Short Synacthen Test (SST)

Indications

The purpose of the test is to diagnose adrenal insufficiency. Under normal circumstances, pituitary ACTH stimulates the secretion of cortisol from the adrenal gland; Synacthen (a synthetic ACTH called tetracosactrin) has a similar effect. However, in patients with adrenal insufficiency, there is inadequate response.

In adrenal insufficiency, there is reduced production of hormones (both mineralocorticoids and glucocorticoids). The most common causes are treatment with glucocorticoids, autoimmune destruction of the adrenal gland, TB and adrenalectomy.

Addison's disease can also be classified as primary (adrenal failure), secondary (a pituitary problem with ACTH synthesis) or tertiary (a hypothalamic problem).

Contraindication

- If 8-10am cortisol >300nmol/L, SST is usually not required for assessment.
- Patients with a previous hypersensitivity reaction to ACTH or who have severe atopic allergies (especially asthma) should avoid SST.
- Pregnancy

Cautions

Avoid in ICU patients or those who are severely unwell. Avoid post pituitary surgery for 6 weeks or with pituitary apoplexy. Discuss with endocrinology if hypoadrenalism suspected.

Preparation

- The assay has significant cross reactivity with 11-deoxycortisol: as such the assay should not be used to monitor patients treated with metyrapone.
- The assay has significant cross reactivity with prednisolone: patients taking prednisolone should wait 24hours from the last dose prior to blood sampling for cortisol
- If the patient is taking any other steroids, please call endocrinology or clinical biochemistry to discuss this before starting the SST.

Ideally, the test is performed between 08:00 and 10:00am. Admission is only required for SST if at risk of Addisonian crisis (virtually never). Short synacthen tests can be performed by primary care through NBT medical day case unit and should be performed before referral to endocrinology. A short synacthen test can be requested on NBT ICE and should be accompanied by a referral to medical day case unit to perform the SST. Results will be reported with an interpretative comment.

Procedure

1. Request a short synacthen test (under the endocrine page) on ICE to generate the correct labels and test code – please **do not** make 3 separate requests for cortisol. A short synacthen test request will generate the 3 labels required for the cortisol samples, and a further label for the ACTH sample.
2. Ensure all sample bottles are correctly labelled with the patient ID and time of collection.
3. At baseline, time 0mins, take cortisol (serum/gold topped tube) and ACTH (EDTA/ purple tube). **Send the ACTH sample to the lab immediately packed on ice.**
4. Give I.M. Synacthen 250mcg (adult dose)
5. At 30 and 60 minutes take cortisol (serum/gold topped tube).
6. Send all the serum/gold topped tubes **together** to the lab, do not send them separately.

Interpretation of Results

- 30min or 60min Cortisol should be greater than 450nmol/L
- If the patient has high oestrogens (e.g. taking OCP or in pregnancy), the cortisol should be greater than 600nmol/L

If there is a suboptimal test, the ACTH will be measured to distinguish primary from secondary adrenal failure. This cannot be sent from primary care due to sampling requirements. If the patient has a normal SST response, then the ACTH will not be sent for analysis.
· If impaired cortisol response, and ACTH >200ng/L then diagnosis is primary adrenal failure.
· If ACTH <10ng/L then diagnosis is secondary adrenal failure

Sensitivity and Specificity

A normal cortisol response does not exclude adrenal failure, since impending adrenal failure might be associated with a much greater loss of zona glomerulosa function. The latter would be suggested by an elevated plasma renin activity.
If equivocal result and no urgency, repeat test after a few weeks.

Use in Congenital Adrenal Hyperplasia

Diagnosis and characterisation of 21-hydroxylase deficiency and other causes of adrenal hyperplasia can use a Short Synacthen Test.
SST should be done in the follicular phase because 17OH progesterone is increased after ovulation.
On the samples taken for cortisol, 17- hydroxy progesterone (17OHP) should be requested.
Response of 17-OH progesterone in suspected 21-hydroxylase deficiency:
Marked rise after ACTH stimulation (>30nmol/L), which varies according to whether the patient is homozygous or heterozygous. Reference for nomogram: New et al., JCEM 57, 320-326 (1983).

Appendix 1: Hazard Data

Hypersensitivity reactions: Synacthen rarely can provoke hypersensitivity reactions, which tend to be more severe (anaphylactic shock) in patients susceptible to atopic allergies (especially asthma). Hypersensitivity reactions may include skin reactions at the injection site, dizziness, nausea, vomiting, urticaria, pruritus, flushing, malaise, dyspnoea, and angioneurotic oedema. When hypersensitivity reactions occur, they tend to set in within 30 minutes after the injection. The patient should therefore be kept under observation during this time.

In case of anaphylaxis: Administer Adrenaline 0.5 mg as 0.5 ml of 0.1% solution (1:1000) by intramuscular injection, repeat adrenaline as necessary (every 5 minutes) followed by Hydrocortisone 200 mg i.v. and Chlorpheniramine 10 mg i.v., slowly over at least 1 min

For further information see http://www.medicines.org.uk/emc/medicine/30030

Appendix 2: Laboratory issues

Our cut off limits have been agreed after a review of the literature, verification of the assay, and taking into account the published cut offs relating to our assay method (BCUK).
Patients taking oestrogens have a significant positive bias post Synacthen due to increased cortisol binding globulin and its interference in the assay.
Other factors that can alter CBG include: increased in pregnancy, COP, HRT and may be decreased in liver and renal disease.

References

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2. le Roux, Meeran K and Alaghband-Zadeh Is a 0900-h cortisol useful prior to a short Synacthen test in out patient assessment? *Ann Clin Biochem* 2002; **39**: 148-50.

3. Abdu TAM, Elhadd TA, Neary R and Clayton RN. Comparison of the low dose short Synacthen test (1µg), the conventional dose short Synacthen test (250µg) and the insulin tolerance test for the assessment of the hypothalamo-pituitary-adrenal axis response in patients with pituitary disease. *J Clin Endocrinol Metab* 1999: **84**; 838-43.

4. Walsh JP and Dayan CM. Role of biochemical assessment in the management of corticosteroid withdrawal. *Ann Clin Biochem* 2000: **37**; 279-287.

5. Wallace I, Cunningham S and Lindsay J. The diagnosis and investigation of adrenal insufficiency in adults. *Ann Clin Biochem* 2009: **46**; 351-67.