PIPADOR REVISION

MRCOG Part 1 Revision Notes

Progesterone

ENDOCRINOLOGY • LECTURE 171

VISUAL EXAMINATION REVISION NOTES

2026 Edition

171

MRCOG PART 1 REVISION NOTES | ENDOCRINOLOGY

Progesterone

Synthesis and sources, receptors, actions, progestogens and antiprogestogens, and clinical uses

> 30 nmol/L	7–9 wk	≈ 500–600	PR-A / PR-B
Mid-luteal level confirming ovulation	Luteo-placental shift	nmol/L at term	Nuclear receptor isoforms

■ **KEY FACTS: Learning objectives**

- Describe the synthesis, sources, transport and metabolism of progesterone.
- Describe progesterone receptors and the actions of progesterone in the cycle and pregnancy.
- Classify synthetic progestogens and antiprogestogens and their clinical uses.
- Describe evidence-based uses of progesterone in obstetrics and gynaecology.

171.1 Synthesis, sources and levels

Cholesterol → **pregnenolone** (CYP11A1) → **progesterone** (3β-HSD). It is the precursor of all other steroid hormones. Sources: **corpus luteum** (LH/hCG-dependent), **placenta** (from maternal LDL-cholesterol — does not need fetal precursors), adrenal cortex (small amounts).

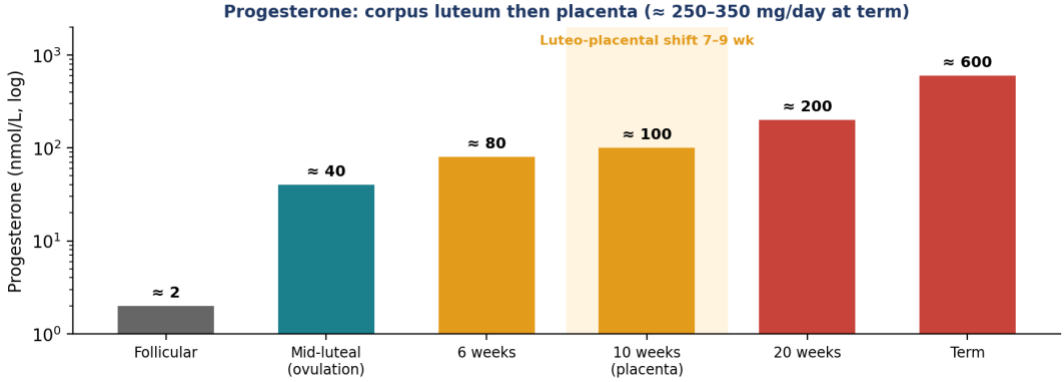


Figure 171.1 — Progesterone in the luteal phase and pregnancy

- Transported bound to **albumin** (≈ 80%) and **CBG** (≈ 18%); short half-life; hepatic metabolism to **pregnanediol** (urine).
- **Neuroactive metabolites** (5α-reduced: **allopregnanolone**) act on **GABA-A** receptors — sedation, anxiolysis; withdrawal implicated in PMDD and postnatal depression (brexanolone/zuranolone are analogues).
- Oral micronised progesterone has low bioavailability (first-pass) → vaginal, intramuscular or synthetic progestogens used clinically.

171.2 Receptors

Receptor	Notes
PR-B	Full-length; main transcriptional activator of progesterone actions
PR-A	Truncated; represses PR-B (and ER) — ↑ PR-A : PR-B ratio in myometrium at term = functional progesterone withdrawal (Lecture 147)
Membrane PRs (mPRs), PGRMC1	Rapid non-genomic effects (e.g. oocyte, sperm, myometrium)

Receptor	Notes
Induction	PR expression is induced by oestrogen — oestrogen priming is required for progesterone action

171.3 Actions

Target	Action of progesterone
Endometrium	Secretory transformation, decidualisation, implantation window; ↓ ER; anti-proliferative (protects against hyperplasia); withdrawal → menstruation
Cervix / tubes	Thick, scanty cervical mucus (sperm-hostile); altered tubal motility
Myometrium	Quiescence: ↓ oxytocin receptors, connexin-43, PG synthesis; hyperpolarisation
HPO axis	Slows GnRH pulse frequency; with oestrogen, negative feedback (contraception); small pre-ovulatory rise helps LH surge
Breast	Lobuloalveolar development; inhibits lactogenesis until withdrawal at birth
Smooth muscle	Relaxation: LOS (reflux), gut (constipation), ureters (hydroureter), veins (varicosities), gallbladder (stasis)
Respiratory	↑ Sensitivity of respiratory centre to CO_2 → hyperventilation of pregnancy (Lecture 131)
Metabolic / renal	Thermogenic (BBT ↑ 0.3–0.5 °C); natriuretic (aldosterone antagonism); insulin resistance (pregnancy)
Immune	Th2 shift, progesterone-induced blocking factor — maternal tolerance

171.4 Progestogens and antiprogestogens

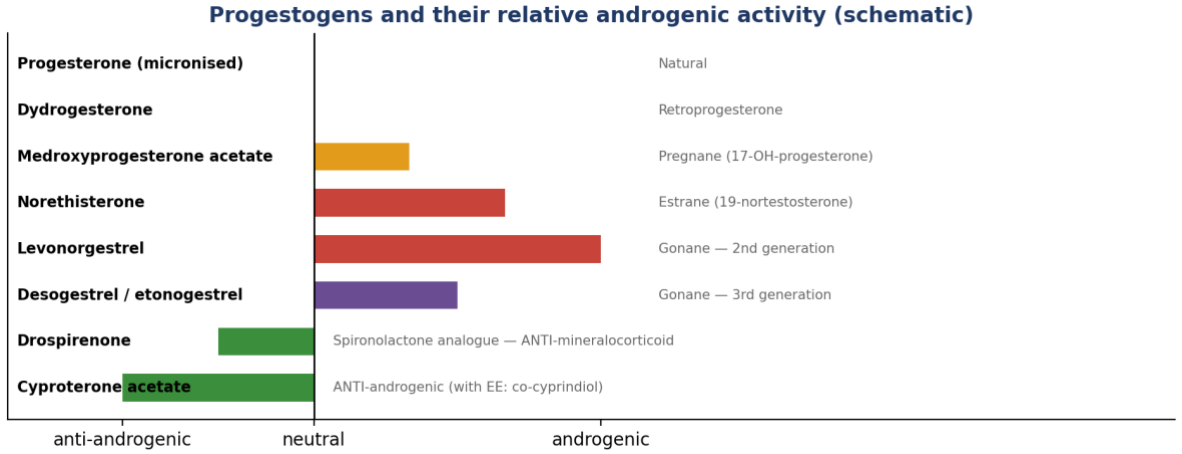


Figure 171.2 — Classes of progestogens and androgenicity

Progestogen feature	Clinical significance
Androgenic (levonorgestrel, norethisterone)	Acne, lipid effects; levonorgestrel CHCs have the lowest VTE risk
3rd-generation (desogestrel, gestodene)	Less androgenic; higher VTE risk in combination with EE (Lecture 149)
Drospirenone	Anti-mineralocorticoid (↓ fluid retention; monitor K^+) and anti-androgenic
Cyproterone acetate	Strongly anti-androgenic (acne, hirsutism) — co-cyprindiol ↑ VTE
Medroxyprogesterone acetate	DMPA contraception, HRT, HMB; glucocorticoid activity; bone density effects
Dydrogesterone / micronised progesterone	Closest to natural; used in pregnancy support and HRT (micronised — lower breast cancer and VTE signals than synthetic in observational data)

Antiprogestogen	Mechanism	Uses
Mifepristone	PR (and glucocorticoid receptor) antagonist	Medical abortion and miscarriage management (with misoprostol), IOL after fetal death, cervical priming

Antiprogestogen	Mechanism	Uses
Ulipristal acetate	Selective progesterone receptor modulator	Emergency contraception (delays ovulation, up to 120 h); fibroids (restricted — hepatotoxicity)

171.5 Clinical uses in obstetrics and gynaecology

Indication	Evidence / guidance
Threatened miscarriage with previous miscarriage	Vaginal micronised progesterone 400 mg twice daily until 16 weeks (PRISM trial; NICE NG126, 2021)
Preterm birth prevention	Vaginal progesterone for a short cervix (≤ 25 mm at 16–24 wk) or previous preterm birth (NICE NG25) — alternative to cerclage
IVF luteal phase support	Vaginal/IM progesterone (GnRH analogues and egg collection impair CL function)
Contraception	POP, implant, injectable, LNG-IUS (Lecture 149)
Endometrial protection in HRT	Any woman with a uterus on oestrogen
HMB / endometrial hyperplasia	LNG-IUS (first line), oral progestogens; hyperplasia without atypia — LNG-IUS (RCOG/BSGE)
Not effective	Recurrent miscarriage without bleeding (PROMISE), established preterm labour, twin preterm birth prevention (unclear)

171.6 Must-know summary

■ EXAM TIP

- Progesterone: CL (LH/hCG) → **placenta from 7–9 wk** (uses maternal cholesterol); mid-luteal > 30 nmol/L confirms ovulation.
- **PR-B activates, PR-A represses**; ↑ PR-A:PR-B at term = functional withdrawal; PR requires oestrogen priming.
- Actions: secretory endometrium, thick mucus, myometrial quiescence, smooth-muscle relaxation, ↑ ventilation, thermogenesis.
- Levonorgestrel CHC lowest VTE; drospirenone anti-mineralocorticoid; cyproterone anti-androgenic.
- Vaginal progesterone: **short cervix** and **threatened miscarriage with prior loss** (400 mg bd to 16 wk).

■ MNEMONIC / MEMORY AID

Progesterone in pregnancy — 'Pro-Gestation': keeps the uterus quiet, the cervix closed, the breasts preparing and the mother breathing deeper.