

Insulin Tolerance Test

This test is potentially dangerous and is not carried out routinely at RMCH. Consult with the paediatric endocrine team at RMCH if you are considering undertaking this test. It should only be carried out in specialist centres by experienced staff.

Test Name: CHILD INSULIN TOLERANCE TEST DFT

Principle

The insulin tolerance test is the gold standard test for assessing the integrity of the hypothalamo-pituitary-adrenal axis. Stress, in this case hypoglycaemia, leads to the secretion of the hypothalamic hormones growth hormone releasing hormone (GHRH) and corticotrophin releasing hormone (CRH) which in turn stimulate the pituitary to produce GH and ACTH. ACTH production is assessed by the measurement of adrenal cortisol production. This test is dangerous as it relies on the induction of symptomatic hypoglycaemia which must be treated immediately if the symptoms become severe.

Indication

- This test is not routinely used at RMCH, although it is considered the gold standard test to assess the integrity of the hypothalamo-pituitary-adrenal axis. We are most likely to use the ITT when re-testing a young person for the presence of persistent GH deficiency at the end of growth. The test may also be required for some research protocols.

Precautions

- This test should not be carried out in a child with a history of epilepsy or cardiac arrhythmias.
- The test should be used with particular caution in young children as the symptoms of hypoglycaemia may be difficult to detect.
- This test should not be carried out on patients with severe panhypopituitarism or hypoadrenalism.
- This test should not be carried out in a patient with a glycogen storage disorder.
- A doctor must be present throughout this test with the patient being closely monitored for symptoms of hypoglycaemia which may require treatment.

Side Effects

- Sweating
- Palpitations
- Impaired or loss of consciousness

Preparation

- The patient must be fasted overnight (4 hours for infants), although drinks of water are allowed.
- Ensure that glucose (10% glucose) and hydrocortisone are available for i.v. injection if necessary.
- A glucose drink must be available. This may be ~40g glucose powder (4 heaped teaspoons) dissolved in approximately half a glass of squash, alternatively POLYCAL or rapilose can be administered.
- Child must remain on the ward and eat for at least an hour after the test before the cannula is removed and the patient discharged.

Protocol

Children can become severely hypoglycaemic after insulin administration. Check glucose levels (by glucose meter) at the time of every sample and observe the child continuously for symptoms of severe hypoglycaemia. Check that the child is responsive at the time of every sample. If they do not respond, then follow instructions for the emergency management of hypoglycaemia.

1. Start the test between 0800h and 0900h. Weigh the patient and insert an indwelling cannula and take a basal blood sample (t = -30) for glucose, growth hormone and cortisol. Wait 30 minutes before taking the baseline (t = 0) sample for glucose, growth hormone and cortisol as cannulation may cause GH to rise. The patient should be resting throughout the test.
2. Check glucose level by meter.

- If glucose <3.5 mmol/L do not administer insulin.
 - If glucose level 3.5 – 4.5 mmol/L then administer **half the dose of insulin**
 - If glucose > 4.5 mmol/L then continue with the test as indicated
3. Dilute soluble insulin (Actrapid) with normal saline to give a solution containing 1 unit per ml. **Give an i.v. dose of 0.1 units per kg body weight**

This dose should be reduced to 0.05 units per kg in patients who might be unduly sensitive to insulin, such as patients with suspected hypopituitarism, severe malnutrition, or those with a baseline blood glucose between 3.5 and 4.5 mmol/L.

4. Monitor blood glucose closely until adequate hypoglycaemia has been established (<2.2 mmol/L) or the child shows signs of hypoglycaemia (e.g. sweating or drowsiness). Administer glucose drink of ~40g glucose powder (4 heaped teaspoons) dissolved in approximately half a glass of squash, or POLYCAL or rapilose can be administered. If there are more severe symptoms of hypoglycaemia (e.g., impaired consciousness), i.v. glucose may be required.
5. Take further blood samples for glucose, growth hormone and cortisol at 15, 30, 60 and 90 min post insulin administration
6. Remember to check the child's glucose level by meter and the responsiveness at every sample.

Time Points:

Time post insulin (min)	Procedure	Blood Sample
-30	Check blood glucose using meter	Glucose, Growth hormone & Cortisol
0	Check blood glucose using meter	Glucose, Growth hormone & Cortisol
15	Check blood glucose using meter	Glucose, Growth hormone & Cortisol
30	Check blood glucose using meter	Glucose, Growth hormone & Cortisol
60	Check blood glucose using meter	Glucose, Growth hormone & Cortisol
90	Check blood glucose using meter	Glucose, Growth hormone & Cortisol
120	Check blood glucose using meter	Glucose, Growth hormone & Cortisol

Samples

- Growth Hormone** 1.2 mL clotted blood (white top)
- Cortisol** 1.2 mL lithium heparin (orange top) or clotted blood (white top)
- Glucose** 1.2 mL venous blood in a fluoride oxalate tube (yellow top)

Record actual sample collection times on the printed barcodes.

Management of hypoglycaemia

- If symptomatic, give glucose (3 mL/kg of i.v. 10% glucose) - **INFORM DOCTOR**
- Give feed if able to tolerate, if not intravenous maintenance fluids, 10% glucose + sodium chloride (e.g., 10% glucose/0.45% sodium chloride)
- Recheck finger prick BG every 15 min until glucose >4.0mol/L
- If BG remains low, consider further bolus and increase glucose concentration/ fluid rate. Consider hydrocortisone bolus.
- **CONTACT ENDOCRINE CONSULTANT ON CALL IF ANY CONCERNS**

Interpretation

Interpretation is only possible if adequate hypoglycaemia (plasma glucose <2.2 mmol/L) has been achieved.

If the *laboratory* plasma glucose falls to 2.2 mmol/L or less, the imposed stress should be sufficient to stimulate a plasma GH concentration exceeding 7 µg/L.

Hypoglycaemia of this magnitude should also cause an increase in the plasma cortisol to concentrations exceeding 430 nmol/L.

References

1. Managed clinical network of Scottish Paediatric Endocrine Group (SPEG MCN) Dynamic function test handbook for Clinicians January 2012
2. Galloway P.J., McNeill E., Paterson W.F. & Donaldson M.D.C. (2002) Safety of the insulin tolerance test. *Arch Dis Child* **87**: 354-356