

Gonadotrophin-releasing hormone (GnRH) test

Test name: CHILD GNRH STIMULATION DFT

Principle

Gonadotrophin-releasing hormone (GnRH), secreted by the hypothalamus, stimulates the release of luteinising hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary gland.

Indication

- Investigation of pubertal disorders: precocious puberty and delayed puberty.
- Investigation of hypogonadotrophic hypogonadism suspected pre-pubertally.
- Monitoring of children with precocious puberty treated with GnRH analogues.

Precautions

- Avoid human chorionic gonadotrophin injections prior to the test and do not perform following priming for an arginine test.

Side Effects

- GnRH may rarely cause nausea, headache and abdominal pain.

Preparation

The patient need not be fasted (unless combined with a test of GH secretion).

Protocol

1. Insert a reliable cannula. Take blood for LH, FSH, testosterone or oestradiol (t = 0).

Administer GnRH:

Age	Generic	Route	Dose	Frequency
<1 year	Gonadorelin	<i>i.v</i>	2.5 micrograms/kg	<i>Bolus</i>
≥ 1 year	Gonadorelin	<i>i.v</i>	100 micrograms	<i>Bolus</i>

3. Take blood at
 - + 30 min
 - + 60 min
 after the GnRH bolus for LH & FSH only

Samples

LH & FSH 1.2 mL lithium heparin (orange top)

Testosterone or Oestradiol 1.2 mL clotted blood (white top)

Interpretation

The GnRH test should be interpreted in the clinical context (including pubertal staging, testicular volume/ovarian ultrasound) and along with other biochemical markers of puberty such as serum oestradiol or testosterone levels.

Prepubertal

Basal LH usually <1.0 IU/L. LH peak post-GnRH <6.0 IU/L. FSH peak greater than LH peak.

Peripubertal

Higher increments, especially if LH dominant, provide evidence of a pubertal pattern of gonadotrophin response. LH peak ≥6.0 IU/L, with LH peak greater than FSH peak.

See table below for the reference ranges from Resende *et al.* 2007, for serum LH and FSH concentrations (AutoDELFIA assays) in normal subjects at different pubertal stages (n=316 for basal levels, n=106 for GnRH stimulated levels).

Pubertal Delay and Pubertal failure

In children with suspected hypogonadotrophic hypogonadism, a complete lack of response supports the diagnosis. A measurable but low response has limited predictive value (may also occur in constitutional delay of puberty). In primary gonadal failure, the basal LH and FSH are elevated and the response to GnRH is exaggerated. High basal FSH levels in the presence of low oestradiol levels may suggest ovarian failure.

Premature thelarche and thelarche variant

There may be a FSH predominant response, with LH usually in the pre-pubertal range.

Precocious puberty

In gonadotrophin-independent precocious puberty, spontaneous gonadotrophin secretion is suppressed by the autonomous sex steroid secretion: basal LH and FSH are low and the response to GnRH is flat.

In gonadotrophin-dependent precocious puberty basal LH and FSH levels are usually elevated and the response to GnRH is exaggerated. A LH dominant rise is usually observed, with LH levels usually >7.0 IU/L and more commonly >10.0 IU/L in established puberty.

Precocious puberty (treated)

Suppressed basal LH and FSH and flat response to GnRH indicate adequate treatment with GnRH analogues.

Table - Concentration of serum LH and FSH (AutoDELFIA assays), expressed as mean and 5th and 95th percentiles, in normal subjects at different pubertal stages (n=316 for basal levels, n=106 for GnRH stimulated levels)

Pubertal Stage	Males				Females			
	Basal		GnRH-stimulated peak		Basal		GnRH-stimulated peak	
	LH (IU/L)	FSH (IU/L)	LH (IU/L)	FSH (IU/L)	LH (IU/L)	FSH (IU/L)	LH (IU/L)	FSH (IU/L)
T₁ (<2.6 yr)	<0.6	1.0 (1.0-1.4)	N/A	N/A	<0.6	3.7 (1.0-8.3)	N/A	N/A
T₁₂	<0.6	1.1 (1.1-1.6)	2.2 (1.1-3.3)	5.7 (2.4-10.6)	<0.6	1.6 (1.0-3.4)	2.1 (0.6-4.2)	11.7 (1.9-27.1)
T_{II}	1.3 (0.6-2.7)	1.8 (1.0-4.3)	15.6 (1.9-31.0)	3.6 (1.4-10.2)	1.0 (0.6-N/A)	2.3 (1.0-4.8)	5.3 (0.6-12.5)	6.5 (1.8-13.2)
T_{III}	1.4 (0.6-2.5)	2.1 (1.0-5.5)	16.1 (7.3-32.0)	4.2 (1.1-13.0)	2.9 (0.6-5.0)	3.9 (2.6-5.1)	21.0 (14.6-31.0)	7.9 (5.9-12.0)
T_{IV}	1.6 (0.7-2.5)	2.1 (1.0-5.2)	17.3 (12.0-28.0)	4.8 (1.7-12.0)	3.1 (1.0-6.0)	4.0 (1.5-7.2)	26.2 (10.4-54.5)	8.6 (4.0-18.0)
T_V	4.7 (2.4-8.2)	3.2 (1.2-5.7)	28.9 (9.5-56.3)	5.3 (1.8-12.0)	5.7 (0.6-15.4)	4.1 (1.0-7.3)	37.9 (9.7-114.0)	9.2 (2.8-18.8)

References

1. Resende E.A., Lara B.H., Reis J.D., Ferreira B.P., Pereira G.A. & Borges M.F. (2007) Assessment of basal and gonadotropin-releasing hormone-stimulated gonadotropins by immunochemiluminometric and immunofluorometric assays in normal children. *JCEM* **92**:1424-9
2. Brito V.N., Batista M.C., Borges M.F., Latronico A.C., Kohek M.B., Thirone A.C., Jorge B.H., Arnhold I.J. & Mendonca B.B. (1999) Diagnostic value of fluorometric assays in the evaluation of precocious puberty. *JCEM* **84**: 3539-44
3. Trueman J.A., Tillmann V., Cusick C.F., Foster P., Patel L., Hall C.M., Price D.A. & Clayton P.E. (2002) Suppression of puberty with long-acting goserelin (Zoladex-LA): effect on gonadotrophin response to GnRH in the first treatment cycle. *Clin Endocrinol (Oxf)*. **57**: 223-30