PIPADOR REVISION

MRCOG Part 1 Revision Notes

Drugs that Cross the Placenta

PHARMACOLOGY • LECTURE 368

VISUAL EXAMINATION REVISION NOTES

2026 Edition

368

MRCOG PART 1 REVISION NOTES | PHARMACOLOGY

Drugs that Cross the Placenta

Mechanisms and determinants of placental transfer, examples and intentional fetal therapy

< 500 Da	> 1000 Da	Ion trapping	FcRn
Cross readily	Heparin, insulin — do not cross	Weak bases in acidotic fetus	IgG biologics in 3rd trimester

■ KEY FACTS: Learning objectives

- Describe mechanisms and determinants of placental drug transfer.
- Give examples of drugs that do and do not cross the placenta and their fetal effects.
- Describe intentional fetal therapy via maternal administration.

368.1 Mechanisms and determinants

- Mechanisms: **passive diffusion** (most drugs), facilitated diffusion, **active transport** (efflux by P-glycoprotein/BCRP protects the fetus; FcRn transports IgG), pinocytosis.
- Fetal exposure also depends on placental blood flow, gestation (membrane thins, ↑ surface area in late pregnancy) and **placental metabolism**.

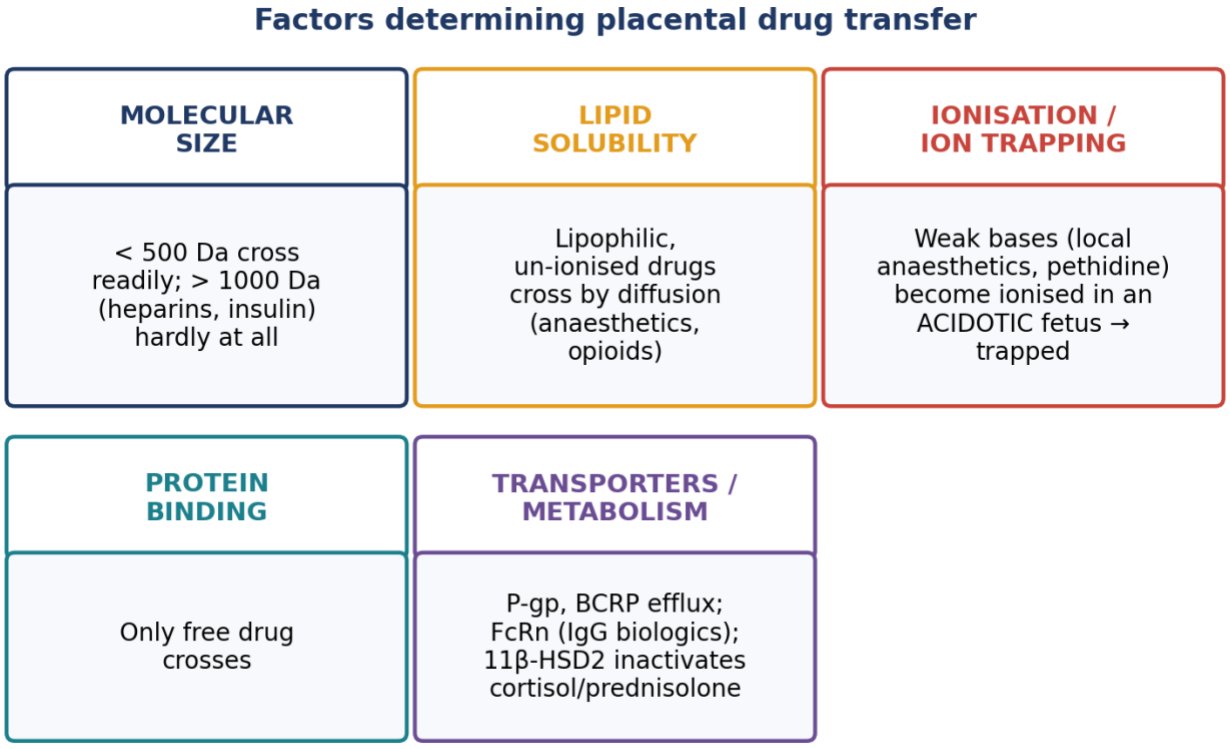


Figure 368.1 — Determinants of placental transfer

368.2 Examples

Placental transfer — key examples

Heparin / LMWH	SAFE	Do NOT cross (large, charged) — anticoagulant of choice
Insulin	SAFE	Does not cross (fetal hyperinsulinism is from glucose)
Warfarin	AVOID	Crosses — embryopathy, fetal bleeding
Betamethasone / dexamethasone	CAUTION	Cross (resist 11β-HSD2) — fetal lung maturation
Prednisolone	SAFE	Largely inactivated by placenta (≈ 10% reaches fetus)
IgG monoclonals (anti-TNF)	CAUTION	Actively transported (FcRn) in 3rd trimester
Opioids, benzodiazepines	CAUTION	Cross — neonatal respiratory depression, withdrawal
$MgSO_4$	CAUTION	Crosses — neuroprotection; neonatal hypotonia
Labetalol / β-blockers	CAUTION	Cross — neonatal bradycardia, hypoglycaemia

Figure 368.2 — Key examples

- **Ion trapping**: local anaesthetics (bupivacaine) and pethidine are weak bases — in a hypoxic, acidotic fetus more becomes ionised and trapped, increasing fetal levels.
- **Opioids** (pethidine metabolite norpethidine, morphine) → neonatal respiratory depression
  - **Benzodiazepines** → floppy infant
  - Chronic opioids → **neonatal abstinence syndrome**.
- **Antithyroid drugs** (PTU, carbimazole) cross → fetal hypothyroidism/goitre if over-treated; maternal TRAb also crosses.
- **Labetalol/β-blockers** → neonatal hypoglycaemia, bradycardia (monitor glucose).

368.3 Intentional fetal therapy

Indication	Maternal drug
Fetal lung maturity	Betamethasone/dexamethasone
Neuroprotection (< 30–32 wk)	Magnesium sulphate
Fetal SVT	Digoxin, flecainide, sotalol
Fetal hyperthyroidism (TRAb)	Carbimazole/PTU
Congenital heart block risk (anti-Ro)	Hydroxychloroquine (prevention)
CMV (early primary infection)	Valaciclovir
HIV	ART (and neonatal PEP)

Indication	Maternal drug
FNAIT	IVIG ± prednisolone

368.4 Must-know summary

■ **EXAM TIP**

- Most drugs cross by passive diffusion: small, lipophilic, un-ionised, free drug.
- Heparin and insulin don't cross; warfarin does.
- Betamethasone/dexamethasone cross (resist 11β-HSD2); prednisolone mostly inactivated.
- Ion trapping of local anaesthetics/pethidine in acidotic fetus; IgG via FcRn.

■ **MNEMONIC / MEMORY AID**

'Small, Slippery (lipid), Uncharged, Unbound' cross the placenta.