**Pharm-00A12 Outline the pharmacology of oxytocin.**

**Background**

Oxytocin is an endogenous nonapeptide hormone synthesised by the hypothalamus and stored and secreted from the posterior pituitary.

Main physiological roles are:
1. Mammary gland contraction → milk let down
2. Uterine contraction esp. during labour
3. Modulate mood

Syntocinon is synthetic oxytocin and is commonly used clinically for:
1. Induction of labour + acceleration of labour
2. Treat/prevent postpartum haemorrhage as a result of uterine atony
3. Facilitate lactation

**Physicochemical**

**Class**
oxytocin – agent that ↑uterine tone

**Presentation**
syntocinon vials containing clear colourless solution at 5 ~ 10 IU/mL
syntometrine suppositories containing 10 IU oxytocin and 500 microg ergotamine

**Dose**
Managed third stage of labour → 10 units IM or 5 ~ 10 units slow IV
Induction of labour → 2 ~ 30 mIU/min IV infusion, slow up-titration

**Pharmacokinetics**

**Absorption**
IV, IM, intranasal, intrauterine
Poor oral availability due to rapid inactivation
Avoid giving together with blood/plasma product → degradation by oxytocinase

**Distribution**
Vdss ≈ 0.2 L/kg
Minimal plasma protein binding

**Metabolism**
Rapid plasma hydrolysis via oxytocinase (up-regulated during pregnancy)

Minimal oxytocinase is found in men, non-pregnant women and cord blood

**Elimination**
t1/2 = 1 ~ 7 min
Pharmacodynamics

Mechanism of action
Pregnancy → oestrogen → ↑ oxytocin receptors → sensitises uterus to oxytocin
Oxytocin binds oxytocin receptors → GPCR (Gq) → ↑ PLC → ↑ IP$_3$/DAG →
↑ intracellular calcium → ↑ smooth muscle contraction

Low dose oxytocin = ↑ force + ↑ frequency of contraction; complete relaxation in between contractions
High dose oxytocin = sustained contraction with incomplete relaxation → may impair uterine/placental blood flow

Time to onset ≈ 1 min (IV) or 2 ~ 4 min (IM)
Duration of effect ≈ 30 ~ 60 min (IM), less for IV

CVS effects
Vasodilatation → ↓ MAP, ↑ HR
↓ Coronary artery perfusion → may precipitate myocardial ischaemia

RENAL effects
ADH-like effect (agonist at V$_2$ receptors) → water retention → may precipitate fluid overload and hyponatraemia

ENDO effects
Mammary gland myoepithelial cell contraction → lactation

FETAL effects
High doses → uterine spasm + incomplete relaxation → may precipitate fetal hypoxia/asphyxia and fetal distress