## Arginine Stimulation Test

Test Name: CHILD ARGININE STIMULATION DFT

### Principle
Arginine is used as a provocative agent during a stimulation test in the diagnosis of children with suboptimal growth. Arginine reduces somatostatin release and stimulates α-adrenergic receptors resulting in GHRH release. The test has a sensitivity of 75% with a specificity of 85% using a diagnostic cut-off of 7 µg/L[1]. This can be increased to a sensitivity of 100% and specificity of 98% if clinical evidence of GHD is also present[2].

### Indication
• See *Diagnosis of Growth Hormone Deficiency*

### Precautions
• None

### Side Effects
• Arginine may cause nausea and some irritation at the infusion site, ensure that the cannula works well prior to arginine administration. **Arginine can cause chemical burn injury if administered incorrectly**. Administer the infusion of arginine over 15 min time period.
• Arginine may also rarely cause anaphylaxis.
• In children with suspected hypopituitarism prolonged fasting may induce hypoglycaemia. Blood glucose should be checked by POCT in these patients whenever a sample is taken.

### Preparation
• Thyroid function should be normal; this must be ascertained before commencing the test.
• GH should be stopped for at least 4 weeks prior to the test.
• Sex steroid priming may be necessary, see *Diagnosis of Growth Hormone Deficiency*
• Patients should have water only for 8 hours prior to the test.
• For very young children, particularly those <1 year of age, a smaller duration of fast, possibly 4 hours should be adequate. This should be discussed with the consultant endocrinologist.
• A small amount of water may be swallowed during the test (no i.v).

### Protocol

1. Insert an indwelling cannula and take a basal blood sample (t= -30). Cannulation may cause growth hormone to rise; therefore, the patient should rest for 30 min before the test is commenced.

2. If the blood glucose meter <2.6 mmol/l at the start if the test, take a sample for glucose and growth hormone before administering glucose. DO NOT PROCEED WITH TEST – discuss with endocrine team first. It may be necessary to administer 10% glucose bolus.

3. If hypoglycaemia occurs during the test (blood glucose meter < 2.6 mmol/L administer 10 % glucose 2ml/Kg throughout the rest of the test.

4. Take a blood sample before commencing the infusion of arginine (t = 0).

| Generic | Route | Dose | Frequency |
|---|---|---|---|
| L-arginine monohydrochloride (10% solution in 0.9% sodium chloride) | i.v | 0.5g/kg body weight up to a maximum of 30g | Infusion over 15 mins |

5. Take blood samples for growth hormone 15, 30, 45, 60, 90 and 120 min after **the start** of the arginine infusion (i.e., 15 min sample should be taken after the arginine infusion has been completed). At each time point also check the blood glucose of the patient using a blood glucose meter.

**Time Points:**

| Time post arginine infusion (min) | Procedure | Blood Sample |
|---|---|---|
| -30 | Check blood glucose using meter. Check ketones using meter if blood glucose <3.0 mmol/L. | Growth hormone |
| 0 | Check blood glucose using meter | Growth hormone |
| 15 | Check blood glucose using meter | Growth hormone |
| 30 | Check blood glucose using meter | Growth hormone |
| 45 | Check blood glucose using meter | Growth hormone |
| 60 | Check blood glucose using meter | Growth hormone |
| 90 | Check blood glucose using meter | Growth hormone |
| 120 | Check blood glucose using meter | Growth hormone |

## Samples
*Growth Hormone*          1.2 mL clotted blood (white top)

## Interpretation

- A peak plasma GH concentration of ≥7 µg/L indicates a normal response to the test and no further investigations are required.

- A peak plasma GH concentration of <5 µg/L is diagnostic of growth hormone deficiency but requires a second GH provocation test to confirm.

- A peak plasma GH concentration of 5 – 7 µg/L may still be indicative of GH deficiency and requires further investigation.

- In adults, a peak plasma GH concentration of <3 µg/L is diagnostic of growth hormone deficiency.

- The percentage of children who are not GH deficient and who show a normal response to this test varies from 45 – 93%. Generally, 20% of normal children fail to respond to a formal test and this is the reason for doing 2 tests before proceeding to GH therapy. For example, 71% of normal individuals will respond to both insulin tolerance and arginine stimulation tests. However, the others will respond to at least one test: 13% to insulin, 16% to arginine.

## References
1. Van Vught A.J.A.H., Nieuwenhuizen A.G., Gerver W.J., Veldhorst M.A.B., Brummer R.J.M. & Westerterp-Plantenga M.S. (2009) Pharmacological and Physiological Growth Hormone Stimulation. Tests to Predict Successful GH Therapy in Children. *JPEM* **22**:679 – 694
2. Binder G. (2011) Growth hormone deficiency: new approaches to the diagnosis. *Paediatric Endocrinol Rev* **9**(1): 535-537