

3-week HCG Stimulation Test

Test Name: CHILD 3 WEEK STIMULATION TEST 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

- In the event of an equivocal result from the 3-day HCG stimulation test, the 3-week HCG stimulation test should be used.

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) if as hCG has a long half-life.

Side Effects

- Headaches and/or tiredness are reported side effects.

Preparation

- None required.

Protocol

3 Week Protocol:

Described in table below

- Day 1** - Between 8.00a.m and 9.00a.m collect baseline blood samples for testosterone (also androstenedione and dihydrotestosterone if a steroid biosynthetic defect is suspected).
- 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 on days 1, 4, 8, 11, 15 & 18.

- Day 4** - Repeat blood sample for testosterone, dihydrotestosterone and androstenedione (72 hours after human chorionic gonadotrophin injection).
- Administer human chorionic gonadotrophin and continue to administer human chorionic gonadotrophin twice weekly for the next 2 weeks (see table below).
- Collect the final blood sample for testosterone, DHT and androstenedione 4 days after the last injection of human chorionic gonadotrophin.

Also document the clinical response in terms of testicular descent and change in phallic size.

Time Points:

Week	1		2		3		4
Day	Mon	Thurs	Mon	Thurs	Mon	Thurs	Mon
hCG administration	✓	✓	✓	✓	✓	✓	
Blood Sample for testosterone, DHT, A-dione	✓	✓					✓
Urine Steroid profile		✓					✓

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.

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. A 5- to 10-fold increment from the basal testosterone constitutes a normal response in the prolonged test.

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