



Norfolk and Norwich
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**Joint Trust Guideline for the Management of Adult Patients with
Suspected Adrenal Suppression Due to Long Term Steroids**

A Clinical Guideline

For Use in:	A&E, Medical Assessment Unit, ITU/HDU Medical and Surgical wards, Medical out patients
By:	Medical and Surgical staff
For:	Adult patients on long term glucocorticoid replacement therapy.
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This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

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Joint Trust Guideline for the Management of Adult Patients with Suspected Adrenal Suppression Due to Long Term Steroids

Quick Reference guidelines

Joint Trust Guideline for the Management of Adult Patients with Suspected Adrenal Suppression Due to Long Term Steroids

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Version Number	Date of Update	Change Description	Author
3	16/09/2020	Change to key words, hyperlinks and references.	Rupa Ahluwalia Frankie Swords Sondra Gorick

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Objectives

The safe and consistent management of patients with suspected adrenal suppression using validated, evidence based data to ensure optimal outcomes, and to prevent unnecessary investigations.

Rationale

The clinical investigation unit received 265 requests for short Synacthen® tests in 2012. Of these 30% (84 tests) came from departments other than endocrinology, of which the majority are requested in patients taking long term steroid therapy, rather than suspected Addison's disease or adrenal failure from other causes.

This guideline was written in 2009, and updated in 2013 to ratify the investigation of these patients, and prevent repeated and unnecessary tests being requested in a small number of patients.

The guideline was renewed again in 2015 for 3 reasons. Firstly the cortisol assay has changed so that there is a new reference range for cortisols and for Synacthen tests. Secondly, the price of hydrocortisone therapy changed dramatically in 2014 and there is a national move to switch more people with adrenal suppression back to prednisolone therapy, modern replacement doses of which are much lower than previously widely used. Thirdly, the department of endocrinology has audited the used of the guideline and confirmed good recovery of adrenal suppression in patients on prednisolone and hydrocortisone where the presenting Synacthen test result was borderline, and 40% recovery of adrenal function overall.

This was then reviewed again in 2018 in view of further evidence showing that 100% patients with a 9am cortisol over 350nmol/L on the Abbott assay went on to have a normal response to Synacthen testing.

All recommendations are evidence based.

The adrenal reserve of patients on long term glucocorticoid therapy can be difficult to predict or assess clinically. Adrenal suppression has been confirmed in patients taking topical, inhaled, intra-nasal, intra-articular, intra-muscular and oral steroid preparations

Joint Trust Guideline for the Management of Adult Patients with Suspected Adrenal Suppression Due to Long Term Steroids

despite tailored and weight adjusted doses, and the use of newer agents. The prolonged duration of action of some agents e.g. Depo-Medrone, and of oral prednisolone may also lead to adrenal suppression at surprisingly low doses due to overnight supraphysiological glucocorticoid exposure. Furthermore, the risk of adrenal suppression from inhaled steroids is dramatically increased with the concurrent use of some medications such as itraconazole in patients with Cystic fibrosis.

Any of these patients may develop acute adrenal insufficiency at times of stress or illness, which is a potentially life threatening emergency.

Clear identification of these patients in advance is therefore essential.

Patients on long term steroids can be defined as more than 3 weeks of continuous treatment with more than 7.5 mg prednisolone, 0.75 mg dexamethasone, or 20 mg hydrocortisone daily. All of these patients will definitely have hypothalamic-pituitary-adrenal axis suppression during treatment. It is thus unnecessary and inappropriate to perform any cortisol assessments including Synacthen® tests in these patients prior to dose reduction, though other drugs and lower doses may have unpredictable results mandating formal testing of the adrenal axis as above.

Recovery of adrenal suppression is usual following withdrawal or reduction in glucocorticoid dose, but this can be unpredictable. Patients on lower doses of steroids e.g. 5mg prednisolone or 0.5mg dexamethasone therefore require assessment as below.

Broad recommendations

Prior to a synacthen test

Always ensure that patients are **not** taking oestrogen containing medications prior to testing serum cortisol as this leads to increased cortisol binding globulin levels, and uninterpretable (elevated) serum cortisol. (If the test is inadvertently performed in a patient taking oestrogen, low results are still valid, but normal or high results are not reliable, and the test must be repeated 6 weeks off treatment.) Patients need to stop oestrogens for at least 6 weeks prior to testing. Progesterone only pills, depots and the Mirena IUD do not affect the test.

Always assess a pre-dose serum cortisol (also known as a 9 am serum cortisol test) before requesting a Synacthen® test as this will prevent the need for many of these tests. Ask the patient to omit their morning dose of steroid (any form), as well as any dose they usually take the evening before performing this pre dose test. Ask the patient to take their normal dose as soon as blood has been taken.

When requesting a Synacthen® test always document a complete medication history including non-prescribed agents, and oral, inhaled, intra-nasal, topical and intra-articular medications as patients may not realise, or report this steroid use and this will affect interpretation. Please also request this as a single Synacthen® test on ICE rather than requesting repeated individual cortisol levels, as this helps the laboratory interpret results and ensures a formal report is produced.

Joint Trust Guideline for the Management of Adult Patients with Suspected Adrenal Suppression Due to Long Term Steroids

9am cortisol Results

Pre-dose 9 am cortisol results above 350nmol/L

A Pre-dose serum cortisol >350nmol/L confirms normal adrenal reserve. No further investigations including Synacthen® test are required. Steroids can be stopped abruptly and safely, from an endocrine view point, depending on the clinical indication.

Pre-dose 9 am cortisol results below 100nmol/L

These are grossly abnormal, confirm that the adrenal gland is fully suppressed, and **obviate the need for a Synacthen® test**. Steroids must be continued in some form. Patients should usually be asked to continue the lowest dose of prednisolone at which they feel well (typically 3-mg prednisolone). Alternatively, when the original indication for steroid has passed, and the steroids would otherwise be stopped, consider prescribing either low dose prednisolone or hydrocortisone replacement therapy.

Pre-dose 9 am cortisol results between 100-350nmol/L: possible adrenal suppression, Synacthen® test required

These patients require further evaluation. Please write to the Clinical Investigation Unit to arrange Synacthen® test to be performed according to trust protocol, or use the standard short Synacthen® test request form given in Appendix 2.

Synacthen Test Results

Cortisol >450nmol/L at 30 minutes = normal response

A normal response is defined by serum cortisol rise to > 430nmol/L at 30 minutes. Safe to stop steroids from an adrenal point of view.

Stimulated Cortisol at 30 minutes, 350-450nmol/L = mild adrenal suppression

This group of patients have a good chance of adrenal axis recovery with correct treatment. They should receive sick day rules counselling guidance for patients taking long term steroid therapy see patient information leaflet – Guidance for taking long term steroid therapy - sick day rules [Trustdocs Id: 12101](#) as below, but a supervised wean off prednisolone should be considered to maximise the chance of adrenal recovery. The speed of wean will depend on the current dose and duration but typically for prednisolone would reduce by 1mg / week down to 5mg, then reducing by 1mg / month in a well patient. A repeat Synacthen® test should then be performed to confirm complete axis recovery.

Alternatively, where a more rapid wean is required, consider adding hydrocortisone 10mg waking, and 5mg mid-afternoon and stopping the prednisolone abruptly, and referring to endocrinology for further advice.

60 minute cortisol <350nmol/L: severe adrenal suppression

If adrenal suppression is confirmed, steroid treatment must be continued long term. The patient must also receive education and be given verbal and written information about long term steroid treatment, emergency identification, and what to do in the event of emergencies. This is the responsibility of the prescribing doctor. A patient information leaflet is available through the Trust Intranet under [Trustdocs Id: 12101](#).

Joint Trust Guideline for the Management of Adult Patients with Suspected Adrenal Suppression Due to Long Term Steroids

Further patient education, including training on the use of emergency hydrocortisone injections, will be provided to patients referred to a named endocrinology consultant.

If severe adrenal suppression is confirmed, **but the patient would otherwise be ready to have steroid treatment withdrawn**, then some form of long term glucocorticoid replacement therapy is required. Patients should be offered the choice of how best to do this. It is usual to continue prednisolone therapy long term, with the warning that the longer the patient has been on prednisolone, the more likely they are to require lifelong treatment. In this case, as a minimum, the approximate total daily dose requirement of 3mg prednisolone should be continued long term, with the usual sick day rules advice. In patients hoping to come off steroids in time, interim monitoring of 9am cortisol may be continued to help guide dose reduction.

In selected patients, very keen to come off steroids, consider prescribing hydrocortisone replacement therapy to allow their other steroid therapy to be withdrawn safely. Typical starting doses are 10mg on waking, 5mg at lunchtime and 5mg at tea time (at time 0, 5 and 9 hours). Please refer the patient to endocrinology to supervise this if required, and for long term follow up. Once patients are safely taking low dose hydrocortisone replacement therapy, other steroids can be withdrawn. Serum cortisol should then be tested prior to their early morning (9am) hydrocortisone dose every 3-6 months (depending on previous level and total treatment duration). When pre-dose cortisol rises, a repeat Synacthen® test may be arranged, and the dose reduced or stopped according to the results.

Patients in whom there is no likelihood of steroid withdrawal

Patients who are on maintenance prednisolone for many years do not require assessment to confirm adrenal suppression. However, these patients do require standard 'steroid education' and should be given verbal and written information about long term steroid treatment, emergency identification, and what to do in the event of emergencies. The 'Sick day rules' for patients taking long term steroid therapy' [Trustdocs Id: 12101](#) and a clinical guideline, Management of Peripartum Pyrexia and Sepsis [Trustdocs Id: 855](#) is also available. Further formal steroid education including the use of emergency intramuscular hydrocortisone, will be provided to patients referred to a named endocrinology consultant only.

If patients have been switched to long term hydrocortisone replacement therapy, and require a further short course of high dose steroids (e.g. for an exacerbation of asthma), this should be added to the hydrocortisone, and may then be stopped abruptly, provided that hydrocortisone replacement therapy has been continued throughout.

If the patient needs to revert to long term high dose steroids, hydrocortisone should be stopped, and only restarted when the prednisolone dose has been reduced to below 7.5mg (or equivalent) as above.

If there is any possibility of adrenal suppression in an unstable or acutely unwell patient, e.g. patients with severe sepsis, hypotension, vomiting, or trauma, always assume that they are adrenally insufficient and treat with high dose hydrocortisone as see clinical guideline Management of Adults on Long-term Glucocorticoid Replacement Therapy during Acute Illness [Trustdocs Id: 1246](#).

Joint Trust Guideline for the Management of Adult Patients with Suspected Adrenal Suppression Due to Long Term Steroids

Clinical audit standards

- 1 9am cortisol documented in all patients prior to arranging Synacthen[®] tests.
- 2 9am cortisol between 100 and 350nmol/L in all patients undergoing Synacthen[®] tests.
- 3 Prednisolone or hydrocortisone replacement therapy continued, or clear reason for not prescribing documented in all patients with suboptimal response to Synacthen[®].
- 4 Full medication history documented in all patients referred for Synacthen[®] test.

Summary of development and consultation process undertaken before registration and dissemination

The authors listed above drafted this guideline on behalf of the endocrinology directorate, which has agreed the final content. During its development it has been circulated for comment to all endocrine consultants, endocrine specialist nurses, and consultants in gastroenterology, respiratory medicine and rheumatology. This guideline was approved by the clinical governance committee of the endocrine directorate.

This version has been endorsed by the Clinical Guidelines Assessment Panel.

Distribution list/ dissemination method

Trust intranet, plus emailed specifically to all consultants in endocrinology, respiratory medicine, gastroenterology and rheumatology.

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Joint Trust Guideline for the Management of Adult Patients with Suspected Adrenal Suppression Due to Long Term Steroids

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