PIPADOR REVISION

MRCOG Part 1 Revision Notes

Eicosanoids: Structure and Synthesis

BIOCHEMISTRY • LECTURE 233

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG PART 1 REVISION NOTES | BIOCHEMISTRY

233 Eicosanoids: Structure and Synthesis

Arachidonic acid cascade, COX/LOX pathways, actions of prostaglandins, prostacyclin, thromboxane and leukotrienes, and O&G pharmacology

C20	PLA_2	COX-1 / COX-2	Seconds
Eicosa- = 20 carbons (arachidonic acid)	Rate-limiting release	Constitutive / inducible	Local, rapidly inactivated (lungs)

■ KEY FACTS: Learning objectives

- Describe the structure of eicosanoids and their synthesis via COX, LOX and cytochrome P450 pathways.
- Describe the actions of prostaglandins, thromboxane, prostacyclin and leukotrienes in reproduction.
- Describe the pharmacology of drugs targeting eicosanoids in O&G.

233.1 Structure and synthesis

Eicosanoids are **C20 oxygenated fatty acid derivatives**, mainly from **arachidonic acid** (C20:4 n-6; from dietary linoleic acid). Prostanoids contain a **cyclopentane ring** (prostaglandins) or an oxane ring (thromboxane); series number = number of double bonds (PGE_2, $PGF_{2\alpha}$ from arachidonic acid; series-3 from EPA — less pro-thrombotic). They are **autocrine/paracrine**, act via **GPCRs** (EP1–4, FP, IP, TP, DP), and are **rapidly inactivated** (15-PGDH; lungs clear ≈ 90% in one pass).

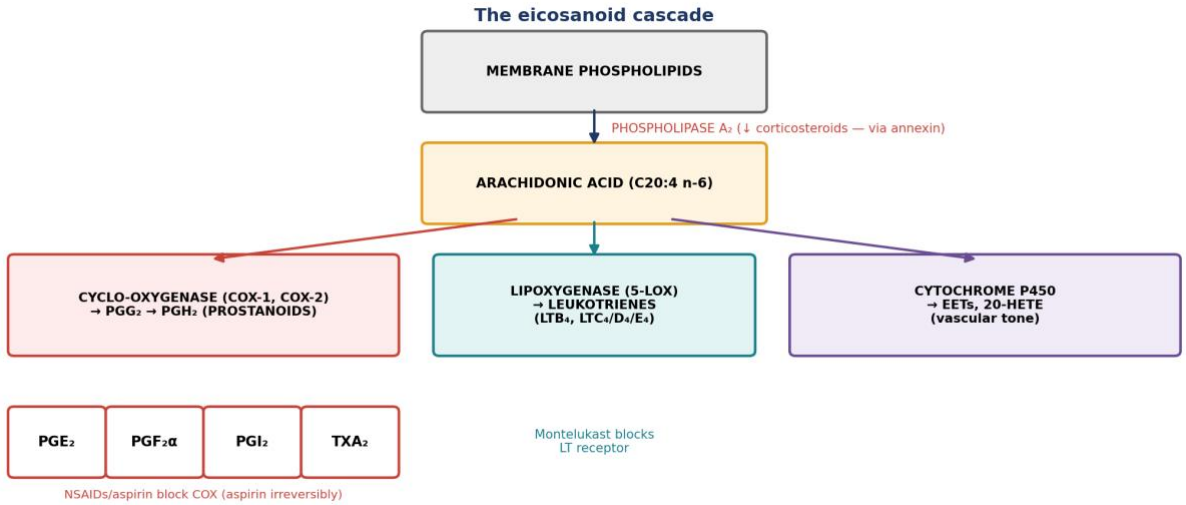


Figure 233.1 — The eicosanoid cascade

Enzyme	Features
Phospholipase A_2	Releases arachidonic acid from membrane phospholipids — rate-limiting; ↑ by Ca^{2+}, cytokines, stretch; ↓ by glucocorticoids (annexin-1)
COX-1	Constitutive — gastric mucosa, platelets (TXA_2), kidney, vessels
COX-2	Inducible (inflammation, labour) — amnion/decidua at term; also constitutive in kidney, fetal ductus
Terminal synthases	Tissue-specific: PGE synthase (amnion), PGF synthase (decidua), prostacyclin synthase (endothelium), thromboxane synthase (platelets)

233.2 Actions in reproduction

Eicosanoid	Receptor	Actions	Drug / clinical
PGE_2	EP1–4	Cervical ripening (EP2/4), myometrial contraction (EP1/3) or relaxation (EP2/4), fever, ductus arteriosus patency, gastric protection	Dinoprostone (IOL); misoprostol (PGE_1 analogue); alprostadil (PGE_1 — duct-dependent CHD)
$PGF_2\alpha$	FP (Gq)	Myometrial contraction, luteolysis, menstrual vasoconstriction, bronchoconstriction	Carboprost (PPH — avoid in asthma); ↑ in dysmenorrhoea
PGI_2 (prostacyclin)	IP (Gs)	Vasodilatation, inhibits platelet aggregation, ↑ in normal pregnancy (endothelium)	Epoprostenol (pulmonary hypertension)
TXA_2	TP (Gq)	Vasoconstriction, platelet aggregation	Low-dose aspirin irreversibly blocks platelet COX-1 → ↓ TXA_2 (platelets can't make new COX) while endothelial PGI_2 recovers
Leukotrienes	CysLT1, BLT	Bronchoconstriction (LTC_4/D_4), neutrophil chemotaxis (LTB_4), ↑ permeability	Montelukast (asthma — continue in pregnancy)

233.3 Clinical applications

Situation	Eicosanoid physiology / pharmacology
Pre-eclampsia	PGI_2 : TXA_2 imbalance (↓ PGI_2, ↑ TXA_2) → vasoconstriction, platelet activation → aspirin 75–150 mg from 12 wk for high-risk women (NICE NG133)
Labour	↑ COX-2, ↓ chorionic PGDH at term → $PGE_2/PGF_2\alpha$ ↑ (Lecture 185); amniotomy and membrane sweep release PGs
Dysmenorrhoea / HMB	↑ Endometrial $PGF_2\alpha$ and PGE_2 → NSAIDs (mefenamic acid) ↓ pain and loss
Preterm labour tocolysis	Indomethacin (COX inhibitor) — ductus arteriosus constriction, oligohydramnios, NEC; avoid > 30–32 weeks
NSAIDs in pregnancy	Avoid in 3rd trimester (ductus, renal); early-pregnancy use linked to miscarriage in some studies
Patent ductus arteriosus	Kept open by PGE_2 — closed with ibuprofen/indomethacin/paracetamol; PGE_1 (alprostadil) keeps it open in duct-dependent lesions
Gastric protection	COX-1 PGs maintain mucus/bicarbonate — misoprostol used with NSAIDs

233.4 Must-know summary

■ **EXAM TIP**

- Arachidonic acid (C20) from membrane phospholipids via **PLA_2** (blocked by steroids) → **COX** (prostanoids), **LOX** (leukotrienes), **CYP450** (EETs).
- PGE_2 ripens cervix and keeps ductus open; **$PGF_2\alpha$** contracts uterus, luteolysis; PGI_2 vasodilates/anti-platelet; TXA_2 constricts/aggregates.
- Low-dose aspirin ↓ TXA_2 (pre-eclampsia prevention); NSAIDs/indomethacin constrict ductus; carboprost avoided in asthma.

■ **MNEMONIC / MEMORY AID**

'E for Effacement (PGE_2), F for Force ($PGF_2\alpha$), I for Inhibits platelets (PGI_2), T for Thrombosis (TXA_2)'.