PIPADOR REVISION

MRCOG Part 1 Revision Notes

Puberty

ENDOCRINOLOGY • LECTURE 165

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG PART 1 REVISION NOTES | ENDOCRINOLOGY

165 Puberty

Activation of the HPG axis, pubertal sequence and staging, precocious and delayed puberty, primary amenorrhoea

≈ 10–11 yr	≈ 12.5–13 yr	< 8 / < 9 yr	> 13 / > 14 yr
Thelarche — first sign in girls	Menarche (UK)	Precocious puberty (girls / boys)	Delayed puberty (girls / boys)

■ KEY FACTS: Learning objectives

- Describe activation of the hypothalamic–pituitary–gonadal axis at puberty and its triggers.
- Describe the sequence and staging of puberty in girls and boys, adrenarche and the growth spurt.
- Classify and investigate precocious and delayed puberty and primary amenorrhoea.

165.1 Activation of the HPG axis

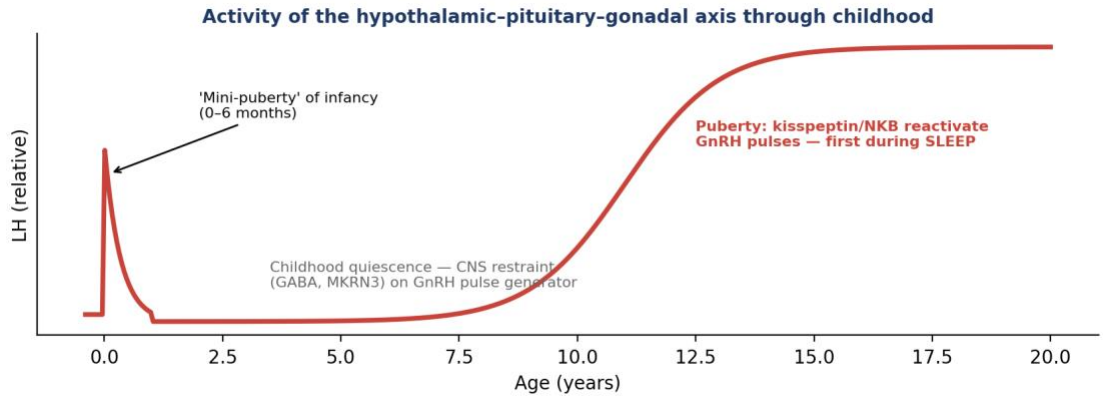


Figure 165.1 — HPG axis activity from fetal life to adulthood

Factor	Role
Kisspeptin (KISS1 → KISS1R) / neurokinin B	Gatekeeper — stimulates GnRH neurons; loss-of-function → hypogonadotrophic hypogonadism
MKRN3 (paternally expressed, imprinted)	Brake on puberty; loss-of-function → familial central precocious puberty
Leptin / energy status	Permissive signal of adequate fat stores (critical body weight); low leptin → delayed puberty/amenorrhoea (anorexia, athletes)
Genetics, ethnicity, environment	Earlier puberty with obesity, better nutrition; endocrine disruptors
Sleep-related pulses	Early puberty: nocturnal LH pulses → then daytime; ↑ LH:FSH response to GnRH

Adrenarche (≈ 6–8 yr) — maturation of the adrenal **zona reticularis** → ↑ **DHEAS** → pubic/axillary hair, body odour, acne; **independent** of the gonadal axis (occurs in gonadal agenesis). Premature adrenarche is associated with later PCOS.

165.2 Sequence of puberty

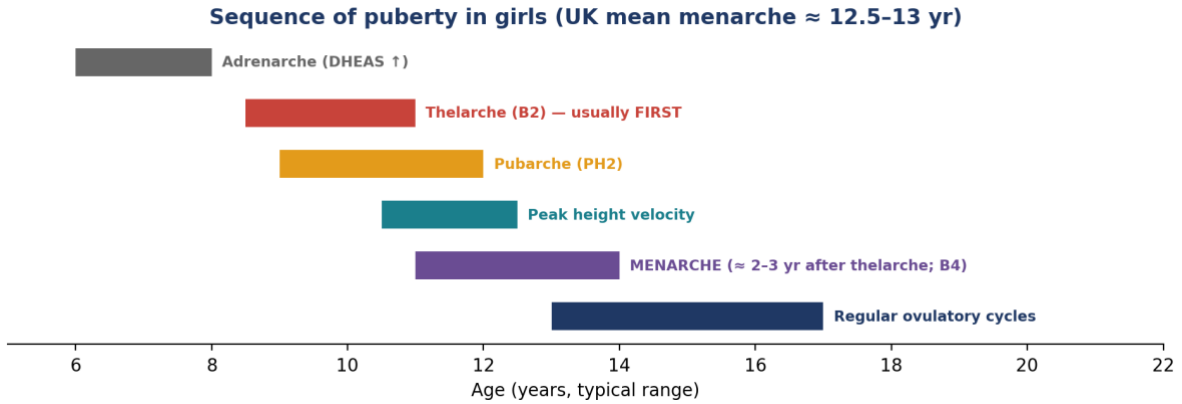


Figure 165.2 — Timing of pubertal events in girls

Tanner stage	Breast (girls)	Pubic hair	Boys — genitalia
1	Pre-pubertal	None	Pre-pubertal; testicular volume < 4 mL
2	Breast bud (thelarche)	Sparse, long, labia/base of penis	Testicular volume ≥ 4 mL (first sign, ≈ 11.5 yr)
3	Breast and areola enlarge (one contour)	Darker, coarser, over pubis	Penis lengthens
4	Areola forms secondary mound; menarche usually here	Adult type, not on thighs	Penis widens; scrotum darkens
5	Adult contour	Spreads to medial thighs	Adult (testes ≈ 15–25 mL)

- **Growth spurt**: girls early (peak height velocity ≈ 8 cm/yr at B2–3, before menarche); boys ≈ 2 years later and greater (≈ 10 cm/yr) — accounts for the ≈ 13 cm sex difference in adult height. Driven by **sex steroids → ↑ GH/IGF-1**; **oestrogen fuses the epiphyses in both sexes** (aromatase deficiency → tall stature).
- Early cycles are often **anovulatory** (immature positive feedback) → irregular, sometimes heavy bleeding; regular ovulation within ≈ 2–5 years.

165.3 Precocious puberty

	Central (GnRH-dependent)	Peripheral (GnRH-independent)
Mechanism	Early activation of HPG axis — normal sequence	Sex steroids from gonads, adrenals or exogenous; gonadotrophins suppressed
Causes	Girls: idiopathic (≈ 90%), MKRN3/KISS1 variants; boys: CNS lesions more likely (hamartoma, tumour, hydrocephalus, irradiation)	McCune–Albright, ovarian cysts/granulosa cell tumour, CAH, adrenal tumours, testicular tumours (hCG-secreting), exogenous oestrogen, severe hypothyroidism
Tests	LH ↑ after GnRH stimulation; advanced bone age; pelvic USS (uterine growth); MRI brain	Low LH/FSH with high sex steroids; 17-OH-progesterone, DHEAS, hCG, USS
Treatment	GnRH agonist depot (downregulation) to preserve height and psychosocial wellbeing	Treat cause (aromatase inhibitors, surgery)

Benign variants: **premature thelarche** (isolated breast development, < 2 yr, non-progressive) and **premature adrenarche**.

165.4 Delayed puberty and primary amenorrhoea

Category	Causes	Hormones
Constitutional delay	Commonest (especially boys); family history; delayed bone age; spontaneous puberty	Low (as for bone age)
Hypogonadotrophic	Kallmann syndrome (anosmia; ANOS1), isolated GnRH deficiency, functional (anorexia nervosa, excessive exercise, chronic illness — coeliac, IBD, CF), hyperprolactinaemia, pituitary tumours (craniopharyngioma), hypothyroidism	↓ FSH/LH, ↓ E2
Hypergonadotrophic	Turner syndrome (45,X) — commonest cause of primary ovarian failure; 46,XY gonadal dysgenesis (Swyer), POI (chemo/radiotherapy, galactosaemia)	↑↑ FSH/LH, ↓ E2
Normal breast development but no menses	MRKH (Müllerian agenesis, 46,XX), complete AIS (46,XY; no pubic hair), imperforate hymen/transverse septum (cyclical pain, haematocolpos)	Normal female (MRKH); male testosterone (AIS)

■ **CLINICAL CORRELATION**

- **Primary amenorrhoea**: investigate if no menses by **15** with secondary sexual characteristics, or by **13** without breast development.
- Assess growth and BMI, Tanner stage, smell, dysmorphic features (Turner: short stature, webbed neck, wide carrying angle), pelvic ultrasound; FSH, LH, E2, prolactin, TSH, testosterone, **karyotype**.
- **Turner**: oestrogen induction (low-dose, gradually increasing) for puberty and bone; GH for height; cardiac (coarctation, bicuspid valve, aortic dissection — high risk in pregnancy) and renal assessment; egg donation for fertility.

165.5 Must-know summary

■ **EXAM TIP**

- Girls: **thelarche → pubarche → peak height velocity → menarche** (≈ 2–3 yr after thelarche, at Tanner B4).
- Boys: **testicular enlargement ≥ 4 mL** first; height spurt later.
- Kisspeptin activates GnRH; leptin is permissive; adrenarche (DHEAS) is independent of gonadarche.
- Precocious: < 8 (girls) — mostly idiopathic central; boys — exclude CNS lesion; peripheral = suppressed LH/FSH.
- Delayed: Turner (↑ FSH) vs Kallmann/functional (↓ FSH); normal breasts + no menses → MRKH or AIS.

■ **MNEMONIC / MEMORY AID**

Order in girls — 'Boobs, Pubes, Grow, Flow': thelarche, pubarche, growth spurt, menarche. **Kallmann — 'Kall-man can't smell'** (anosmia + hypogonadotrophic).