

Table 4 Approach to treatment of CHH

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Target population	Goals	Treatment	Clinical monitoring	Laboratory monitoring	Comments
Neonatal and childhood					
Male individuals with cryptorchidism with or without micropenis	Testicular descent	Cryptorchidism: orchidopexy (patients aged <1 year)	Testicular volume	Testosterone, LH, FSH, inhibin B and AMH levels	Baseline levels of testosterone, LH and FSH between days 14–90; for later timepoints, measure after GnRH agonist stimulation No current indication for female individuals
	Penis growth	Micropenis: testosterone, DHT or gonadotropin therapy (patients aged 1–6 months)	Penile growth		
Adolescent					
Patients aged 14–15 years (earlier in the presence of specific signs such as anosmia)	Virilization or estrogenization Sexual function Growth and bone health Gonadal maturation and future fertility Psychological wellbeing	Male patients: testosterone (oral, injectable or transdermal) Gonadotropins?	Genital development Growth and epiphyseal closure Virilization Sexual function Wellbeing Adherence Reversibility	Morning serum testosterone levels (trough levels for injections), LH, FSH and inhibin B levels, haemocrit	Testosterone treatment will not induce testicular growth or fertility
		Female patients: estradiol (oral or transdermal) followed by estradiol + progesterone or progestin	Breast development Growth and epiphyseal closure Estrogenization Feminized body Menses Sexual function Bone health Wellbeing Adherence Reversibility		
Adulthood					
All patients	Sexual function Fertility Limiting comorbidities Psychological wellbeing Puberty induction	Male patients: Testosterone (injectable or transdermal) hCG ± FSH FSH, FSH + hCG GnRH pump	Pubertal development Sexual function and libido Bone health Wellbeing Adherence Fertility Reversibility	Tough serum testosterone levels, LH, FSH and inhibin B levels, haematocrit, PSA levels	Sex steroid replacement will not induce fertility
		Female patients: Estradiol (oral or transdermal) Progesterone or progestin FSH + hCG or GnRH pump	Pubertal development Sexual function and libido Bone health Wellbeing Adherence Fertility Reversibility		
Abbreviations: AMH, anti-Müllerian hormone; CHH, congenital hypogonadotropic hypogonadism; DHT, dihydrotestosterone; FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; hCG, human chorionic gonadotropin; LH, luteinizing hormone; PSA, prostate-specific antigen.					