PIPADOR REVISION

MRCOG Part 1 Revision Notes

Hypothalamic Hormones

ENDOCRINOLOGY • LECTURE 168

VISUAL EXAMINATION REVISION NOTES

2026 Edition

168

MRCOG PART 1 REVISION NOTES | ENDOCRINOLOGY

Hypothalamic Hormones

GnRH, TRH, CRH, GHRH, somatostatin and dopamine — physiology, pharmacology and clinical disorders

10 aa	3 aa	41 aa	Inhibitory
GnRH (decapeptide)	TRH (tripeptide)	CRH	Dopamine = prolactin-inhibiting factor

■ KEY FACTS: Learning objectives

- Describe the hypothalamo-pituitary connections and the portal circulation.
- Describe the structure, secretion, receptors and actions of GnRH, TRH, CRH, GHRH, somatostatin and dopamine.
- Explain GnRH pulsatility and the pharmacology of GnRH agonists and antagonists.
- Apply to Kallmann syndrome, functional hypothalamic amenorrhoea, drug-induced hyperprolactinaemia, stress and pregnancy.

168.1 Hypothalamo-pituitary anatomy



Figure 168.1 — Portal and neural links between hypothalamus and pituitary

Hypothalamic **parvocellular** neurons release releasing/inhibiting hormones at the **median eminence** into the **hypophyseal portal system**, delivering high concentrations to the anterior pituitary. **Magnocellular** neurons of the supraoptic and paraventricular nuclei send axons to the **posterior pituitary** (ADH, oxytocin — Lecture 169).

168.2 The hypothalamic hormones

Hormone	Structure / receptor	Pituitary target	Regulation and notes
GnRH	Decapeptide; GnRH-R (Gq)	↑ LH, FSH	Pulsatile (KNDy — kisspeptin/neurokinin B/dynorphin). ↓ by sex steroids (via kisspeptin), prolactin, CRH/cortisol, opioids, low leptin. Fast pulses → LH; slow → FSH
TRH	Tripeptide; Gq	↑ TSH, ↑ prolactin	↓ by T_3/T_4; primary hypothyroidism → ↑ TRH → hyperprolactinaemia, pituitary hyperplasia

Hormone	Structure / receptor	Pituitary target	Regulation and notes
CRH	41 aa; CRH-R1 (Gs)	↑ ACTH (POMC)	Circadian (peak early morning), stress; synergises with ADH; cortisol negative feedback. Placental CRH rises exponentially (Lecture 147)
GHRH	44 aa; Gs	↑ GH	Pulsatile, sleep; ghrelin also stimulates GH
Somatostatin	14/28 aa; Gi (SSTR)	↓ GH, ↓ TSH	Also gut/pancreas (↓ insulin, glucagon, gastrin); analogues (octreotide) for acromegaly, variceal bleeding
Dopamine	Amine; D_2 (Gi)	↓ Prolactin (tonic inhibition)	Tuberoinfundibular neurons; only anterior hormone under predominantly inhibitory control → stalk compression ↑ prolactin

168.3 GnRH pulsatility and pharmacology

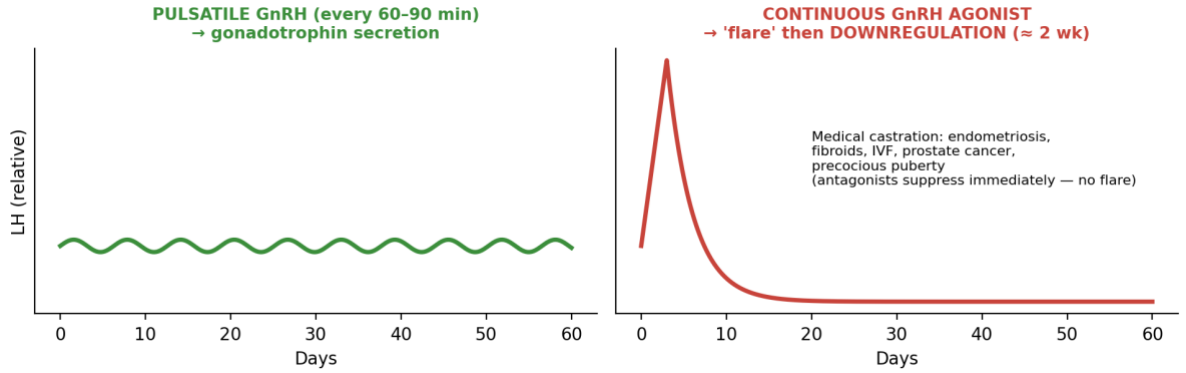


Figure 168.2 — Pulsatile vs continuous GnRH stimulation

Agent	Mechanism	Uses
Pulsatile GnRH (pump)	Restores physiological pulses	Ovulation induction in hypothalamic amenorrhoea (low multiple-pregnancy/OHSS risk)
GnRH agonists (goserelin, leuprorelin, triptorelin, buserelin nasal)	Initial flare, then receptor downregulation and desensitisation within ≈ 2 weeks → hypogonadotrophic state	Endometriosis, fibroids (pre-op), IVF (long protocol), central precocious puberty, prostate/breast cancer, trigger for final oocyte maturation (antagonist cycles — ↓ OHSS)
GnRH antagonists (cetrorelix, ganirelix; oral elagolix/relugolix)	Competitive blockade — immediate suppression, no flare	IVF (prevent premature LH surge), endometriosis/fibroids (oral, with add-back)

Side effects of prolonged suppression: menopausal symptoms and **bone loss** — limit to 6 months or use **add-back HRT**.

168.4 The HPA axis and stress

Stress, circadian clock, cytokines ▶ Hypothalamic **CRH** (+ ADH) ▶ Pituitary **ACTH** (from POMC) ▶ Adrenal **cortisol** ▶ Negative feedback; stress also ↓ **GnRH** → amenorrhoea

■ CLINICAL CORRELATION

- **Pregnancy**: placental CRH ↑ (≈ 1000-fold by term) but **CRH-binding protein** limits activity until late gestation; maternal **free cortisol rises** (≈ 2–3-fold; ↑ CBG raises total); diurnal rhythm preserved. Placental **11β-HSD2** protects the fetus.
- **Long-term steroid use** suppresses CRH/ACTH → adrenal insufficiency risk in labour/surgery — give **parenteral hydrocortisone cover**.

168.5 Clinical correlations

Condition	Mechanism / features
Kallmann syndrome	Failure of GnRH neuron migration from the olfactory placode (ANOS1/KAL1, FGFR1…) → hypogonadotrophic hypogonadism + anosmia; induce puberty/fertility with gonadotrophins or pulsatile GnRH
Functional hypothalamic amenorrhoea	Energy deficit (↓ leptin), exercise, psychological stress (↑ CRH/cortisol, opioids) → ↓ GnRH pulses; low E2 → bone loss; restore weight/energy balance
Drug-induced hyperprolactinaemia	Dopamine antagonists: antipsychotics (risperidone, haloperidol), metoclopramide, domperidone; also opioids, SSRIs, oestrogens. Treat by stopping/switching (aripiprazole), not routinely with dopamine agonists
Hypothalamic lesions	Craniopharyngioma, sarcoid, irradiation, trauma → multiple deficiencies, diabetes insipidus, ↑ prolactin (stalk effect), obesity, temperature dysregulation
Primary hypothyroidism	↑ TRH → galactorrhoea/amenorrhoea; resolves with thyroxine

168.6 Must-know summary

■ EXAM TIP

- Releasing hormones reach the anterior pituitary via the **portal veins**; ADH/oxytocin are made in hypothalamus and released from the **posterior** pituitary.
- **Dopamine (D_2)** tonically inhibits prolactin — stalk compression or D_2 antagonists ↑ prolactin.
- **TRH ↑ TSH and prolactin**; somatostatin ↓ GH and TSH.
- Pulsatile GnRH stimulates; continuous agonist → **flare then downregulation**; antagonists act immediately.
- Kallmann = GnRH deficiency + **anosmia**.

■ MNEMONIC / MEMORY AID

Hypothalamic hormones — 'Get The Cortisol & Growth Started, Don't': GnRH, TRH, CRH, GHRH, Somatostatin, Dopamine (last two inhibitory).