

## PITUITARY FUNCTION TEST PROTOCOL

### INTRODUCTION

The Insulin Stress Test is used to assess the ability of the anterior pituitary to secrete growth hormone and indirectly ACTH, in response to the stress of hypoglycaemia. As serum cortisol is measured, the whole hypothalamic-pituitary-adrenal cortex axis is tested. Thyrotrophin-Releasing Hormone (TRH) and LHRH can be administered with insulin to provide a single test assessing anterior pituitary reserve.

### CONTRAINDICATIONS AND SIDE EFFECTS

The test is potentially dangerous and should be done under direct medical supervision. It should NOT be performed in the following patients:

1. Age > 60 years.
2. This test should not be performed on children outside a specialist paediatric endocrine unit
3. Ischaemic heart disease – ECG MUST be normal.
4. Epilepsy
5. Severe panhypopituitarism, hypoadrenalism (09:00 cortisol < 100 nmol/L)
6. Untreated hypothyroidism (impairs GH and cortisol response)

It is advisable that all patients with suspected primary or secondary hypoadrenalism or on glucocorticoids have a SYNACTHEN test performed first to ensure adequate adrenal response. Hypothyroidism impairs the GH and cortisol response but corticosteroid replacement should be done before thyroxine is given. Glucose for intravenous administration should be immediately available in case severe hypoglycaemia develops. At the end of the test the patient should be given something to eat. If it is necessary to administer glucose during the test **continue with blood sampling**; the stress will have been adequate.

### PATIENT PREPARATION

Hydrocortisone, cortisone and prednisolone interfere with cortisol assay. If necessary the patient should be transferred to alternative medication (e.g. dexamethasone) 7 days prior to the test.

Patient should fast overnight (at least 10 hours) and the test performed in the morning, in a recumbent position.

**PROTOCOL**

Samples must be accompanied by pro-forma (PF-BSM-CP-25)

1. After an overnight fast, insert indwelling intravenous cannula and wait at least **30 minutes** for hormone levels to return to basal levels.
2. Take basal blood samples according to sample pro-forma.
3. Inject soluble insulin intravenously (for dosage guidelines see below). If required, inject 100ug of LHRH and 200ug TRH intravenously immediately after insulin – **note times on sample pro-forma**.
4. Continue to take samples as per pro-forma (30, 60, 90 and 120 minutes).
5. Check whole blood glucose on glucometer every time a sample is taken. Adequate hypoglycaemia is defined as glucose <2.2 mmol/L with symptoms. Once this has been achieved, patients need not remain hypoglycaemic. The lowest glucose level following insulin is usually at 20-30 minutes, with spontaneous resolution.
6. At least two samples must be obtained following hypoglycaemia.
7. Once the test is completed, give a supervised meal and ensure glucose is within normal limits prior to discharge.
8. Patient should be advised not to drive for two hours after the test.

If symptoms of hypoglycaemia occur at other times, additional sample(s) for glucose only should be taken: this is important in cases of suspected growth hormone deficiency.

**Insulin Dosage:** Insulin sensitivity will vary depending on the endocrine status of the patient and care should be taken in selecting the correct dose. Guidelines on insulin dosage are as follows:

- Probably normal patients – 0.15 units/kg body weight.
- Suspected hypopituitary patients (the most sensitive) 0.10 units/kg.
- Suspected Cushings, diabetes or Acromegaly (the most resistant) 0.2 - 0.3 units/kg.

**INTERPRETATION****CRITERIA FOR ADEQUATE HYPOGLYCAEMIA**

The blood glucose level must fall to less than 2.2 mmol/l; preferably with clinical signs of hypoglycaemia (N.B. glucose meters are unreliable for detecting hypoglycaemia). If after 60 mins adequate hypoglycaemia has not been obtained, collect the 60 min blood to complete LHRH and TRH tests. The IV dose of insulin can be repeated and the procedure recommenced (i.e. collect SST and fluoride samples at 30, 60, 90 and 120 mins post repeat dose). In this case please complete a separate sample proforma for insulin tolerance test.

**NORMAL RESPONSES**

**ITT:** It is necessary for the plasma glucose to fall to less than 2.2 mmol/l for this test to be valid. There should be a marked rise in cortisol and growth hormone levels with the different responses peaking at 20-90 minutes. Cortisol should rise to a peak of >450 nmol/L. Severe GHD is defined as GH <3 ug/L and partial GHD as GH <5 ug/L.

**TRH:** Normal result is a TSH rise to >5 mU/L with the 30 minute value exceeding the 60 minute value. If the 60 minute value exceeds the 30 minute value, this usually indicates primary hypothalamic disease. In hyperthyroidism, the TSH remains suppressed and in hypothyroidism there is an exaggerated response.

**LHRH:** The normal peaks occur at either 30 or 60 minutes. LH should exceed 10 IU/L and FSH should exceed 2 IU/L. An inadequate response may be an early indication of hypopituitarism.

Gonadotrophin deficiency is diagnosed on the basal levels rather than dynamic response. In males, a low testosterone in the absence of raised gonadotrophins and in females, a low oestradiol without raised gonadotrophins and no response to clomiphene.

These tests have a low specificity and sensitivity for hypogonadotrophic hypogonadism. Basal gonadotrophins and sex steroid levels are better discriminators.

The degree of the various responses varies widely and reference range limits (particularly for peak responses) should not be regarded too rigidly.

All the responses must be considered together and viewed carefully in the light of the whole clinical context of the patient before final conclusions are drawn as to the assessment of hypothalamic-anterior pituitary reserve function.

***Please note: All ITT/LHRH/TRH tests must be accompanied by a completed sample pro-forma.***

## CONTACTS

Basildon Hospital Biochemists: ext. 3029 / 3095 / 3539

Southend Hospital Biochemist: ext. 8795

## REFERENCES

Imperial endocrinology handbook. <http://imperialendo.co.uk/Bible2018.pdf>. (accessed 25/09/2020)