

3-day HCG Stimulation Test

Test Name: CHILD 3 DAY HCG STIMULATION DFT

Principle

Human chorionic gonadotrophin (hCG) is a polypeptide hormone and shares a common subunit with LH. It stimulates testicular Leydig cells to secrete androgens via the LH receptors. Children aged 6 months to 8 years frequently have undetectable basal gonadal steroids in plasma and gonadal function can only be assessed by Leydig cell stimulation using hCG.

Indication

- To detect functioning testicular tissue in the investigation of male hypogonadism, ambiguous genitalia, micropenis, delayed puberty and/or undescended testes. The test should be performed even if the gonads are impalpable (and the karyotype is XY or XY mosaic).
- To define enzyme blocks in testosterone biosynthesis.
- A urine steroid profile (after 1-3 months of age) may be more helpful for investigation of possible 5-alpha reductase deficiency, as blood results can be misleading.
- For investigation of possible 17-β-hydroxy-steroid dehydrogenase deficiency, a hCG stimulation test is more reliable than a urine steroid profile.

Precautions

- In boys with normal testes there may be some virilisation (increase in testicular size, erections).
- The test should not be performed before 2 weeks of age.
- If a GnRH test is planned, this should be carried out before the HCG test (or > 6 weeks after) as HCG has a long half-life.

Side Effects

- Headaches and/or tiredness are reported side effects.

Preparation

- None required.

Protocol

3 Day Protocol:

1. **Day 1** - Between 8.00 a.m. and 9.00 a.m. collect baseline blood samples for testosterone, androstenedione and dihydrotestosterone
2. Immediately following collection of baseline blood samples, **give human chorionic gonadotrophin as follows:**

Generic	Route	Dose	Frequency
human chorionic gonadotrophin	i.m	500 units if weight < 5kg 1000 units if weight 5 - 10kg 1500 units if weight 10 - 15kg 3000 units if weight above 15kg	Bolus

3. **Day 4** - Repeat blood sample 72 hours after hCG injection for testosterone, dihydrotestosterone and androstenedione.

If the results of the 3-day test are equivocal then consider performing the 3-week hCG stimulation test.

Samples

Testosterone, DHT & Androstenedione 1.2 mL clotted blood (white top)

Urinary Steroid Profiling 24hr timed urine in a plain bottle if indicated (collection after injection usually preferred e.g., 24hr prior to day 4)

visit, check with consultant). Random/ 4-hour timed sample less reliable but is acceptable. Collection on day 4 usually preferable to day 1.

Interpretation

The normal testosterone response depends on the age of the patient. In infancy, a normal testosterone increment after hCG may vary from 2-fold to 10- or even 20-fold. During childhood, the increment is between 2- and 9-fold. During puberty, as the basal concentration is higher, the increment is less, i.e. 2- to 3-fold. In the absence of testes, no response to testosterone occurs.

An absent response with an exaggerated LH/FSH response to LHRH stimulation indicates primary gonadal failure or anorchia. If there is a defect in testosterone biosynthesis, there will be an increase in precursor steroid secretion following HCG stimulation.

There are reported errors in the interpretation of the hCG stimulation test in boys ~8yrs of age with increased Testosterone: DHT in the 5 α -reductase range.

Samples are sent to Leeds General Infirmary for analysis.

Interpretation (from Leeds):

	Testosterone (nmol/L)	DHT (nmol/L)	Testosterone /DHT ratio post hCG*	Androstenedione (nmol/L)	Androstenedione/ Testosterone ratio post HCG
Normal male adults	8 - 27	0.4-1.9	< 15	1.3 -5.8	<1.0
Normal children (6 months – puberty)	< 0.9	< 0.25	< 15	<1.4	<1.0
5 α -reductase deficiency (6 months – puberty)	<0.5	N/A	> 20	N/A	N/A
17- β -hydroxy-steroid dehydrogenase deficiency	N/A	N/A	N/A	N/A	Raised >2.0**

* Testosterone /DHT ratio post hCG 15-20: 5-alpha-reductase deficiency cannot be excluded

** Androstenedione/ Testosterone ratio post HCG: Males, all ages: <1.0 – Likely excludes 17 β -hydroxysteroid dehydrogenase deficiency. Adults: >3.0 – Indicative of 17 β -hydroxysteroid dehydrogenase deficiency.

References

1. Maimoun L., Philibert P., Cammas B., Audran F., Bouchard P., Fenichel P., Cartigny M., Pienkowski C., Polak M., Skordis N., Mazen I., Ocal G., Berberoglu M., Reynaud R., Baumann C., Cabrol S., Simon D., Kayemba-Kay's K., De Kerdanet M., Kurtz F., Leheup B., Heinrichs C., Tenoutasse S., Van Viet G., Gruters A., Eunice M., Ammini A.C., Hafez M., Hochberg Z., Einaudi S., Mawlawi H.A., del Valle Nunez C.J., Servant N., Lumbroso S., Paris F. & Sultan C. (2011) Phenotypical, Biological and molecular heterogeneity of 5 α -Reductase deficiency: An extensive international experience of 55 patients. *JCEM* **96**: 296 - 307
2. Segal T.Y., Mehta A., Anazodo A., Hindmarsh P.C. & Dattani M.T. (2009) Role of gonadotropin-releasing hormone and human chorionic gonadotropin stimulation tests in differentiating patients with hypogonadotropic hypogonadism from those with constitutional delay of growth and puberty. *JCEM* **94**(3): 780 – 785
3. Leeds Children’s Hospital Paediatric Endocrinology Dynamic Function Tests: Valid Jan 2022 to Jan 2025. hCG Stimulation Test