Adrenal Insufficiency - Short Synacthen Test in Adults – Full Clinical Guideline

Reference no.: CHISCG1

1. Introduction

Adrenal insufficiency is a condition in which the adrenal glands do not produce adequate amounts of steroid hormones, primarily cortisol; but may also include impaired production of aldosterone (a mineralocorticoid), which regulates sodium conservation, potassium secretion, and water retention.

There are three major types of adrenal insufficiency:

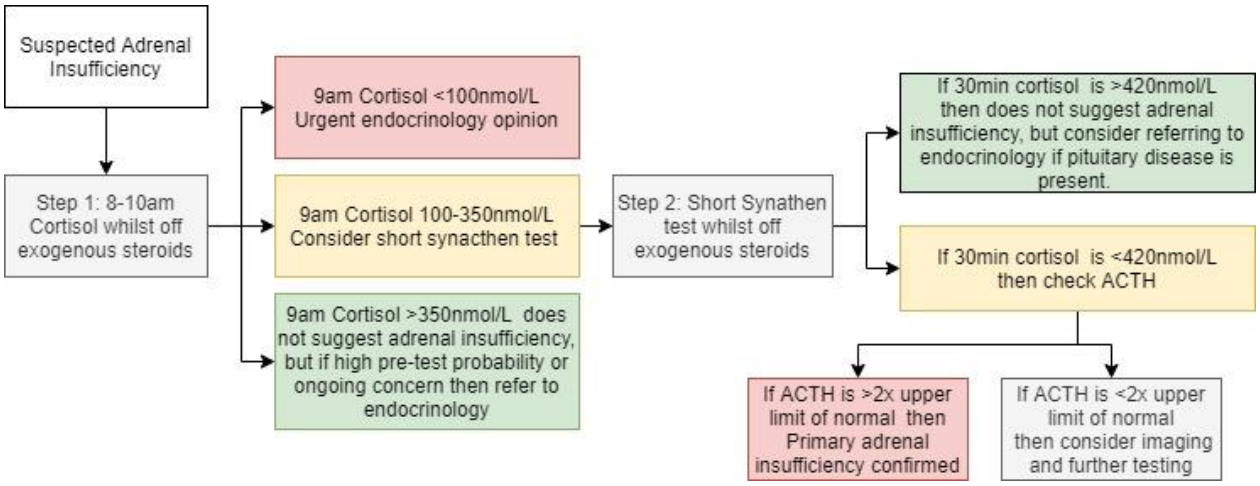
- Primary adrenal insufficiency is due to impairment of the adrenal glands (e.g. Addisons, bilateral adrenal TB, congenital adrenal hyperplasia, etc.)
- Secondary adrenal insufficiency is caused by impairment of the pituitary gland (e.g. pituitary tumours or apoplexy)
- Tertiary adrenal insufficiency is due to hypothalamic disease and a decrease in the release of corticotropin releasing hormone (CRH) (e.g. withdrawal of long-term exogenous steroids or brain tumours)

Synacthen (Tetracosactrin) is a synthetic analogue, comprising amino acids 1-24 of the 39 amino acid peptide Adenocorticotrophic Hormone (ACTH). This sequence retains the full biological activity of intact ACTH. Synacthen stimulates the normal adrenal cortex to secrete cortisol, which can then be measured in serum.

2. Guideline

INDICATIONS

The short Synacthen test is a simple procedure for investigating reduced adreno-cortical function and adrenocortical reserve. It is in itself a preliminary test and abnormal responses need to be followed-up with an endocrinology opinion being sought. It is advised that patients should be screened for adrenal insufficiency with a 9 a.m. cortisol before considering a short synacthen test.



N.B. The use of a 9 a.m. cortisol with the cut off values in this diagram is only appropriate for use in Outpatients or Inpatients that are not critically unwell. In all other situations Endocrine advice should be sought if there is concern about adrenal insufficiency.

It should be noted that prednisolone and hydrocortisone cross react with cortisol assays (i.e. can give falsely raised cortisol levels), but dexamethasone and budesonide do not. The short synacthen test is only suitable for patients that have been off exogenous steroids for an appropriate length of time – see the section on 'patient preparation' for more information. The contraceptive pill or other hormone replacement therapy can also affect results within 6 weeks, so a clinician should discuss with the patient about stopping temporarily or consult Endocrinology about whether proceeding with the test is appropriate.

CONTRAINDICATIONS

- Pregnancy
- Previous hypersensitivity to ACTH, Synacthen or Synacthen depot
- The first six weeks following pituitary surgery

SIDE EFFECTS

Local or systemic hypersensitivity reactions have been reported very rarely following Synacthen injection, particularly if a history of allergic disorders.

PRECAUTIONS

Patient should be kept under observation throughout the period of this test.

PREPARATION

Planning

The test can be carried out as an outpatient at any time, but **should ideally be performed as near to 9am as possible.** Cortisol levels decline throughout the day and cortisol responses between the morning and late afternoon may differ by as much as 100 nmol/L at 30 minutes post Synacthen, making interpretation of afternoon tests difficult if the response is abnormal. An adequate response to synacthen is a valid result at any time of day.

Patient

- Fasting is not necessary
- Patients on exogenous steroids should withhold their steroid for the following times, but take them immediately after completing the synacthen test:
    - Hydrocortisone - withhold for 18hrs before the test
    - Prednisolone - withhold for 24hrs before the test
    - Topical steroids and inhaled steroids - withhold for 48hr prior to the test
    - Steroid joint injections - withhold for 8 weeks prior to the test
- Patients on dexamethasone or budesonide should be discussed with the endocrine team before testing
- All medication should be noted on the request form

Equipment

Obtain the Synacthen from a Pharmacy or Chemist (1 mL ampule, containing 250 micrograms).
You will also require 2 SST (yellow top) vacutainer tubes and an EDTA (purple top) tube.

PROCEDURE

The short synacthen test procedure is shown below.
Samples must be clearly labelled with patient name, date and time, e.g. 09:30

- A basal (0 min) ACTH sample (4 ml EDTA purple top tube) should always be collected, but the laboratory will only process this if the 30min cortisol is <420nmol/L
- Samples for ACTH must not be taken after administering Synacthen

Time (mins)	Test	Tube type
Basal sample	• Cortisol • ACTH *(Always send but will not be processed if SST is normal)*	SST (yellow top) EDTA (purple top)
0 min	Inject 250 micrograms of Synacthen i.m. or i.v.	
30 min	• Cortisol	SST (yellow top)

Send both cortisol samples and ACTH sample with a completed Chemical Pathology request form to the Chemical Pathology Department as soon as the test is finished.

INTERPRETATION

A normal response is defined as 30 minute serum cortisol concentration greater than 420 nmol/L. (NOTE: Roche generation II cortisol assay in use from 11/01/16).

Consideration of the increment in cortisol can add to interpretation in some circumstances but a high baseline cortisol due to concurrent stress may often preclude a further significant rise in cortisol without indicating adrenal insufficiency.

A normal result excludes primary adrenocortical insufficiency, but **does not necessarily exclude ACTH deficiency**. Partial ACTH deficiency may result in a normal or reduced response to Synacthen.

A decreased response may indicate:

1. Primary adrenal failure (such as Addison's disease). Results typically show a low baseline cortisol with little or no response to Synacthen.

2. Adrenal atrophy secondary to prolonged ACTH deficiency.

3. Adrenal atrophy secondary to long term steroid therapy (including topical, nasal or inhaled steroids).

Values for baseline and post-Synacthen cortisol levels do not apply to women taking oral contraceptives.

The response to Synacthen is not affected by obesity.

Failure to respond normally to Synacthen may require further investigation.

Reliable assessment of hypothalamic-pituitary-adrenal axis reserve is difficult in severely ill patients or those with hepatic impairment, because cortisol-binding globulin (CBG) levels fall substantially during the acute phase response. 80% of total cortisol is bound to CBG and variation in CBG

significantly affects total cortisol levels, which should be interpreted with caution. If necessary, repeat the Synacthen test in 3 months.

Certain drugs, particularly steroids (Hydrocortisone and Prednisolone) may interfere with cortisol estimation. Please note all drug therapy, including topical, nasal or inhaled steroids on the request form so this possibility can be checked.

If a diagnosis of hypoadrenalism is made, please take a sample for ACTH before starting steroid replacement. All such patients must be referred to an endocrinologist.

ASSAYING LABORATORY
Cortisol is measured at RDH and QHB.
Samples for ACTH are referred to Nottingham.

TURNAROUND TIME
Results will normally be available within 2 working days following completion of the test, although ACTH results can take up to 2 weeks.

3. References

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4. Documentation Controls

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Version / Amendment History	Version	Date	Authors	Reason
	12.0.0	21/01/2021	Mrs Helen Seddon Dr David Hughes Dr Antonia Ugur	Review & Update in consultation with Departments of Biochemistry and Endocrinology
Intended Recipients: All staff undertaking Synacthen tests.				
Training and Dissemination:				
Development of Guideline: Biochemistry / Endorinology MDT **Job Title:** Consultant Endocrinologists, Consultant Biochemists				
Consultation with: Biochemistry / Endorinology MDT				
Linked Documents:				
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