

Glucagon Stimulation Test for Cortisol and Growth Hormone

Author: D Ismail, M Lazner, C Chadwick. Adapted from Endocrine Dynamic Function Test Protocols for use in neonates and children – Manchester University NHS Foundation Trust November 2021 (H Beeston et al).

Approved by: UHSussex Medicines Governance Committee July 2022

Publication date: September 2022. Version 1

Review date: September 2024

Diagnosis of growth hormone deficiency (GHD)

If the patient is likely to become hypoglycaemic during GHD testing (due to a known issue with hypoglycaemia), an individualised plan should be implemented prior to GHD testing.

- GHD may present as an isolated problem or in combination with multiple pituitary hormone deficiency (MPHD).
- Evaluation for GHD in short stature (defined as height ≥ 2 SD below the population mean) should not be initiated until other chronic, non-endocrine causes of growth failure (e.g. hypothyroidism, chronic systemic disease, Turner's syndrome, skeletal disorder) have been excluded.

Principle

- This test can be used as an alternative to the insulin-induced hypoglycaemia test in the evaluation of central adrenal insufficiency. Glucagon requires endogenous ACTH to cause cortisol secretion.

Indication

To identify secondary adrenal insufficiency or combined ACTH/GH deficiency

Precautions

- ! The test should not be performed on a patient with pheochromocytoma or insulinoma as it may provoke an attack.
- ! The test should not be carried out following starvation of >48 hours or in the presence of a glycogen storage disease. The inability to mobilise glycogen may result in hypoglycaemia.
- ! The test should not be carried out in patients with severe hypocortisolaemia (9 am level <100 nmol/L)
- ! Thyroid function must be normal as thyroxine deficiency may reduce the GH and cortisol response.

Side Effects

Nausea and abdominal pain are common (30%) and patients may rarely vomit.

Preparation

- Thyroid function and cortisol must be checked to rule out panhypopituitarism
- GH should be stopped for at least 4 weeks prior to the test.
- All glucocorticoid therapy (other than dexamethasone or betamethasone) interferes with the assay of cortisol.
 - If the patient is on prednisolone therapy, it must be discontinued for 24 hours prior to the test.
 - If the patient is on a supra-physiological dose of hydrocortisone, it should be reduced to a physiological level (6 mg/m²/day) prior to the test. Omit the dose the night before and on the morning of the test. In cases of severe adrenal insufficiency, the paediatric endocrine consultant may advise that only the dose on the morning of the test is omitted.

Patients should take their usual dose of corticosteroid as soon as the test is completed.

- Patients must fast for 8 hours prior to the test (water only is allowed).
- A small amount of water may be swallowed during the test.
- Sex steroid priming may be necessary, see **sex steroid priming protocol below**

Protocol

Children can become hypoglycaemic after glucagon administration, usually 90 – 120 minutes post dose. Children <8 years of age are at particular risk.

- ! **Check glucose levels (by glucose meter) at the time of every sample.**
- ! **Check that the child is responsive at the time of every sample. If they do not respond, follow instructions for the emergency management of hypoglycaemia.**

Time (mins)	Medication to be administered	Samples to be taken		
-30		Cap. blood glucose	Cortisol	Growth Hormone
0		Cap. blood glucose	Cortisol	Growth Hormone
0	Glucagon			
30		Cap. blood glucose	Cortisol	Growth Hormone
60		Cap. blood glucose	Cortisol	Growth Hormone
90		Cap. blood glucose	Cortisol	Growth Hormone
120		Cap. blood glucose	Cortisol	Growth Hormone
150		Cap. blood glucose	Cortisol	Growth Hormone
180		Cap. blood glucose	Cortisol	Growth Hormone

1. Insert a 22G blue cannula and take -30 minute samples for capillary blood glucose, cortisol and growth hormone.
2. Wait 30 minutes before taking the baseline (t=0) sample for cortisol, growth hormone and cap. blood glucose.

NB. If glucose < 2.6 mmol/L at the start of the test **DO NOT PROCEED WITH TEST and DO NOT ADMINISTER GLUCAGON**

Discuss with endocrine team. It may be necessary to administer 10% glucose 2 ml/kg throughout the test. Take a sample for glucose and growth hormone before administering glucose.

3. If glucose level >2.6 mmol/L then administer **glucagon** intramuscularly
Dose: 100 microgram/kg. Max 1 mg.
4. Take further blood samples for cortisol and GH at 30, 60, 90, 120, 150, and 180 min post glucagon administration.
5. Observe for signs of hypoglycaemia throughout the test and record in patient's notes
6. Remember to check the child's glucose level by meter and the responsiveness at every sample.
7. A sweet drink and a full meal must be eaten and tolerated after the test and the child should be observed for 1 hour after the test. Blood glucose (by meter) must be >4 mmol/L before discharge.

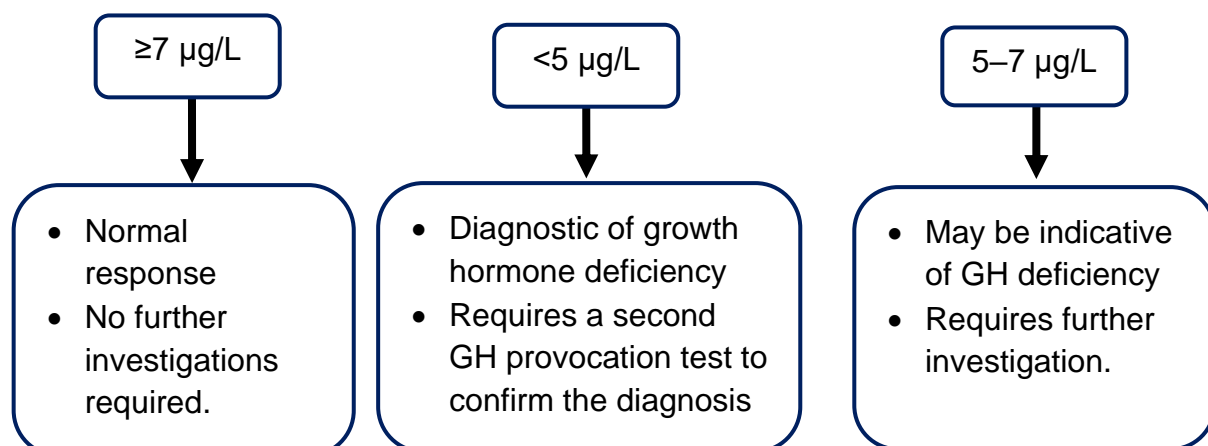
Samples

Cortisol & Growth Hormone 2 mL clotted blood (yellow / gold top)

**Record actual sample collection times on the printed labels.
SEND ALL SAMPLES TO THE LABORATORY TOGETHER**

Interpretation

- A peak plasma cortisol concentration of ≥ 420 nmol/L is indicative of a normal response and normal adrenal function.
- **Peak plasma Growth Hormone concentration** interpretation:



- In adults, a peak plasma GH concentration of <3 micrograms/L is diagnostic of growth hormone deficiency.
- Peak GH responses are also highly dependent on both short term nutritional status and on BMI – higher peak GH levels after short term fasting and in those with lower BMI.

Sex Steroid Priming protocol:

- Please refer to the BSPED guidance via <https://www.bsped.org.uk/clinical-resources/guidelines/> (Paediatric endocrine guidelines > growth > BSPED UK Consensus National Guidelines for Sex Hormone Priming for Growth Hormone (GH) Stimulation Testing)

Paediatric Endocrine Guidelines

Category	Guideline	Type	Source	Date of document	Review date
Adrenal Insufficiency	Steroid Treatment Card for Adrenal Insufficiency (link to patient resources page)	BSPED	BSPED	Nov 2020	Nov 2023
Bone	Vitamin D: supplement use in specific population groups	Endorsed	NICE	Nov 2014	
Bone	Recommendation of Endocrine & Bone Monitoring in Duchenne Muscular Dystrophy (DMD) in the UK NorthStar Network	Endorsed	DMD Care UK	Aug 2020	Aug 2023
Bone	Adrenal Insufficiency in DMD / Puberty and Testosterone Treatment in DMD - Patient Information Leaflets	Endorsed	DMD Care UK	Aug 2020	Aug 2023
DSD	UK Guidance on the Initial Evaluation of an Infant or an Adolescent with a Suspected Disorder of Sex Development	Endorsed	Society for Endocrinology	April 2021	April 2024
Growth	BSPED UK Consensus National Guidelines for Sex Hormone Priming for Growth Hormone (GH) Stimulation Testing	BSPED	BSPED	Apr 2021	April 2024
Growth	Human growth hormone (somatropin) for the treatment of growth failure in children	Endorsed	NICE	May 2010	
Growth	Shared care guidelines: Paediatric use of Recombinant Human Growth Hormone (r-hGH)	BSPED	BSPED	Aug 2015	May 2020

References

1. Basildon and Thurlow University Hospitals NHS Foundation Trust Clinical Biochemistry Department paediatric department Glucagon Stimulation test Paediatric protocol
2. Lim S.H., Vasanwala R., Lek N. and Yap F. (2011) Quantifying the risk of hypoglycaemia in children undergoing the glucagon stimulation test. *Clinical Endocrinology* **75**: 489 – 494
3. Strich D., Terespolsky N. and Gillis D. (2009) Glucagon stimulation test for childhood Growth Hormone deficiency: Timing of the peak is important. *The Journal of Pediatrics* 415 – 419
4. Secco A., di Iorgi N., Napoli F., et al. (2009) The Glucagon Test in the diagnosis of growth hormone deficiency in children with short stature younger than 6 years. *JCEM* **94**(11): 4251-4257
5. GH Research society (2000) *JPEM* **14**: 377 – 382
6. Binder G. (2011) Growth hormone deficiency: new approaches to the diagnosis. *Pediatr Endocrinol Rev* **9** (Suppl 1): 535 - 537
7. Kumaran A. & Dattani M. (2008) Growth hormone deficiency – Difficulties in Diagnosis and Management. *Touch Briefings*
8. Stanley T. (2012) Diagnosis of Growth Hormone Deficiency in childhood. *Curr Opin Endocrinol Diabetes Obes* **19**:47-52
9. Petersenn S., Quabbe H.J., Schöfl C., et al. (2010) The Rational Use of Pituitary Stimulation Tests. *Dtsch Arztebl Int* **107**(25):437-43