Pathology at the Royal Derby Hospital Standard Clinical Guidelines Chemical Pathology Department **Document Code: CHISCG1**	Short Synacthen Test Valid Until 31st March 2015

Short Synacthen Test for the Investigation of Adrenal Insufficiency

INTRODUCTION

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.

INDICATIONS

The short Synacthen test is a simple procedure for investigating reduced adreno-cortical function and adrenocortical reserve. It is a screening test and abnormal responses need to be followed up with further tests and an endocrinology opinion should be sought.

It should be noted that Prednisolone and hydrocortisone cross react with cortisol assays, but the short synacthen test is suitable for patients that have recently started steroid replacement or are on low dose steroids. For these patients, the steroid dose should be omitted the evening before the test (if possible) and on the morning of the test.

CONTRAINDICATIONS

Pregnancy, history of hypersensitivity to ACTH, Synacthen or Synacthen depot.

The synacthen test gives unreliable results in the six weeks following pituitary surgery.

Patients on the contraceptive pill or on hormone replacement therapy should stop this 6 weeks prior to the test.

For the assessment of adrenal status in patients receiving long term steroid treatment who are having difficulty coming off steroids, referral to the Endocrine team is suggested.

SIDE EFFECTS

Local or systemic hypersensitivity reactions have been reported very rarely following Synacthen injection, particularly in children with 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 in cortisol is abnormal. An adequate response to synacthen is a valid result at any time of day.

Patient

No special preparation of the patient is required and fasting is unnecessary.
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 plain (red top) vacutainer tubes. If ACTH is to be measured you will need an EDTA tube (see below).

PROCEDURE

The short synacthen test procedure is described in Table 1. Samples must be clearly labelled with patient name, date and time, eg 09.30

A basal (0 min) ACTH sample (4 ml EDTA purple top tube) may also be collected. Samples for ACTH must be placed on ice immediately and taken to the laboratory within 10 minutes. Samples for ACTH must not be taken after administering Synacthen and will only be analysed if the cortisol response is inadequate.

TABLE 1

Time (mins)	Test	Tube type	Comments
Basal sample	Cortisol ACTH (if required)	Plain (red top) EDTA (purple top)	 Place ACTH samples on ice and take to the laboratory within 10 minutes
0 min	Inject 250 micrograms of Synacthen i.m. or i.v. (Infant dose 36 micrograms per kg)		
30 min	Cortisol	Plain (red top)	

Send both cortisol samples with a completed Chemical Pathology request form to the Chemical Pathology Department on the day of the test.

INTERPRETATION

A normal response is defined as a 30 minute serum cortisol concentration greater than 540 nmol/L. The increment of cortisol at 30 minutes above the basal level is a measure of adrenal reserve whereas the absolute level gives an indication of adrenal sufficiency. However, the interpretation of results must take into account the stress level of the patient and the time of day of the test. For example, a stressed patient that is secreting all the cortisol that their adrenal gland can synthesise may have a basal cortisol >540 nmol/L with very little increment after 30 minutes but does not have adrenal insufficiency. When a raised basal level is not seen, a rise in cortisol at 30 minutes of at least 200 nmol/L should be expected.

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).

Females show a small but significantly greater incremental and stimulated cortisol value than males. There are no age-related changes in adults.

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 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
Pathology at the Royal Derby Hospital

TURNROUND TIME
Results will normally be available within 2 working days following completion of the test, although ACTH results can take up to 3 weeks.

NOTE
Several studies in recent years suggest that a low dose Synacthen test (using as little as 1µg) might help uncover subtle defects of hypothalamic-pituitary adrenal axis function. These studies are at a preliminary stage, and good reference data do not exist as yet. Routine use of lower doses than the conventional 250 µg cannot be recommended at present.

REFERENCES AND FURTHER READING
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Reviewed by:	Date:	Valid Until:
SCG group	October 1995	May 2000
SCG group	November 2001	October 2004
SCG group	May 2005	May 2007
H Seddon	May 2007	May 2008
H Seddon	August 2008	May 2009
H Seddon	August 2009	August 2011
R Stanworth/H Seddon	March 2012	March 2015