PIPADOR REVISION

MRCOG Part 1 Revision Notes

Nitric Oxide

BIOCHEMISTRY • LECTURE 234

VISUAL EXAMINATION REVISION NOTES

2026 Edition

234

MRCOG PART 1 REVISION NOTES | BIOCHEMISTRY

Nitric Oxide

Synthesis by NOS isoforms, cGMP signalling, roles in pregnancy, pre-eclampsia and the neonate, and NO-related drugs

L-arginine	3 NOS	cGMP	Seconds
Substrate (→ citrulline)	eNOS, nNOS, iNOS	Second messenger (soluble GC)	NO half-life

■ KEY FACTS: Learning objectives

- Describe the synthesis of nitric oxide by the NOS isoforms and its regulation.
- Describe the mechanism of action of NO (sGC–cGMP–PKG) and its termination.
- Describe the roles of NO in the cardiovascular system, pregnancy, reproduction and the neonate, and related drugs.

234.1 Synthesis and signalling

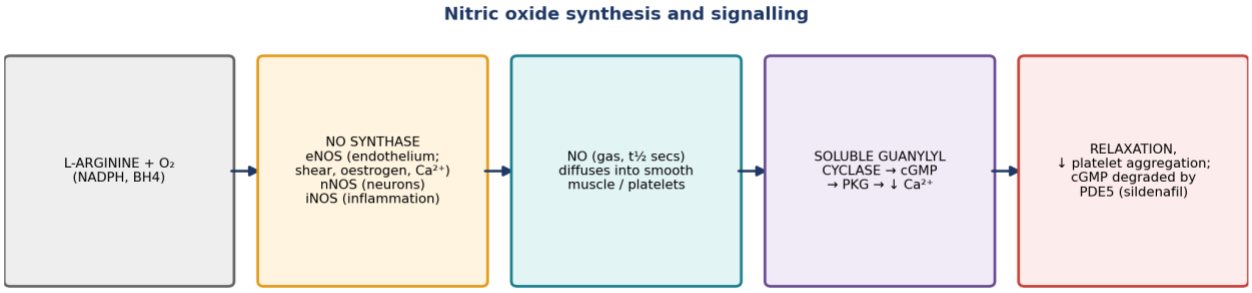


Figure 234.1 — Nitric oxide synthesis and signalling

Isoform	Location	Regulation	Role
eNOS (NOS3)	Endothelium, syncytiotrophoblast	Ca^{2+}/calmodulin; shear stress, ACh, bradykinin, oestrogen, VEGF (Akt phosphorylation)	Vasodilatation, anti-platelet; pregnancy vasodilatation
nNOS (NOS1)	Neurons, skeletal muscle	Ca^{2+}/calmodulin	Neurotransmission (NANC nerves — penile erection, gut relaxation)
iNOS (NOS2)	Macrophages, myometrium	Inducible by cytokines, endotoxin (Ca^{2+}-independent; large amounts)	Host defence; septic shock vasodilatation

- NO is a **free-radical gas** that diffuses across membranes (no receptor needed) → binds the haem of **soluble guanylyl cyclase** → **cGMP** → **protein kinase G** → ↓ intracellular Ca^{2+} and myosin light-chain dephosphorylation → **smooth-muscle relaxation**.
- Terminated by reaction with **haemoglobin** (→ methaemoglobin/nitrate), superoxide (→ **peroxynitrite** — oxidative stress) and **PDE5** breakdown of cGMP.
- **ADMA** (asymmetric dimethylarginine) is an endogenous NOS inhibitor — ↑ in **pre-eclampsia**, renal failure.

234.2 Roles in pregnancy and reproduction

Context	Role of NO
Maternal vasodilatation	↑ eNOS (oestrogen, shear, relaxin) → ↓ SVR, ↑ renal blood flow, refractoriness to angiotensin II (Lectures 126, 178)
Uteroplacental circulation	Spiral artery remodelling; fetoplacental vessels (no autonomic innervation) rely on local NO
Pre-eclampsia	↓ NO bioavailability (↑ ADMA, oxidative stress, sFlt-1 ↓ VEGF-driven eNOS) → vasoconstriction, endothelial dysfunction
Myometrium	NO–cGMP promotes quiescence during pregnancy; NO donors studied as tocolytics (GTN — limited use)
Cervix	NO contributes to cervical ripening (with PGs); NO donors (isosorbide mononitrate) studied for ripening
Neonate	At birth ↑ O_2 and ventilation ↑ pulmonary NO → ↓ PVR; inhaled NO treats PPHN
Male	nNOS/eNOS → cGMP → erection (sildenafil inhibits PDE5)
Ovary / embryo	Ovulation, implantation, trophoblast invasion (NO and VEGF)

234.3 Drugs acting on the NO pathway

Drug	Mechanism	O&G use
Glyceryl trinitrate (GTN)	NO donor	Uterine relaxation for retained placenta/inversion, head entrapment at CS/breech; acute severe hypertension; angina
Inhaled NO	Selective pulmonary vasodilator	PPHN; maternal pulmonary hypertension in critical care
Sildenafil	PDE5 inhibitor (↑ cGMP)	Erectile dysfunction, pulmonary hypertension; STRIDER trial in severe FGR — no benefit and possible neonatal pulmonary hypertension harm — not recommended
Sodium nitroprusside	NO donor	Hypertensive emergency (cyanide toxicity — fetal concern)
Methylene blue	Inhibits sGC/NOS	Refractory vasoplegic shock; methaemoglobinaemia

234.4 Must-know summary

■ EXAM TIP

- L-arginine → NO + citrulline (NOS; NADPH, BH4); eNOS & nNOS Ca^{2+}-dependent, **iNOS inducible** (sepsis).
- NO → **soluble guanylyl cyclase → cGMP → PKG** → relaxation; PDE5 degrades cGMP (sildenafil).
- Pregnancy: oestrogen/relaxin ↑ eNOS → ↓ SVR; **pre-eclampsia ↓ NO** (↑ ADMA).
- Inhaled NO for PPHN; GTN for uterine relaxation; sildenafil not used for FGR (STRIDER).

■ MNEMONIC / MEMORY AID

'NO → GC → cGMP → PKG → relax'.