PIPADOR REVISION

MRCOG Part 1 Revision Notes

Fertilisation

EMBRYOLOGY • LECTURE 43

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 43: Fertilisation

Embryology • Visual revision edition

COLOUR CODE USED THROUGHOUT THESE NOTES

OOCYTE	SPERM	CALCIUM / ACTIVATION	IVF / ICSI	ABNORMAL

LEARNING OBJECTIVES — tick off as you go

- ☐ Describe where and when fertilisation happens, and what the gametes bring.
- ☐ Explain capacitation, zona binding and the acrosome reaction.
- ☐ Describe gamete fusion (IZUMO1–JUNO) and the blocks to polyspermy.
- ☐ Explain oocyte activation by PLCζ and completion of meiosis II.
- ☐ Describe pronuclear formation, syngamy and the first cleavage.
- ☐ Apply to IVF/ICSI, pronuclear assessment, molar pregnancy and triploidy.

1 Where, When and What It Achieves

IN ONE LINE: *Sperm and secondary oocyte fuse in the AMPULLA within ~24 h of ovulation — restoring 46 chromosomes, fixing genetic sex, and starting development.*

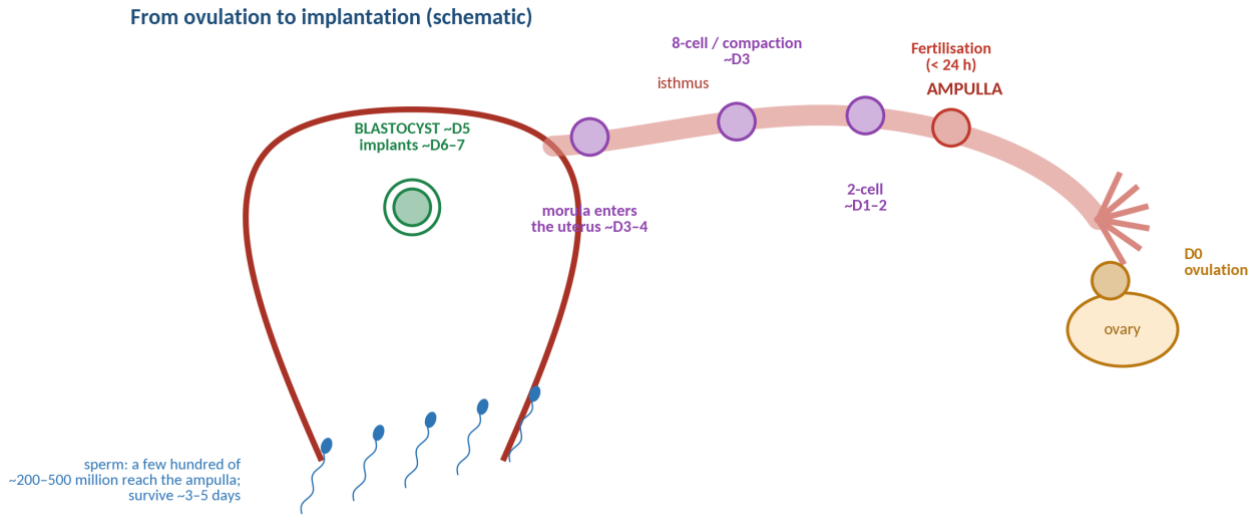


Figure 1. From ovulation to implantation.

THE OOCYTE AT OVULATION

- **Secondary oocyte, arrested at metaphase II** (Lecture 41)
- Zona pellucida + **cumulus** in hyaluronic acid; first polar body in the perivitelline space
- Picked up by the fimbriae; carried to the ampulla by cilia + peristalsis
- Viable for **~12–24 h**

THE SPERM

- ~200–500 million deposited; cervical mucus selects; **a few hundred** reach the ampulla
- Survive **~3–5 days** in the female tract
- **Capacitation (~7 h)**: cholesterol removed, Ca^{2+} + HCO_3^- in → soluble adenylyl cyclase → cAMP/PKA → tyrosine phosphorylation → **hyperactivated motility**

2 The Steps of Fertilisation

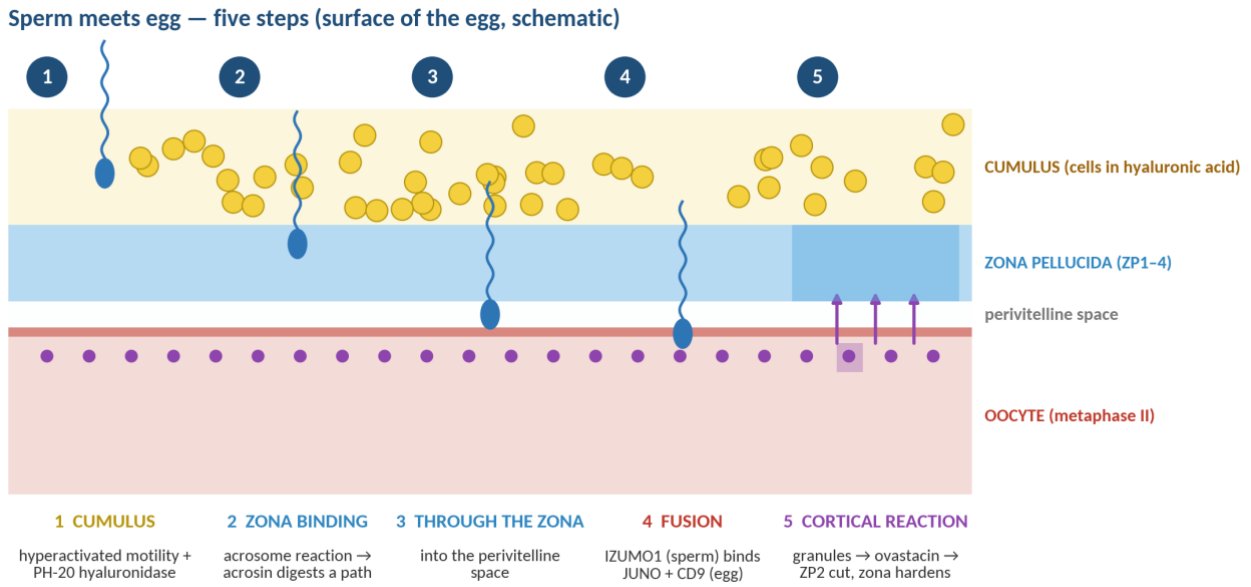


Figure 2. From cumulus to cortical reaction.

Step	What happens
1. Cumulus / corona	Hyperactivated motility + PH-20 (SPAM1) hyaluronidase
2. Zona binding	Zona of ZP1–4. Classic (mouse) model: ZP3 binds sperm and triggers the acrosome reaction; human data point to the ZP2 N-terminus as the key binding site
3. Acrosome reaction	Outer acrosomal membrane fuses with the sperm membrane → acrosin, hyaluronidase released → path through the zona
4. Fusion	Equatorial segment meets the oolemma: IZUMO1 (sperm) binds JUNO (folate receptor 4, egg); CD9 needed
5. Activation	Sperm PLCζ → IP3 → Ca^{2+} oscillations (next section)

MNEMONIC / MEMORY HOOK

'JUNO marries IZUMO' — JUNO is the goddess of marriage (on the egg); IZUMO is a Japanese marriage shrine (on the sperm). Discovered in 2005 (IZUMO1) and 2014 (JUNO).

3 Oocyte Activation and Blocks to Polyspermy

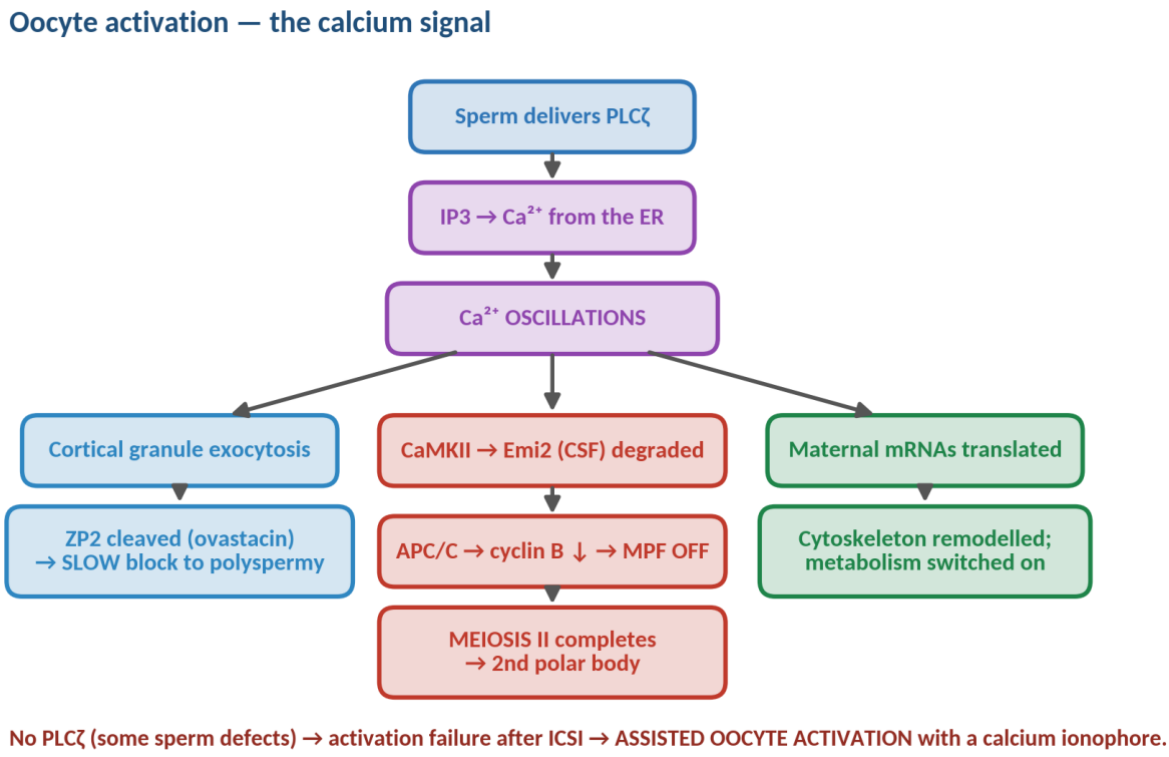


Figure 3. The calcium signal and what it switches on.

Block	Mechanism
Fast (electrical)	Membrane depolarisation — important in sea urchins; little or no role in mammals
Slow — zona reaction	Cortical granules release ovastacin, which cleaves ZP2 → zona hardens and stops binding more sperm
Membrane block	JUNO shed from the oolemma within ~40 min of fusion

4 Pronuclei, Syngamy and First Cleavage

- Meiosis II completes (~3 h) → **second polar body** + the maternal chromosome set (23, 1c).
- Sperm nucleus decondenses; **protamines → maternal histones**; each set gets a nuclear envelope → **male and female pronuclei**, which replicate their DNA.
- **Pronuclei do NOT fuse** in mammals: their envelopes break down and chromosomes gather on **one spindle** (syngamy) → **2-cell embryo at ~24–30 h**; diploidy restored; sex set by the sperm's X or Y.

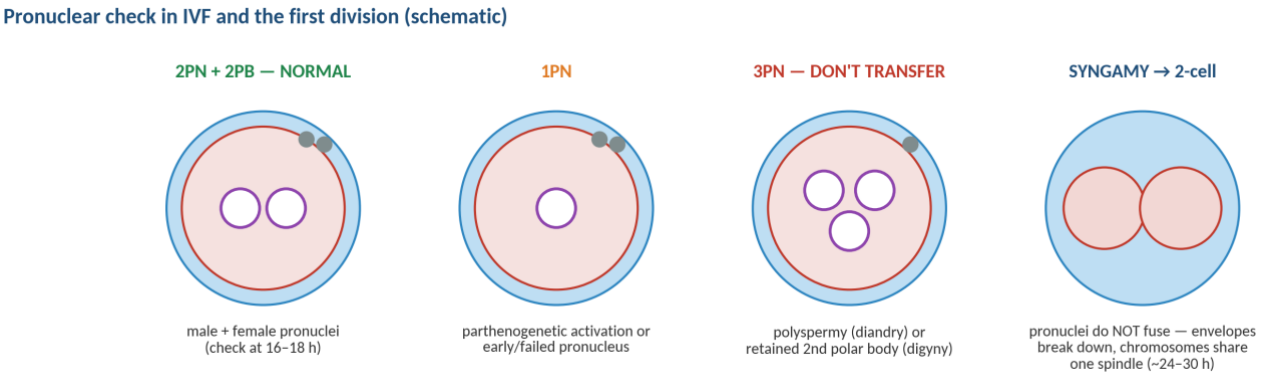


Figure 4. Pronuclear assessment in IVF.

Event	Approximate timing
Capacitation	~7 h
Zona penetration, fusion, cortical reaction	Minutes
Meiosis II complete, 2nd polar body	~3 h
Pronuclei visible	~6–8 h (IVF check at 16–18 h)
First cleavage	~24–30 h
Compaction (8-cell)	Day 3–4
Blastocyst	Day 5

5 IVF, ICSI and Activation Failure

CONVENTIONAL IVF

- Each oocyte with ~50 000–100 000 motile sperm
- ~60–70% fertilise
- **Check at 16–18 h**: **2PN + 2PB = normal**; 1PN uncertain; **3PN — don't transfer**

ICSI

- One sperm injected into the cytoplasm
- For severe male factor, previous fertilisation failure, surgically retrieved sperm, some PGT
- Bypasses natural selection; small ↑ imprinting disorders / anomalies reported
- **Activation failure** (often PLCζ-related) → **calcium ionophore** (assisted oocyte activation)

6 When Fertilisation Goes Wrong

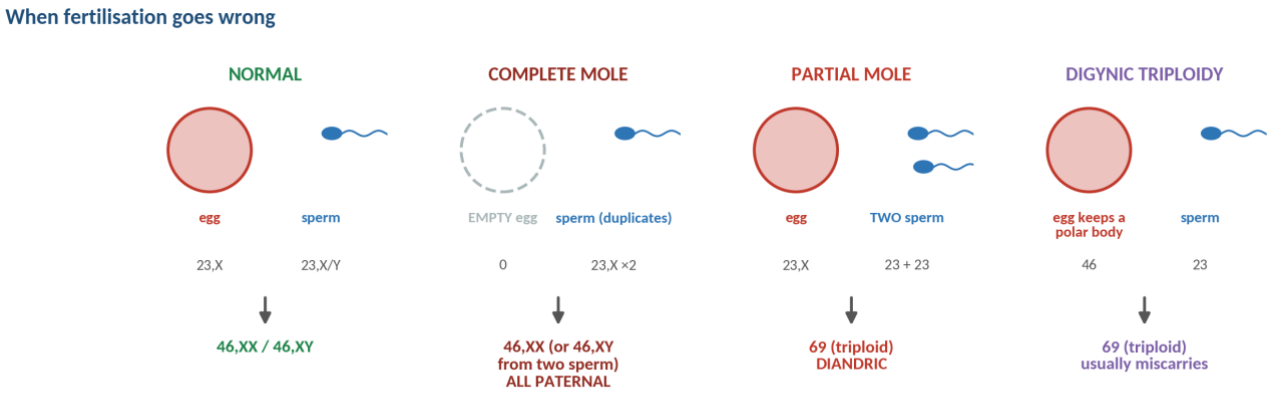


Figure 5. Moles and triploidy by origin.

Condition	Origin
Complete mole	Empty egg + one sperm that duplicates (46,XX) or two sperm (46,XX/XY) — all paternal; no fetus; highest GTN risk
Partial mole	Egg + two sperm (diandric triploidy, 69,XXY / XXX / XYY) — some fetal tissue
Digynic triploidy	Egg retains a polar body + one sperm — usually a small, growth-restricted fetus; miscarriage
Parthenogenesis	Egg activated without sperm — non-viable in humans
Ectopic pregnancy	Implantation outside the cavity — ampulla most often; tubal damage (PID, surgery), previous ectopic, smoking, IVF, conception with an IUD in place
Anti-sperm antibodies	Impair motility / zona binding — after vasectomy reversal, testicular injury

★ **PEARL**

Complete mole = no maternal genome (androgenetic diploid). Partial mole = one maternal + two paternal sets (triploid).

In IVF, **3PN** zygotes are not transferred; **2PN + 2PB** at 16–18 h confirms normal fertilisation.

7 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

< 24 h After ovulation	**12–24 h** Oocyte viability	**3–5 days** Sperm survival	**~7 h** Capacitation
16–18 h IVF pronuclear check	**24–30 h** First cleavage	**Day 5** Blastocyst	**69** Triploidy

HIGH-YIELD CHECKLIST

- ☐ Ampulla, within ~24 h of ovulation; secondary oocyte at metaphase II.
- ☐ Capacitation (~7 h) in the female tract → hyperactivation.
- ☐ PH-20 hyaluronidase through the cumulus; zona binding → acrosome reaction (acrosin).
- ☐ IZUMO1 (sperm) – JUNO (egg) + CD9 → fusion.
- ☐ PLCζ → IP3 → Ca^{2+} oscillations → activation, meiosis II completes.
- ☐ Slow block: cortical granules, ovastacin cleaves ZP2; JUNO shed.
- ☐ Pronuclei don't fuse — common spindle; 2-cell at 24–30 h.
- ☐ 2PN + 2PB normal; 3PN not transferred.
- ☐ Complete mole androgenetic diploid; partial mole diandric triploid.
- ☐ Activation failure after ICSI → calcium ionophore.

Self-assessment — cover the right-hand column

Question	Answer
Main molecular events of capacitation?	Cholesterol loss, Ca^{2+}/HCO_3^- in, cAMP/PKA, tyrosine phosphorylation, hyperactivation
What triggers the acrosome reaction?	Binding to the zona pellucida (classically ZP3)
Sperm and egg fusion proteins?	IZUMO1 (sperm) and JUNO (egg), with CD9
How is polyspermy prevented?	Cortical reaction (ovastacin cleaves ZP2) + JUNO shedding
How does sperm activate the egg?	PLCζ → IP3 → Ca^{2+} oscillations
Do the pronuclei fuse?	No — they share one spindle at the first division
Normal IVF fertilisation at 16–18 h?	2PN + 2PB
Genetic origin of a complete mole?	Paternal only — empty egg + 1 or 2 sperm (46)
Genetic origin of a partial mole?	Egg + two sperm — triploid (69)
Treatment for oocyte activation failure after ICSI?	Assisted oocyte activation — calcium ionophore

8 References

- Sadler TW. Langman's Medical Embryology. 14th ed. 2019.
- Bianchi E et al. Juno is the egg Izumo receptor and is essential for mammalian fertilization. Nature 2014.
- RCOG Green-top Guideline No. 38. Management of Gestational Trophoblastic Disease. 2020.