

Gonadotrophin-releasing hormone (Gonadorelin) test for puberty assessment

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Approved by: UHS Medicines Governance Committee July 2022

Publication date: September 2022. Version 1

Review date: September 2024

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 HCG 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 does not need to be fasted (unless combined with a test of GH secretion).

Protocol

Time (min)	Samples to be taken			Medication to be administered
0	LH	FSH	Oestradiol (for girls) Testosterone (for boys)	
0				Gonadorelin: 2.5 micrograms/kg IV bolus (maximum 100 micrograms)
20	LH	FSH		
60	LH	FSH		

1. Insert a 22G blue cannula. Take blood for LH, FSH, testosterone or oestradiol (t = 0).
2. Give a bolus dose of Gonadorelin intravenously
Dose: 2.5 micrograms/kg. Max 100 micrograms
3. Take blood at + 20 min + 60 min after the GnRH bolus for LH & FSH only

Samples

LH & FSH, Testosterone or Oestradiol 2 mL clotted blood (yellow/gold 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 IU/L. LH peak post-GnRH <6 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 IU/L, with LH peak greater than FSH peak.
- See Table 1 on the following page for the reference ranges from Resende *et al.* 2007, for serum LH and FSH concentrations (AutoDELFIAs 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 hypogonadotropic 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 IU/L and more commonly >10 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 1 - Concentration of serum LH and FSH (AutoDELFIAs 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 ₁ (<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
T1 ₂	<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)
TII	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)
TIII	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)
TIV	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)
TV	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

(adaptation with permission of authors: RMCH Paediatric Endocrine and Clinical Biochemistry L Tetlow, B Hird, H Beeston, Prof I Banerjee, Dr A Chinoy, Prof P Clayton, Prof, Z Mughal, Dr P Murray, Dr R Padidela, Prof L Patel, Dr M Salomon Estebanez, Dr M Skae, E O'Shea).

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