

# **Standard Dose Synacthen Test for Congenital Adrenal Hyperplasia (CAH)**

Test Name: CHILD SYNACTHEN & 170HP DFT

### **Principle**

Adrenal glucocorticoid secretion is controlled by adrenocorticotrophic hormone (ACTH) released by the anterior pituitary. This test evaluates secretion of cortisol and 17-hydroxyprogesterone (17-OHP) by the adrenal cortex following stimulation with Synacthen. In patients with congenital adrenal hyperplasia (CAH; a group of inherited disorders caused by enzyme defects in the steroid synthetic pathway), cortisol may, or may not, be adequately secreted. However, there is excessive secretion of the precursor steroids proximal to the defective enzyme. The commonest cause of CAH is due to 21-hydroxylase deficiency and in these subjects increased secretion of 17-hydroxyprogesterone (17-OHP) occurs.

### Indication

Diagnosis of CAH due to 21-hydroxylase deficiency in children and adults.

# **Precautions**

- The Synacthen test gives unreliable results if performed within 4 weeks of pituitary surgery.
- Do not perform at the same time as an oral glucose tolerance test. However, the oral glucose tolerance may be performed after this test.

# **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 patient for 30 minutes.
- Take basal blood sample for cortisol and 17-OHP (t = 0). Take baseline ACTH sample (if requested)
- Give Synacthen as an i.v. bolus as per the table below:

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Age	Generic	Brand	Route	Dose	Frequency	Comments
<1 month	Tetracosatide	Synacthen	i.v	36 micrograms/kg	Bolus	
1-12 months	Tetracosatide	Synacthen	i.v	125 micrograms	Bolus	Use 36 micrograms/kg for preterm babies who remain in hospital.
>1 year	Tetracosatide	Synacthen	i.v	250 micrograms	Bolus	

4. Take blood samples at + 30 min after Synacthen (for cortisol and 17OHP) + 60 min after Synacthen. (for 17OHP only)

<u>Samples</u>

**Cortisol** 1.2 mL lithium heparin (orange top) or clotted blood (white top)

**17–OHP** 1.2 mL lithium heparin (orange top) or clotted blood (white top)

#### Interpretation

- Unaffected adults and children usually have a basal 17-OHP of <6 nmol/L.</li>
- A minority of patients with non-classical CAH have a normal basal 17-OHP, even on early morning samples.
- A normal response to Synacthen is a stimulated 17-OHP of <9.8 nmol/L at 60 minutes.</li>
- A stimulated 17-OHP between ≥9.8 but ≤30 nmol/L is an equivocal response and CAH is not excluded. Genotyping and/or a urine steroid profile is recommended.
- A stimulated 17-OHP of ≥30 nmol/L is consistent with a diagnosis of CAH. Genotyping of the 21-hydroxylase gene and urine steroid profiling can be used to confirm the diagnosis.
- Milder elevations of 17-OHP may be found in rarer forms of CAH: 11-β-hydroxylase deficiency and 3-β-hydroxysteroid dehydrogenase deficiency.
- An increment of <10 nmol/L in normal individuals compared to >20 nmol/L in CAH has been reported.
- A normal cortisol response is an increase in plasma/serum cortisol to a level of ≥430 nmol/L at 30 minutes.

### References

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