PIPADOR REVISION

MRCOG Part 1 Revision Notes

Oestrogen

ENDOCRINOLOGY • LECTURE 170

VISUAL EXAMINATION REVISION NOTES

2026 Edition

170

MRCOG PART 1 REVISION NOTES | ENDOCRINOLOGY

Oestrogen

Types and sources, transport and receptors, actions, pregnancy oestrogens, synthetic oestrogens and SERMs

E2	E1	E3	≈ 2%
Oestradiol — most potent (reproductive yrs)	Oestrone — main postmenopausal	Oestriol — main in pregnancy	Free E2 (38% SHBG, 60% albumin)

■ KEY FACTS: Learning objectives

- Describe the types, sources, synthesis, transport and metabolism of oestrogens.
- Describe oestrogen receptors and actions on reproductive and non-reproductive tissues.
- Describe oestrogen production in pregnancy (fetoplacental unit).
- Describe synthetic oestrogens, SERMs and aromatase inhibitors and the clinical consequences of oestrogen excess and deficiency.

170.1 Types, sources and synthesis

Oestrogen	Main source	Notes
Oestradiol (E2)	Granulosa cells of the dominant follicle; corpus luteum	Most potent; 17β-hydroxyl
Oestrone (E1)	Peripheral aromatisation of androstenedione (adipose, muscle, skin)	Main oestrogen after menopause; ↑ in obesity (endometrial cancer risk)
Oestriol (E3)	Placenta (from fetal 16-OH-DHEAS)	Weak; ≈ 90% of pregnancy oestrogen; unconjugated E3 (uE3) in quadruple test
Estetrol (E4)	Fetal liver	Used in a newer COC (estetrol + drospirenone)

Synthesis: cholesterol → (StAR, CYP11A1) pregnenolone → androgens (CYP17) → **aromatase (CYP19)** → oestrogens. In the ovary this uses the **two-cell, two-gonadotrophin** system (Lecture 143). Aromatase is also in adipose tissue, brain, bone, breast and placenta.

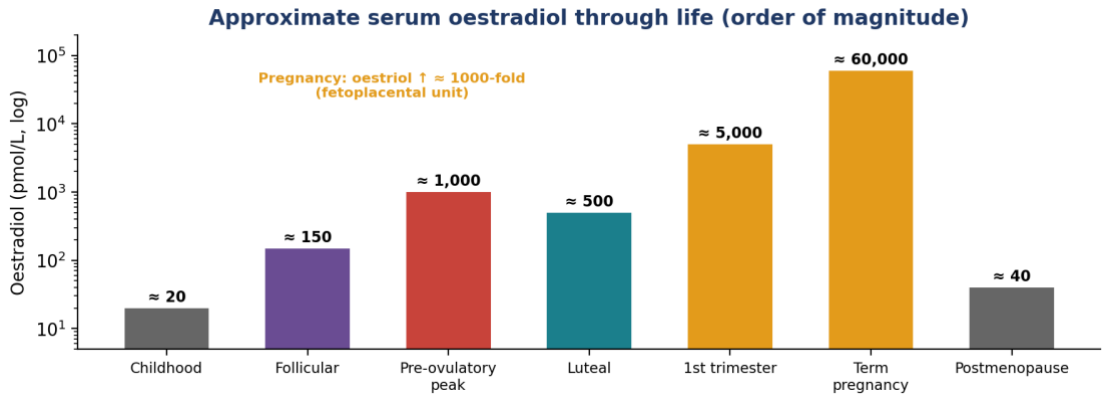


Figure 170.1 — Serum oestradiol through life

170.2 Transport, metabolism and receptors

- Bound to **SHBG** (≈ 38%) and **albumin** (≈ 60%); free ≈ 2%. Oestrogen **↑ SHBG** synthesis (and TBG, CBG, angiotensinogen, clotting factors).

- Hepatic metabolism (hydroxylation by CYP450, glucuronidation/sulphation) → bile → **enterohepatic recirculation** (gut bacteria deconjugate) → urine. **Enzyme inducers** (rifampicin, carbamazepine, St John's wort) ↓ levels → contraceptive failure.
- **Receptors**: nuclear **ERα** (uterus, breast, liver, hypothalamus) and **ERβ** (ovary, prostate, brain, vasculature) → oestrogen response elements; **GPER** membrane receptor (rapid effects). Oestrogen induces **ER and PR** expression; progesterone downregulates ER.

170.3 Actions

System	Actions of oestrogen
Reproductive tract	Endometrial proliferation; myometrial growth and oxytocin/gap-junction expression; thin, clear, stretchy cervical mucus; vaginal epithelial maturation, glycogen → lactobacilli → acidic pH
Ovary / HPO axis	Granulosa proliferation, ↑ FSH/LH receptors; negative feedback (most of cycle) and positive feedback → LH surge
Breast	Ductal growth (progesterone → lobuloalveolar); stromal and fat deposition
Bone	↓ Resorption (↑ OPG, ↓ RANKL); epiphyseal closure (both sexes)
Cardiovascular	Vasodilatation (↑ NO, PGI_2); ↑ HDL, ↓ LDL; ↑ triglycerides (oral)
Liver	↑ SHBG, TBG, CBG, angiotensinogen, clotting factors (II, VII, IX, X, fibrinogen), ↓ antithrombin/protein S → VTE; ↑ bile cholesterol saturation → gallstones, cholestasis
Skin / body	Female fat distribution (gluteofemoral), skin thickness and collagen, ↓ sebum; spider naevi and palmar erythema (pregnancy, liver disease)
Brain	Mood, cognition, thermoregulation (KNDy), sexual behaviour

170.4 Oestrogens in pregnancy

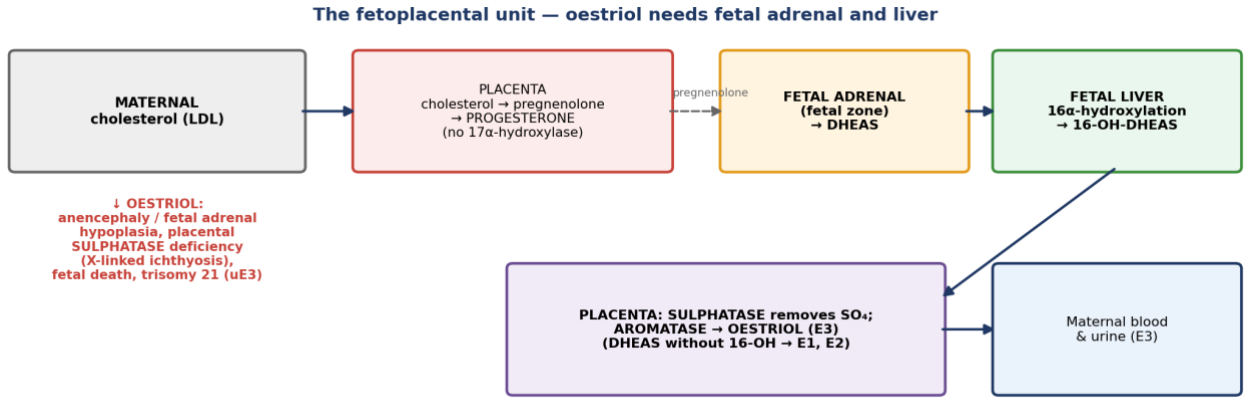


Figure 170.2 — The fetoplacental unit

Pregnancy oestrogens ↑ uteroplacental blood flow, myometrial growth, breast development, prolactin secretion (lactotroph hyperplasia), hepatic protein synthesis (TBG, SHBG, fibrinogen) and, near term, **contraction-associated proteins** (Lecture 147). Low maternal oestriol occurs with **fetal adrenal hypoplasia, anencephaly, placental sulphatase deficiency** (delayed labour; X-linked ichthyosis in boys) and **trisomy 21**.

170.5 Synthetic oestrogens and modulators

Agent	Mechanism	Use / effects
Ethinylestradiol (EE)	17α-ethinyl group resists hepatic metabolism → orally potent, strong hepatic effects	COCs — ↑ SHBG, clotting factors, angiotensinogen (BP), VTE
Estradiol valerate / 17β-estradiol / CEE	Natural/conjugated	HRT; some newer COCs

Agent	Mechanism	Use / effects
Tamoxifen	SERM — antagonist in breast, agonist in endometrium and bone	ER+ breast cancer; endometrial hyperplasia/polyps/carcinoma, VTE, hot flushes; teratogenic (stop 2 months before conception)
Raloxifene	SERM — agonist bone, antagonist breast, neutral endometrium	Osteoporosis; ↓ breast cancer; VTE, flushes
Clomifene	SERM — antagonist at hypothalamus	Ovulation induction (↑ GnRH → FSH); anti-oestrogenic mucus/endometrium; multiple pregnancy ≈ 8–10%
Letrozole / anastrozole	Aromatase inhibitors	Breast cancer (postmenopausal); letrozole first-line ovulation induction in PCOS; bone loss
Fulvestrant	Selective ER degrader	Advanced breast cancer

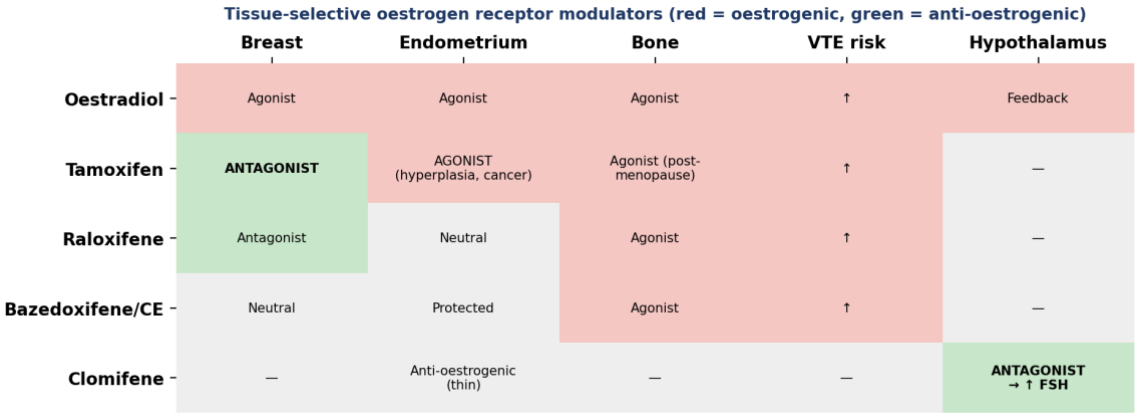


Figure 170.3 — Tissue-selective actions of SERMs

170.6 Oestrogen excess and deficiency

Oestrogen excess (unopposed)	Oestrogen deficiency
Endometrial hyperplasia and endometrioid carcinoma (obesity, PCOS, anovulation, tamoxifen, oestrogen-only HRT with uterus, granulosa cell tumours)	Menopause, POI, hypothalamic amenorrhoea, GnRH analogues, lactation
Breast cancer risk (lifetime exposure: early menarche, late menopause, nulliparity)	Vasomotor symptoms, GSM, osteoporosis, ↑ CVD risk
VTE, hypertension, gallstones (exogenous)	Atrophic endometrium/vagina; ↑ FSH (if ovarian)
Precocious puberty (girls), gynaecomastia (men)	Delayed puberty; tall stature (aromatase deficiency)

170.7 Must-know summary

■ **EXAM TIP**

- E2 (ovary) is most potent; E1 dominates after menopause (adipose); **E3 dominates pregnancy** (needs fetal adrenal DHEAS + fetal liver + placental sulphatase/aromatase).
- Oestrogen ↑ SHBG, TBG, CBG, angiotensinogen and clotting factors (hepatic first-pass — strongest with oral EE).
- **ERα/ERβ** nuclear receptors; oestrogen induces PR.
- Tamoxifen: breast antagonist, **endometrial agonist**; clomifene: hypothalamic antagonist; letrozole: aromatase inhibitor.
- Unopposed oestrogen → endometrial hyperplasia/cancer.

■ **MNEMONIC / MEMORY AID**

Oestrogens by life stage — 'E1 Elders, E2 Everyday, E3 Expecting'.