GH Stimulation Tests

Arginine Infusion

Aim:
To test growth hormone release and, on rare occasions, insulin release (which has a separate indication). The test may, if desired, be followed by an insulin tolerance test (ITT) (See separate protocol, page 118

Patient Preparation
Patient should be fasting overnight, but may drink water.

Contra-indications:
Certain drugs interfere with Arginine/Clonidine stimulation

Precautions:
Antihistamine and adrenaline should be available for treatment of potential allergic reactions to arginine. Excessive infusion rates can result in local irritation, flushing, nausea or vomiting. Inadequate dosage (or prolongation of the infusion period) may result in diminished stimulus to the pituitary and nullification of the growth hormone reserve test.

Materials:
IV equipment, 1 bag 0.9% NaCl, pump and tubing.
Arginine hydrochloride 5% in 500ml bottle (order through Pharmacy).
4 x 4ml EDTA tubes (clearly labelled with times).

Method:
Weigh patient, pulse and BP.
Settle patient comfortably and give explanation.
Insert IV line.
Take -30 minute, and then zero blood samples.
Keep vein open with 0.9% NaCl.
Infuse Arginine Hydrochloride 5% 11ml/kg over 30 minutes, allowing time to flush line with 0.9% NaCl before taking next sample.
Further samples taken at +30, +60.
Breakfast with food and fluid as desired.

Samples:
Growth Hormone (1 - 3ml EDTA tube to Endolab)
Other basal bloods as ordered by doctor.

Interpretation:
Present normal cut off (as accepted for Health Department Childhood GH Advisory Committee) is 4µg/L (normal >7µg/L) (1µg/L = 2.7mU/L). Levels in childhood between 4 and 7µg/L suggest partial GH deficiency. The cut off is very arbitrary, but is the present local criterion. The same cut off applies to any physiologically or pharmacologically stimulated test.

Reference:
1974 - 1990 Micromedex Inc. Vol. 6

Clonidine Test

Aim:
Clonidine is a central α-adrenergic stimulator which induces GH release in normal children⁴, (see references) via stimulation of central adrenergic pathways. Release is impaired or absent in adults or children with hypopituitarism.

Patient Preparation
The patient should be fasting (overnight) and supine.

⁴ JCEM 41:827,1975
**Procedure:**
An IV line inserted and blood samples collected at:
-15, 0, +15, 30, 45, 60, 90 120 minutes.
Clonidine: 0.15 mg/m² is given orally at the time zero.
Measure lying BP at 60 and 120 minutes and when upright at the end of the test.

**Blood samples:**
The six samples are collected for growth hormone estimation and clearly labelled with time of sampling (see growth hormone for details of samples required). Other basal bloods as required by doctor.

**Interpretation**
Present normal cut off (as accepted for Health Department Childhood GH Advisory Committee) is 4µg/L (normal >7µg/L) (1µg/L = 2.7mU/L). Levels in childhood between 4 and 7µg/L suggest partial GH deficiency. The cut off is very arbitrary, but is the present local criterion. The same cut off applies to any physiologically or pharmacologically stimulated test.

**Side Effects:**
Mild fall in BP, care when walking after end of test.
Mild drowsiness for up to three hours.

**References:**

**Glucagon test**

**Indications**
If ITT/Metyrapone testing is contraindicated in patients with possibly impaired HPA function. This is also a reliable test of GH release.

**Preparations**
Fast overnight. Prepare as for ITT.

**Test**
1 mg glucagon s.c. at zero time.
Take bloods at 0, 30, 60, 90, 120, 150, 180, 210, and 240 min for glucose, cortisol (ACTH) and hGH.

**Side effects**
Nausea, vomiting.
Deterioration of blood sugar control in diabetics.

**Interpretation**
Cortisol should rise above 550nmol/L.
Present normal cutoff (as accepted for Health Department Childhood GH Advisory Committee) is 4µg/L (normal >7µg/L) (1µg/L = 2.7mU/L). Levels in childhood between 4 and 7µg/L suggest partial GH deficiency. The cutoff is very arbitrary, but is the present local criterion. The same cutoff applies to any physiologically or pharmacologically stimulated test.

**Insulin Tolerance Test**

**Clinical Applications:**
To assess hypothalamic – pituitary – adrenal axis and growth hormone axis function. Clinical consultation with an Endocrinologist must precede the test being performed.

**Purpose of Test:**
To lower plasma glucose sufficiently to stimulate the secretion of growth hormone, cortisol and in some cases, ACTH. This requires a 50% drop from baseline values at 20 - 30 minutes post insulin and/or a fall of plasma glucose to 2.2 mmol or less.

**Indications:**
As a test of hypothalamic-pituitary function.
**Side Effects:**
Symptomatic hypoglycaemia 20 to 30 min after insulin administered. May provoke cerebral or cardiac complications - (very rare).

**Patient Preparation:**
Ideally an ECG should be done and inspected before the test. The patient is fasted for 8 hours overnight and rests in bed for 1 hour prior to the test beginning and continues to rest in bed throughout the test. The patient should not be receiving any drugs. If patient is on steroids or insulin, special arrangements regarding the doses of these hormones have to be made. Patient must not have consumed alcohol within 24 hr. The tests should not be done if veins are doubtful. At least one "good vein" is essential. The test should not be done in epileptics, in the very old (70 yrs), in patients with ischaemic heart disease or important rhythm disorders.

**Dosage:**
Soluble insulin is used as a rapid intravenous injection and if 20 units per ml solution is used, small doses can be dispensed with accuracy. In all cases the dose of insulin must be calculated and checked by the Registrar administering the insulin, after consultation with consultant Physician.

**Dose schedule:**
Likely Hypopituitary, underweight and not on replacement therapy, also for children under 4 yr age: 0.05 U/kilo body weight.
Possible Hypopituitary, children 4-8 years: 0.1 U/kilo.
Normals, children older than 8 y: 0.15 U/kilo; 0.2U/kilo if sex steroid primed.
Obese patients: 0.2 U/kilo.
Acromegalic or giants: 0.3 U/kilo.

**Equipment:**
1. 1 IV cannula, luer plug, syringes, tegaderm, needles, syringe with saline, Gelofusine.
2. Labelled tubes, observation chart, timing clock.
3. Normal saline, amps 50% Dextrose, drawing up cannula, labels and tubes for samples, insulin.

**Insulin preparation 1 unit/ml:**

**Equipment**
- 1 500ml bag Gelofusine
- 100 units/ml actrapid insulin (penfill)
- 1 20ml syringe
- 1x 1 insulin syringe
- 3x needles

**Method to make 20 units per ml of solution of insulin:**
- Draw up 20ml Gelofusine
- Draw up 20 units of Actrapid insulin (0.2ml on Insulin Syringe)
- Add Insulin 20 units to 20ml Gelofusine.
- Complete additive label and attach to syringe.
- Calculate patient dose using dosing schedule
- Withdraw the required dose from the gelofusine/insulin syringe (1 unit/ml ratio).
Procedure:
1. Insert cannula into suitable vein. Take glucose sample and test. Patient rests 30 minutes. Before beginning test have insulin drawn up.
2. Draw zero sample.
3. Immediately after sampling Physician/RN gives IV insulin and clock started at completion of injection. Flush cannula with IV saline (10ml).
4. Samples drawn as follows:

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Note: Paediatric Department, Christchurch Hospital has a protocol for ITT in small children.

Modified protocol for small children:
After 120’ sample patient given breakfast but must remain resting on bed till after substantial meal. The cannula is removed when BSL levels are stable.

Supervision:
A doctor or Endocrine nurse must maintain continuous supervision throughout the test. A chart must be kept recording pulse and other symptoms eg: sweating, confusion, drowsiness etc. every 5 minutes from the start of the test. If untoward reaction occurs (coma, rapid palpitations, angina etc.) the test should be terminated with bolus of 50% glucose IV. (Adults ONLY). In children, large amounts of intravenous hyperosmolar glucose should be avoided, and hypoglycaemia treated with glucose 200 mg/kg IV over 3 minutes (10% dextrose, 2ml/kg over 3 minutes). If a test is terminated with IV glucose, hormone sampling should continue if the patient stabilises.

Ensure a good (carbohydrate) food intake "as breakfast" and later lunch once the test is completed.

Interpretation
Cortisol should rise above 500nmol/L.
Present normal cut off (as accepted for Health Department Childhood GH Advisory Committee) is 4µg/L (normal >7µg/L) (1µg/L = 2.7mU/L). Levels in childhood between 4 and 7µg/L suggest partial GH deficiency. The cut off is very arbitrary, but is the present local criterion. The same cut off applies to any physiologically or pharmacologically stimulated test.
The consensus criteria for absolute GH deficiency in adults is a stimulated GH <3µg/L.

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