PIPADOR REVISION

MRCOG Part 1 Revision Notes

Oogenesis

EMBRYOLOGY • LECTURE 41

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 41: Oogenesis

Embryology • Visual revision edition

COLOUR CODE USED THROUGHOUT THESE NOTES

OOCYTE / MEIOSIS	FOLLICLE / GRANULOSA	MOLECULAR CONTROL	THECA / HORMONES	CLINICAL

LEARNING OBJECTIVES — tick off as you go

- ☐ Trace primordial germ cells from the epiblast to the gonadal ridge.
- ☐ Give the timeline and numbers of oogenesis from fetal life to menopause.
- ☐ State the chromosome number and DNA content at each stage, and where meiosis arrests.
- ☐ Explain the molecular basis of meiotic arrest and its release by the LH surge.
- ☐ Link oogenesis to folliculogenesis and the two-cell, two-gonadotrophin theory.
- ☐ Apply to maternal-age aneuploidy, ovarian reserve, POI, Turner syndrome and ART.

1 Key Definitions

IN ONE LINE: *Oogenesis starts before birth, stops for decades, and only finishes if the egg is fertilised — slow, discontinuous and wasteful compared with spermatogenesis.*

Cell	Definition
Primordial germ cell (PGC)	Embryonic precursor of all gametes
Oogonium	Diploid cell dividing by mitosis in the fetal ovary
Primary oocyte	Diploid; arrested in prophase I (diplotene/dictyate) from fetal life
Secondary oocyte	Haploid; arrested in metaphase II until fertilisation — the cell that is ovulated
Ootid / ovum	Haploid cell after meiosis II, which happens only at fertilisation

2 Primordial Germ Cells and the Gonad

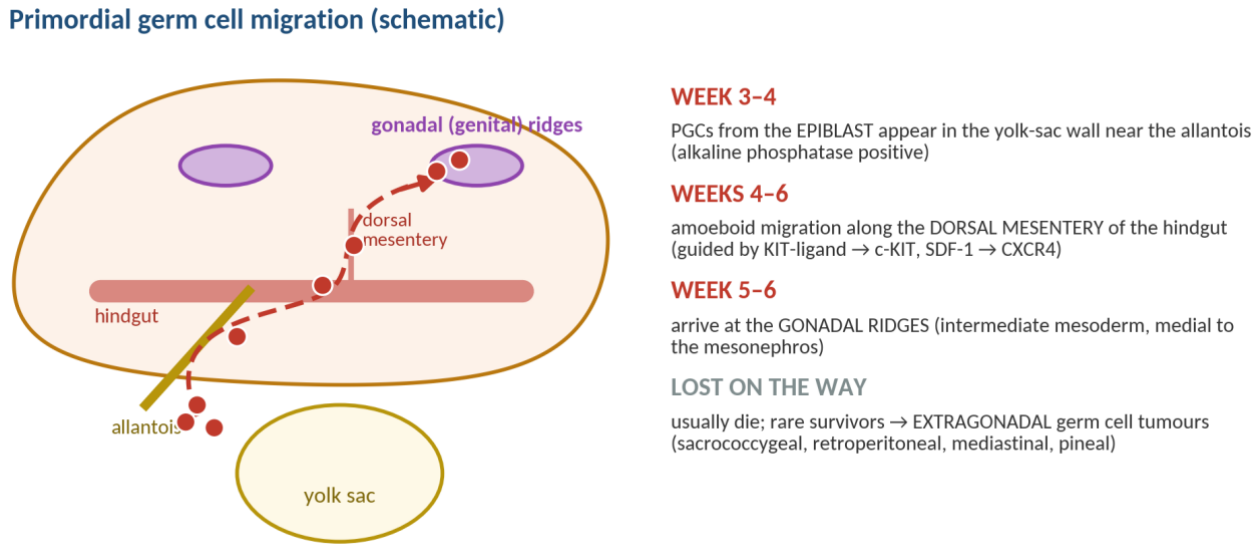


Figure 1. From yolk sac to gonadal ridge.

- The gonad is **indifferent until ~7 weeks**. With no **SRY**, the cortex develops and the medulla regresses → ovary (~10 weeks). Normal ovarian development needs **two functional X chromosomes** — in **45,X** oocytes form but undergo accelerated atresia → **streak gonads**.

3 Fetal Phase and the Oocyte Pool

- PGCs → **oogonia** (mitosis, in clusters joined by cytoplasmic bridges) → peak **~6–7 million at 20 weeks**.
- From **~12 weeks** oogonia enter **meiosis I** (retinoic acid from the mesonephros → **Stra8**) → leptotene, zygotene, pachytene → **arrest in diplotene** (dictyate).
- Each arrested primary oocyte gains a single layer of **flat pre-granulosa cells** → **primordial follicle**.

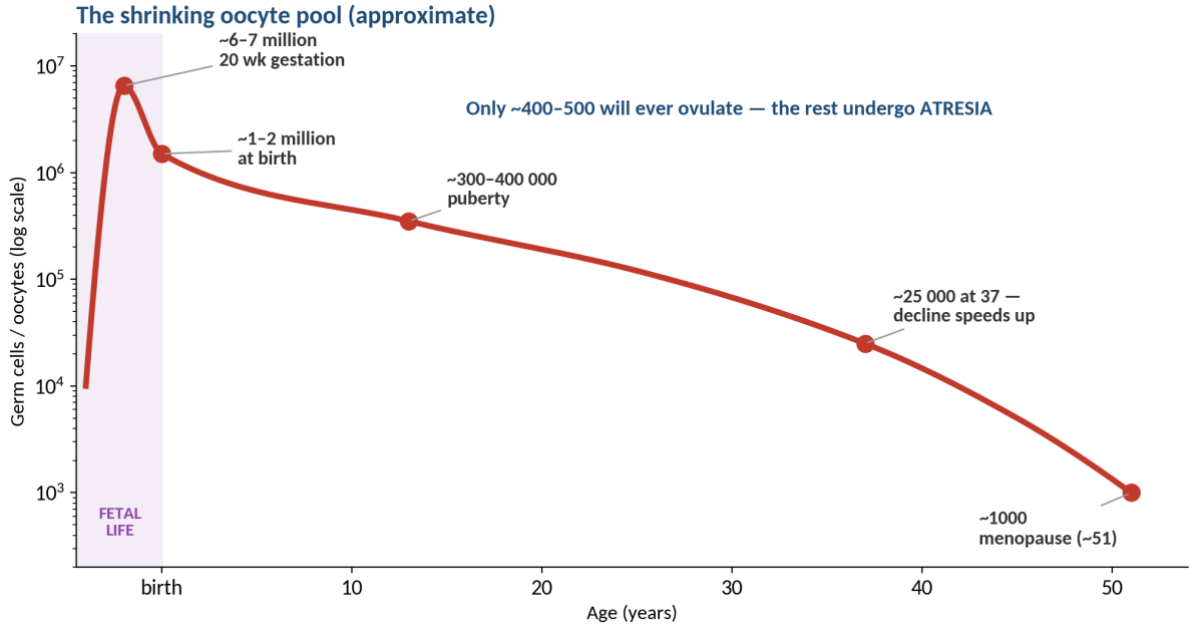


Figure 2. Atresia from mid-gestation to menopause.

MNEMONIC / MEMORY HOOK

7 – 2 – ½ – 1000: ~7 million at 20 weeks • ~2 million at birth • ~½ million (300–400 000) at puberty • ~1000 at menopause. Only ~400–500 ever ovulate.

4 Meiosis: Two Arrests, Two Divisions

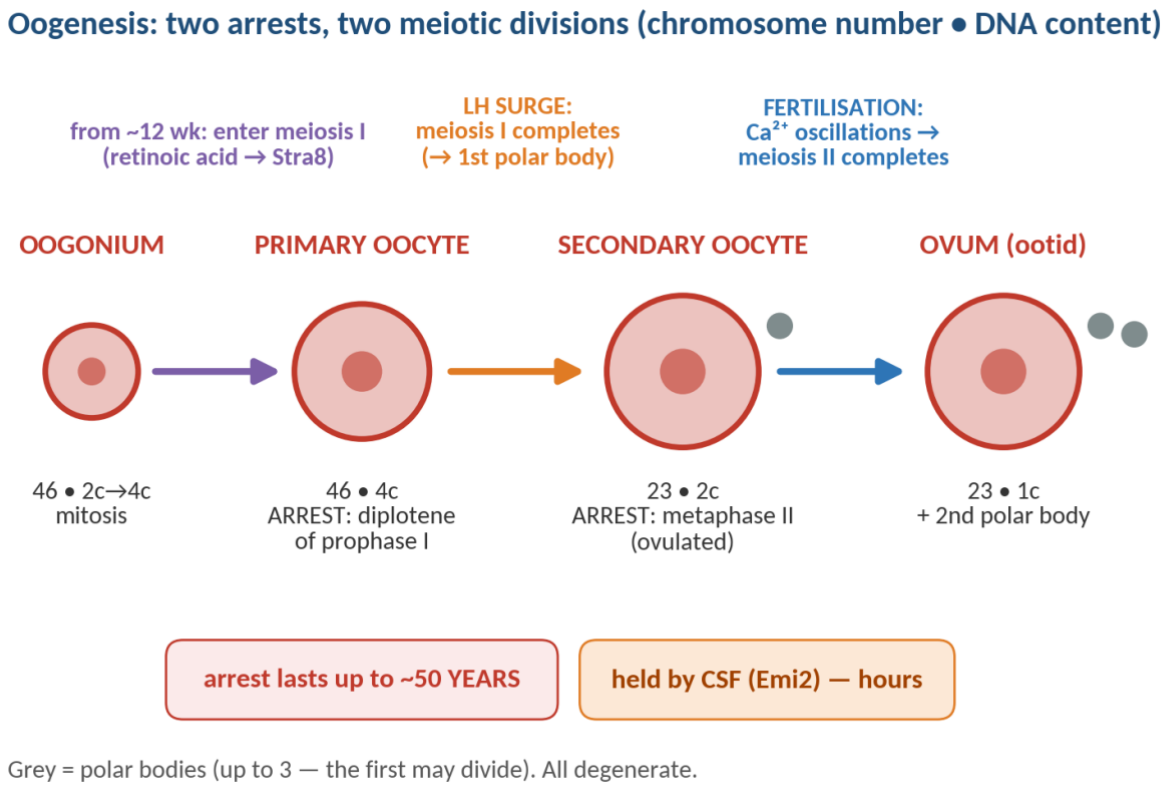


Figure 3. The oogenesis timeline.

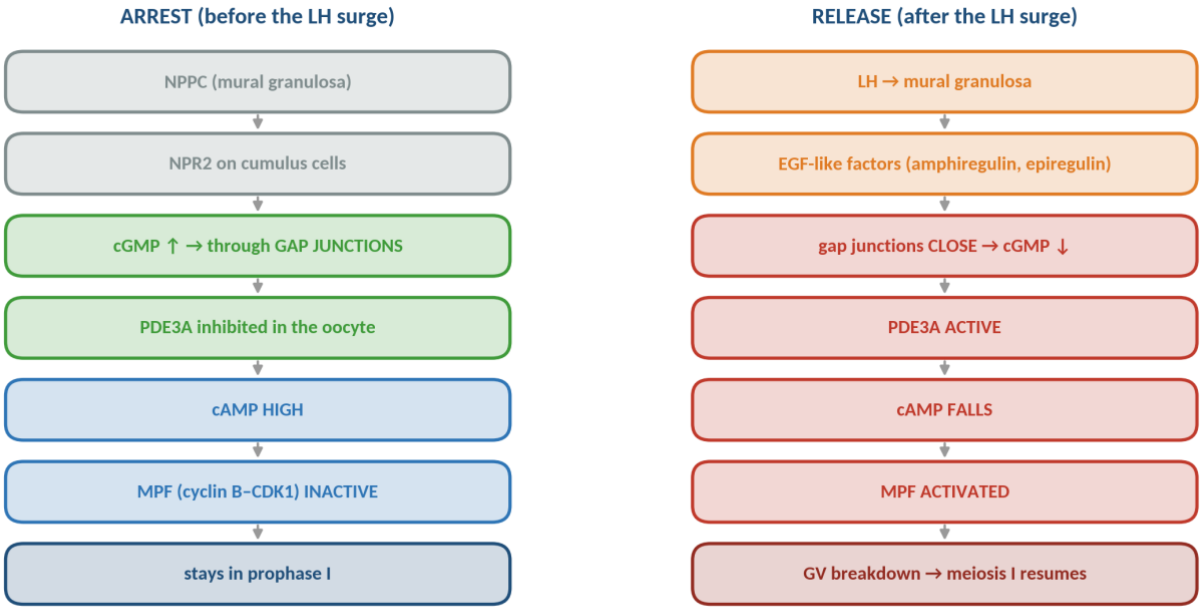
Stage	Chromosomes	DNA (chromatids)	Ploidy
Oogonium	46	2c → 4c after S phase	Diploid
Primary oocyte (arrested diplotene)	46	4c	Diploid
Secondary oocyte (at ovulation)	23	2c — each chromosome still 2 chromatids	Haploid
First polar body	23	2c	Haploid
Ovum / ootid (after meiosis II)	23	1c	Haploid
Second polar body	23	1c	Haploid

EXAM HOOK

The **ovulated egg is a secondary oocyte** arrested at **metaphase II**: haploid in **number (23)** but with **2c DNA** (sister chromatids not yet separated). Meiosis II finishes only when a sperm enters — calcium oscillations destroy **cytostatic factor (Emi2)** and inactivate **MPF**.

- **LH surge** → meiosis I completes (secondary oocyte + first polar body, very unequal cytoplasm) → **ovulation ~36 h after the surge begins**.

5 Why the Oocyte Waits — and What Wakes It



Connexin 37 links oocyte ↔ cumulus; connexin 43 links granulosa ↔ granulosa.

Figure 4. cAMP–cGMP control of meiotic arrest.

- **High intra-oocyte cAMP** keeps **MPF** (cyclin B–CDK1) inactive. Granulosa **NPPC → NPR2** makes cGMP, which passes through **gap junctions** to inhibit **PDE3A**. The **LH surge** (via EGF-like factors) closes the gap junctions → cGMP ↓ → PDE3A active → cAMP ↓ → MPF on → **germinal vesicle breakdown**.

6 Folliculogenesis

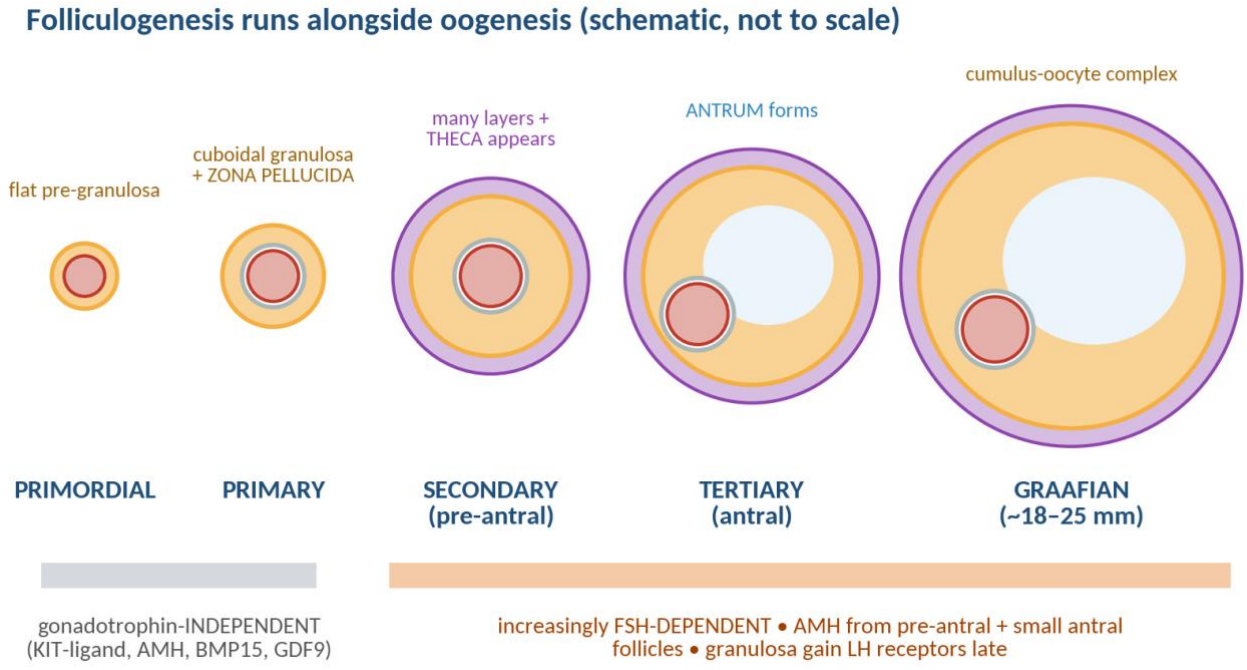


Figure 5. Follicle stages.

Stage	Features
Primordial	Primary oocyte (~25–30 µm) + one layer of flat pre-granulosa — the resting pool
Primary	Granulosa cuboidal; zona pellucida (ZP1–4) laid down
Secondary (pre-antral)	Several granulosa layers; stroma forms theca interna (LH receptors, androgens) and theca externa
Tertiary (antral)	Fluid-filled antrum; oocyte on the cumulus oophorus
Graafian	~18–25 mm, pre-ovulatory; cumulus–oocyte complex projects into the antrum

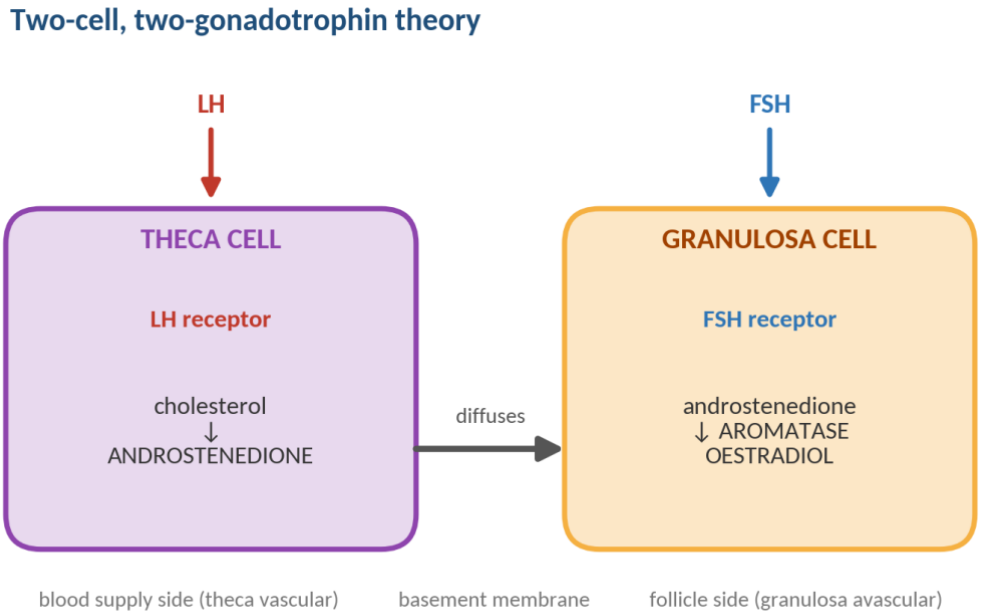


Figure 6. Theca makes androgen; granulosa turns it into oestradiol.

- Early recruitment is **gonadotrophin-independent** (KIT-ligand, AMH, BMP15, GDF9); growth becomes **FSH-dependent** from the secondary stage. **AMH** (pre-antral and small antral granulosa) restrains recruitment and measures ovarian reserve. **Inhibin B** (follicular) and **inhibin A** (luteal) suppress FSH.

7 Oogenesis vs Spermatogenesis

Feature	Oogenesis	Spermatogenesis
Starts	Fetal life (~12 weeks)	Puberty
Pattern	Discontinuous — long arrests	Continuous
Meiosis lasts	Up to ~50 years	~64–74 days (whole cycle)
Gametes per precursor	1 ovum + polar bodies	4 sperm
Cytoplasm	Very unequal	Equal
Lifetime output	~400–500	~10^{12}
Non-disjunction with age	Rises steeply	Much less age-dependent

8 Clinical Correlates

MATERNAL AGE + ANEUPLOIDY

- Decades in diplotene → **cohesins** holding chromosomes together wear out
- Premature separation and **non-disjunction** → aneuploid eggs
- Steep rise in **trisomy 21** risk after 35

OVARIAN RESERVE + POI

- **AMH** and **antral follicle count** are the main markers; early-follicular FSH rises as reserve falls
- **POI**: loss of ovarian function before 40 — 45,X, **fragile X premutation**, autoimmune, chemotherapy/radiotherapy, galactosaemia, idiopathic

DISORDERS OF SEX DEVELOPMENT

- **Turner (45,X)**: accelerated atresia → streak gonads; some (esp. mosaics) have brief ovarian function
- **Swyer (46,XY complete gonadal dysgenesis)**: streak gonads — SRY changes in a minority, other genes in most; **gonadoblastoma risk → gonadectomy**
- **46,XX gonadal dysgenesis**: rare (e.g. FSHR mutations)

ART

- **Polar body biopsy** tests the maternal genome without touching the embryo
- **In vitro maturation** mimics the LH-triggered cascade
- **Oocyte vitrification** stores metaphase II eggs (fertility preservation)

★ PEARL

The egg you **ovulate** is a **secondary oocyte in metaphase II (23 chromosomes, 2c)**. The egg you are **born with** is a **primary oocyte in diplotene of prophase I (46, 4c)**.

The very long first arrest is why egg quality — and aneuploidy — tracks **maternal age**.

9 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

~6–7 million Peak at 20 wk gestation	**~1–2 million** At birth	**~300–400 000** At puberty	**~1000** At menopause
~12 wk Meiosis I begins	**~36 h** LH surge → ovulation	**~400–500** Eggs ever ovulated	**18–25 mm** Graafian follicle

HIGH-YIELD CHECKLIST

- ☐ PGCs: epiblast → yolk sac wall → dorsal mesentery of hindgut → gonadal ridge (c-KIT/KIT-ligand).
- ☐ Stray PGCs → extragonadal germ cell tumours.
- ☐ Oogonia peak ~6–7 million at 20 weeks; meiosis I from ~12 weeks (retinoic acid → Stra8).
- ☐ Arrest 1: diplotene of prophase I — until the LH surge.
- ☐ Arrest 2: metaphase II (CSF/Emi2) — until fertilisation.
- ☐ Secondary oocyte: 23 chromosomes, 2c DNA; ovum: 23, 1c.
- ☐ cAMP high → MPF off; LH closes gap junctions → cGMP ↓ → cAMP ↓ → MPF on.
- ☐ Follicles: primordial → primary (ZP) → secondary (theca) → antral → Graafian.
- ☐ Two-cell theory: LH-theca androgen → FSH-granulosa aromatase → oestradiol.
- ☐ AMH = ovarian reserve; inhibin B follicular, inhibin A luteal.
- ☐ Long arrest → age-related aneuploidy (cohesin loss).
- ☐ 45,X: accelerated atresia → streak gonads.

Self-assessment — cover the right-hand column

Question	Answer
When do oogonia enter meiosis I, and what triggers it?	~12 weeks; retinoic acid → Stra8
Chromosome number and DNA content of the ovulated egg?	23 chromosomes, 2c (secondary oocyte, metaphase II)
How does the LH surge restart meiosis I?	Gap junctions close → cGMP ↓ → PDE3A active → cAMP ↓ → MPF activated
Why is oogenesis 'inefficient'?	One ovum per precursor, polar bodies wasted, massive atresia, ~400–500 ovulated
Link between the long arrest and maternal age?	Cohesin/spindle decay → non-disjunction → aneuploidy
Role of AMH?	From pre-antral/small antral granulosa; restrains recruitment; marker of reserve
Follicle stage where theca first appears?	Secondary (pre-antral)
Two-cell, two-gonadotrophin theory?	LH → theca androgens; FSH → granulosa aromatase → oestradiol
What holds the oocyte in metaphase II?	Cytostatic factor (Emi2) stabilising MPF
Where do stray PGCs cause tumours?	Sacrococcygeal, retroperitoneal, mediastinal, pineal

10 References

- Sadler TW. Langman's Medical Embryology. 14th ed. 2019.
- Strauss JF, Barbieri RL. Yen & Jaffe's Reproductive Endocrinology. 8th ed. 2019.
- ESHRE Guideline: Management of women with premature ovarian insufficiency. 2016 (updated 2024).