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BSPED UK Consensus National Guidelines for Sex Hormone Priming for Growth Hormone (GH) Stimulation Testing

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In peri-pubertal children, sex-steroid priming before growth hormone (GH) stimulation testing increases spontaneous nocturnal GH secretion and reduces the number of conflicting test results (10). Priming may therefore improve the diagnostic accuracy of GH stimulation tests for idiopathic GH deficiency in this age group (13). Children with slow growth and delayed puberty may show low GH peaks during stimulation testing which often normalize as puberty progresses. This transient suboptimal response may therefore lead to unnecessary growth hormone treatment.

A national audit and Delphi consensus process among members of the BSPED (1) confirmed an agreement to priming with sex hormones prior to growth hormone provocation tests in children in the peri-pubertal age for suspected growth disorders. This approach is also supported by a recent multinational Delphi process and a recent audit of worldwide practices.

This guideline is derived from consensus based on current agreed clinical practices and published literature through a comprehensive literature review performed up to August 2025 which showed further evidence to support the use of priming prior to growth hormone stimulation tests in peri-pubertal children but no evidence supporting one specific priming regimen over any other.

PATIENT SELECTION

Children of the peri-pubertal age with minimal signs of puberty, defined as:

- Boys aged over 10 years and with testicular volumes of less than 6mls (Delphi 92%)
- Girls aged over 9 years with breast stage 2 or less (Delphi 87%)

DRUG CHOICE

- An oestrogen preparation should be the preferred drug of choice for both male (Delphi 72%) and females (Delphi 100%)
- Intramuscular testosterone may be used as an alternative in boys
- However, the choice of priming agent may be determined by local availability
- Note, stilboestrol has been removed from this guideline as its use in children is now contraindicated following a recent MHRA notification (add ref no)

EXAMPLES OF SEX STEROID PRIMING REGIMENS OPTIONS

Drug	Dose	Choices	Sex	Pros	Cons
17β-oestradiol e.g. Estradiol Valerate	1 mg daily (< 20kg) 2 mg daily (>20kg) orally for 3 days before GH test (2–4)	Preferred	Males & Females	• Availability • Well tolerated • Side effects uncommon	
Conjugated oestrogen e.g. Premarin®	2.5 mg daily orally for 3 days before GH test	Preferred	Males & Females	• Availability • Well tolerated • Side effects uncommon	
Ethinyl-oestradiol	10 micrograms daily for 3 days before GH test	Preferred	Males & Females	• Availability • Well tolerated • Side effects uncommon in girls	• Intermittent availability • Nausea and vomiting in boys
Testosterone depot (testosterone enanthate Or Sustanon®)	100 mg once only intramuscular administered 5 days before GH test	Alternative	Males	• Availability • Not reliant on patient compliance (administered by health care professional)	• Local inflammation of injection site • Testicular pain, priapism • Hypersensitivity in patients allergic to nuts or soy in some testosterone preparations

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Sex Hormone Priming for Growth Hormone (GH) Stimulation Testing

Reference	Study type	Population	Intervention	Evidence	Included in review?
BSPED UK Consensus National Guidelines for Sex Hormone Priming for Growth Hormone (GH) Stimulation Testing	Current BSPED Guidance 2021 UK	Delphi consensus	Range of preparations	PATIENT SELECTION Children of the peri-pubertal age with minimal signs of puberty, defined as: Boys aged over 10 years and with testicular volumes of less than 6mls (Delphi 92%) Girls aged over 9 years with breast stage 2 or less (Delphi 87%) DRUG CHOICE An oestrogen preparation should be the preferred drug of choice for both male (Delphi 72%) and females (Delphi 100%) Intramuscular testosterone may be used as an alternative in boys However, the choice of priming agent may be determined by local availability	Yes
Duncan G, Kiff S, Mitchell RT. Sex steroid priming for growth hormone stimulation testing in children and adolescents with short stature: A systematic	Systematic review (4 RCTs, 6 case control studies, 5 retrospective cohort studies)	NA	NA	Sex-steroid priming increases the growth hormone response during GHST, resulting in fewer patients meeting the	Yes

review. Clin Endocrinol (Oxf). 2023 Apr;98(4):527-535	2023 UK			threshold required for a diagnosis of GHD. Numerous sex-steroid priming regimens have been used in clinical practice and the majority appear to be effective, but an optimal regimen has not been determined. Two RCTs showing no significant difference between peak GH response both utilized clonidine for GH stimulation, raising the question as to whether effect of priming varies depending on GHST used. Priming might be unnecessary when Tanner stage 4 or more has been achieved Most studies used cut off GH response >7 µg/L	
Arlien-Søborg MC, Radovick S, Boguszewski MCS, Bidlingmaier M, Johannsson G, Grimberg A, Ho KKY, Biller BMK, Choong CS, Hoffman AR, Backeljauw P,	Delphi consensus 2025 14 countries	NA	NA	Paediatric endocrinologists: All children with short stature during the peripubertal period should	Yes

Boguszewski CL, Bollerslev J, Brue T, Chanson P, Christ E, Cianfarani S, Clayton PE, Cohen P, Dauber A, Fleseriu M, Gebauer J, Giustina A, Higham CE, Horikawa R, Höybye C, Juul A, Lodish M, Luo X, Mauras N, Miller KK, Melmed S, Neggers SJCMM, Karavitaki N, Rosenfeld R, Ross R, Savendahl L, Schilbach K, Collett-Solberg PF, Strasburger CJ, Tritos NA, van Santen HM, Yuen KCJ, Jorgensen JOL. Consensus and controversies about diagnosing GH deficiency: a Delphi survey by the GH research society. Pituitary. 2025 May 7;28(3):57				receive sex steroid priming prior to provocative GH testing 65% agreement 60% agreement 69% agreement	
Lennartsson O, Nilsson O, Lodefalk M. Priming Short Children with Sex Steroids prior to Growth Hormone Testing Decreases the Frequency of Divergent Results. Horm Res Paediatr. 2025 Jun 10:1-10. doi: 10.1159/000546884. Epub ahead of print.	Retrospective observational study Sweden, 2025	132 children undergoing arginine-insulin stimulation tests	19% received priming. Ethinyl estradiol, estradiol valerate or testosterone enanthate	Sex steroid priming prior to GH testing is well tolerated, enhances spontaneous nocturnal GH secretion, and reduces the frequency of divergent results between spontaneous and stimulated values. We recommend incorporating priming when evaluating children in prepuberty or early puberty for suspected GHD.	Yes

				Fewer side effects than other studies ? due to use of oestrogen not testosterone	
Yuen KCJ, Johannsson G, Ho KKY, Miller BS, Bergada I, Rogol AD. Diagnosis and testing for growth hormone deficiency across the ages: a global view of the accuracy, caveats, and cut-offs for diagnosis. Endocr Connect. 2023 Jun 12;12(7):e220504.	Review 2023 Worldwide (USA, Australia, Sweden…)	NA	NA	Practice of priming remains controversial and is not universally accepted yet (135, 136). It is noteworthy that the hormonal milieu of puberty is not sustained after priming. With supraphysiologic testosterone levels, endogenous GH secretion may be overestimated, but whether these children who respond to exogenous sex hormones can secrete adequate GH at the time of puberty remains unclear. It is also unclear whether peripubertal children who have lower GH peak levels without priming would benefit from exogenous GH therapy and whether children diagnosed with GHD with or without priming would respond similarly to GH treatment.	Yes

				Furthermore, overestimation of GH levels from priming can lead to false-negative results and deny eligible children from receiving GH therapy. An exception where priming may be considered is in patients with constitutional delay of growth and puberty, where the conditions can be difficult to differentiate (137). Currently, distinct GH cut-offs are only defined for children and adults, and GH cut-offs based on pubertal staging would bridge the continuum. Reassessment of the GH/IGF1 axis when a child treated with GH prepubertally enters puberty has been proposed as an alternative to priming	
Partenope C, Galazzi E, Albanese A, Bellone S, Rabbone I, Persani L. Sex steroid priming in short stature children unresponsive to GH stimulation tests: Why, who, when and how.	Review 2022 Italy & UK	NA	NA	Children with slow growth and delayed sexual development may exhibit low growth hormone peaks under growth hormone stimulation	Yes

Front Endocrinol (Lausanne). 2022 Nov 29;13:1072271. doi: 10.3389/fendo.2022.1072271. PMID: 36523598; PMCID: PMC9744763.				testing which often normalise as puberty progresses. Consequently, this transient suboptimal response to growth hormone stimulation testing may result in growth hormone overtreatment. Assessment of bone age is warranted to evaluate pubertal delay and to select candidates for sex steroid priming.	
Galazzi E. Improda N. Cerbone M. Soranna D. Moro M. Fatti L.M. Zambon A. Bonomi M. Salerno M. Dattani M. Persani L. *Clinical Endocrinology* 2021;94(2): 219.	Retrospective observational study 2021 Italy and UK	134 patients, 3 centres.	Variable sex hormone preparations used prior to GHST and during GH treatment	In peripubertal children, priming before GHST improves diagnostic accuracy of GHST for idiopathic GHD.	Yes
Yackobovitch-Gavan M, Lazar L, Diamant R, Phillip M, Oron T. Diagnosis of Growth Hormone Deficiency in Children: The Efficacy of Glucagon versus Clonidine Stimulation Test. Horm Res Paediatr. 2020;93(7-8):470-476. doi: 10.1159/000513393. Epub 2021 Feb 10. PMID: 33567442.	Retrospective, single-center, observational study	512 children with short stature Median age 9.3 years (IQR 6.2-12.1) 78.3% pre-pubertal, 61% boys	Underwent GHST with GST or CST first with confirmation of opposite stimulus test (if GH <7.5ng/ml) 2015-2018 Primary outcome efficacy of GST	All girls >11.5 years and boys >13.5 years with no evidence of puberty primed 38 (11.7%) primed Stimulation by glucagon does not generate sufficient GH response from somatotrophs in pre-pubertal children while it does so in pubertal	Yes

			or CST in first diagnosing GHD	children (including those primed)	
Kamoun C, Hawkes CP, Grimberg A. Provocative growth hormone testing in children: how did we get here and where do we go now? J Pediatr Endocrinol Metab. 2021 Apr 12;34(6):679-696. doi: 10.1515/jpem-2021-0045. PMID: 33838090; PMCID: PMC8165022.	Review article	NA	NA	No original data	No
Galazzi E, Persani LG. Differential diagnosis between constitutional delay of growth and puberty, idiopathic growth hormone deficiency and congenital hypogonadotropic hypogonadism: a clinical challenge for the pediatric endocrinologist. Minerva Endocrinol. 2020 Dec;45(4):354-375. doi: 10.23736/S0391-1977.20.03228-9. Epub 2020 Jul 23. PMID: 32720501.	Narrative review	NA	NA	No original data	No
Binder G, Reinehr T, Ibáñez L, Thiele S, Linglart A, Woelfle J, Saenger P, Bettendorf M, Zachurzok A, Gohlke B, Randell T, Hauffa BP, Claahsen van der Grinten HL, Holterhus PM, Juul A, Pfäffle R, Cianfarani S. GHD	Audit of national guidelines and practice	Spain, France, Poland, UK, Netherlands, Denmark, Italy, US, Germany		Priming recommended in 5 of 9 countries US 11y boys, 10y girls, tanner stage 1, 2mg E2 UK Netherlands 10y boys, 8y girls, tanner limit stage 3,	Yes

Diagnostics in Europe and the US: An Audit of National Guidelines and Practice. Horm Res Paediatr. 2019;92(3):150-156. doi: 10.1159/000503783. Epub 2019 Nov 8. PMID: 31707392.				100mg testosterone enanthate / 50ug ethinyl E2 Denmark 12-13y boys, 11-12y girls, tanner limit 1, 100mg testosterone enanthate, 1-2 mg oral E2 or transdermal E2 Germany 10y boys, 8y girls, tanner limit 1, 63mg testosterone enanthate, 1mg E2 valerate	
Dori EB, Avnon Ziv C, Auerbach A, Greenberg Y, Zaken H, Levy-Khademi F. The inter - Test variability of growth hormone stimulation tests and factors affecting this variability. Growth Horm IGF Res. 2020 Dec;55:101361. doi: 10.1016/j.ghir.2020.101361. Epub 2020 Oct 17. PMID: 33096344.	Cohort, cross-sectional	Israel 200 108M 92F, Av age 9.2 years F >11.6y and M>13y primed	Variability of second stim test Clonidine 1st test then, arginine or glucagon as second test	100mg testosterone enanthate 7-10d prior male 1mg estrofem BD twice daily 3 days prior in girls In those primed in 1st test GH peak was higher but not statistically significant. In second test statistically sig higher GH peak in those primed	No
ABSTRACTS					
Leka-Emiri, S; et al. Sex steroid priming prior to growth hormone stimulation testing in peripubertal adolescents with short stature? Endocrine Abstracts 2025; 110 EP747.	Retrospective case series	141 children with SS were evaluated for GHD in a 2 year period	Standard GHST (glucagon or clonidine) with prior steroid priming (n=76, 53.9%) compared to a	For priming – testosterone enanthate 100mg IM 5-7 days before for boys 1-2mg oestradiol valerate PO girls	Yes

			group without prior sex steroid priming (n=65, 46.1%)	Pre-pubertal (tanner 1) had significantly higher GH response after priming as opposed to pubertal (Tanner 2) Not statistically significant Also comments about E2 lvels	
Alyafei F. Soliman A. Qusad M. Hamed N. Alaaraj N. Ahmed S. Elsayed N. Elsiddig S. Hormone Research in Paediatrics 2024;97(Supplement 3): 593.	Prospective observational study	40 children randomised into with or without priming	With or without priming	The primed group exhibited a higher peak GH response (6.53) compared to the non-primed group (5.18), and a lower incidence of GH deficiency GH response in peripubertal children. No significant difference in GH peak levels is observed (p = 0.3234). However, 4/20 and 8/20 were diagnosed with GHD (peak < 7 ng/dl) in the non-primed vs primed groups. IGF1SD	No
Vuralli D. Ozon A. Gonc N. Priming with sex steroids increases the specificity of GH tests in the diagnosis of True isolated growth hormone deficiency. Hormone Research		115 peripubertal boys who were diagnosed with isolated GHD as a result of	Sixty (52.2%) of these patients were primed with sex steroids (125 mg sustanon	Peak GH similar in those primed and not primed at baseline At retest (one year of GH therapy) peak GH during the retest was <10 ng/ml	Yes

in Paediatrics 20243; 96 (supplemnent 4): 293		inadequate GH response in two GH stimulation tests (L-dopa and clonidine). Bone ages of all patients were >= 9 years, pubertal stages were either Tanner 1 (54/115, 47%) or Tanner 2 (61/115, 53%), and testosterone levels were <200 ng/dl in all patients	intramuscularly) one week before at least one of the two GH stimulation tests during the diagnosis of GHD. GH treatment at a dose of 0.033 mg/kg/day was started in all patients and GH stimulation tests were repeated in the first year of treatment	in 70% (42/60) of the patients primed with sex steroids, and in 47.3% (26/55) of those who were not primed (p<0.001).): Individuals diagnosed with GHD by GH stimulation test under priming with sex steroids have better height gain and a higher probability of a diagnosis of GHD in the repeat test. In other words, priming with sex steroids increases the specificity of the GH stimulation test in identifying GHD.	