ICE test name: Child Synacthen test (base)

**Principle**
Adrenal glucocorticoid secretion is controlled by adrenocorticotrophic hormone (ACTH) released by the anterior pituitary. This test evaluates the ability of the adrenal cortex to produce cortisol after stimulation by synthetic ACTH (tetracosactrin: Synacthen). The Synacthen test is a useful investigation in suspected secondary adrenal insufficiency as it correlates reasonably well with the ‘gold-standard’ insulin tolerance test, but is safer and less unpleasant. Chronic ACTH deficiency results in adrenal atrophy which leads to a reduced response to exogenous ACTH.

**Indication**
- Screening test for suspected adrenal insufficiency.

**Precautions**
- The Synacthen test is unreliable if performed within 4 weeks of pituitary surgery as ACTH deficiency may not have been sufficiently prolonged to result in adrenal atrophy. An 8 - 9 am plasma ACTH and cortisol can be informative in these situations.
- The test is unreliable in patients taking the oral contraceptive pill.

**Side Effects**
- Severe allergic reactions to Synacthen have been described, particularly in children with a history of allergic disorders, but are very rare. In children with prior known synacthen sensitivity, a repeat synacthen test is not advisable. In such cases, morning basal ACTH and cortisol levels can alternatively test for adrenal function.

**Preparation**
- The test should preferably be performed in the morning between 0800 and 0900 hrs.
- The patient does not need to be fasted.
- All glucocorticoid therapy (other than dexamethasone or betamethasone) interferes with the assay of cortisol. If the patient is on prednisolone therapy, this must be discontinued for 24 hours prior to the test. If the patient is on a supra-physiological dose of hydrocortisone, this should be reduced to a physiological level (6 micrograms/m²/day) prior to the test. Omit the dose the night before and on the morning of the test. If the paediatric endocrine consultant is very anxious about the degree of adrenal insufficiency, then omit only the morning hydrocortisone dose. However, the patient should take their usual dose of corticosteroid as soon as the test is completed.

**Protocol**
A number of different protocols with different synacthen doses are available. We have taken a pragmatic approach, considering the ease of use.

1. Insert a reliable cannula and, if possible, rest the patient for 30 minutes.
2. Take basal blood sample for cortisol (t = 0).
3. **Give Synacthen as an i.v. bolus**
   - For children <1 month use a dose of 36 micrograms/kg
   - For children 1 - 12 months use a dose of 125 micrograms
   - For children >1 year use a dose of 250 micrograms
4. Take a blood sample at + 30 min after Synacthen for cortisol.

**Samples**
- **Cortisol**: 1 mL lithium heparin (orange top) or clotted blood (white top)

Record actual sample collection times on the printed barcodes.

**SEND ALL SAMPLES TO THE LABORATORY TOGETHER**

**Interpretation**
- A normal response is an increase in plasma/serum cortisol to a level of ≥430 nmol/L at 30 minutes.
• An impaired response does not distinguish between adrenal and pituitary failure, as the adrenal glands may be atrophied secondary to ACTH deficiency.

• The dose of Synacthen used is supra-physiological and may give a normal response in patients with mild adrenal insufficiency.

• The sensitivity of the Synacthen test is higher in primary adrenal insufficiency compared with secondary adrenal insufficiency. Sensitivity is particularly low in recent-onset ACTH deficiency (within 4 – 6 weeks of an insult to the pituitary).

• Cortisol results may be misleadingly low in the presence of low cortisol binding globulin (for example in severe illness, in conjunction with low albumin).

• In patients on long-term glucocorticoids it is difficult to differentiate underlying adrenocortical disorders from the adrenal-suppressive effects of the treatment. A urine steroid profile may also be misleading after only 24 hours off hydrocortisone. The urine steroid lab at King’s College Hospital recommend changing the glucocorticoid to dexamethasone and stimulating with depot Synacthen for up to 5 days before sample collection, unless glucocorticoid treatment has been brief. Please discuss with the paediatric endocrine team and the laboratory.

References