PIPADOR REVISION

MRCOG Part 1 Revision Notes

Spermatogenesis

EMBRYOLOGY • LECTURE 42

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 42: Spermatogenesis

Embryology • Visual revision edition

COLOUR CODE USED THROUGHOUT THESE NOTES

SPERMATOGONIA	SPERMATOCYTES	SPERMATIDS	SPERMATOZOA	LEYDIG / HORMONES

LEARNING OBJECTIVES — tick off as you go

- ☐ Describe the seminiferous tubule, Sertoli cells, the blood–testis barrier and Leydig cells.
- ☐ Outline the three phases of spermatogenesis with chromosome number and DNA content.
- ☐ Describe spermiogenesis and the structure of the spermatozoon.
- ☐ Explain maturation in the epididymis, capacitation and the acrosome reaction.
- ☐ Describe hormonal control of spermatogenesis.
- ☐ Know the WHO 2021 semen reference limits and causes of impaired spermatogenesis.

1 Overview

IN ONE LINE: *Continuous from puberty into old age: diploid spermatogonia → haploid spermatozoa in ~64–74 days, ~100–300 million a day, FOUR sperm from each primary spermatocyte.*

- Three phases: **(1) mitosis** of spermatogonia • **(2) meiosis** (spermatocytes → spermatids) • **(3) spermiogenesis** (spermatid → spermatozoon, no division).
- Germ cells come from **primordial germ cells** that reach the gonadal ridge in week 5; under **SRY** the gonad becomes a testis, and germ cells stay quiet inside the sex cords until puberty.

2 The Seminiferous Tubule

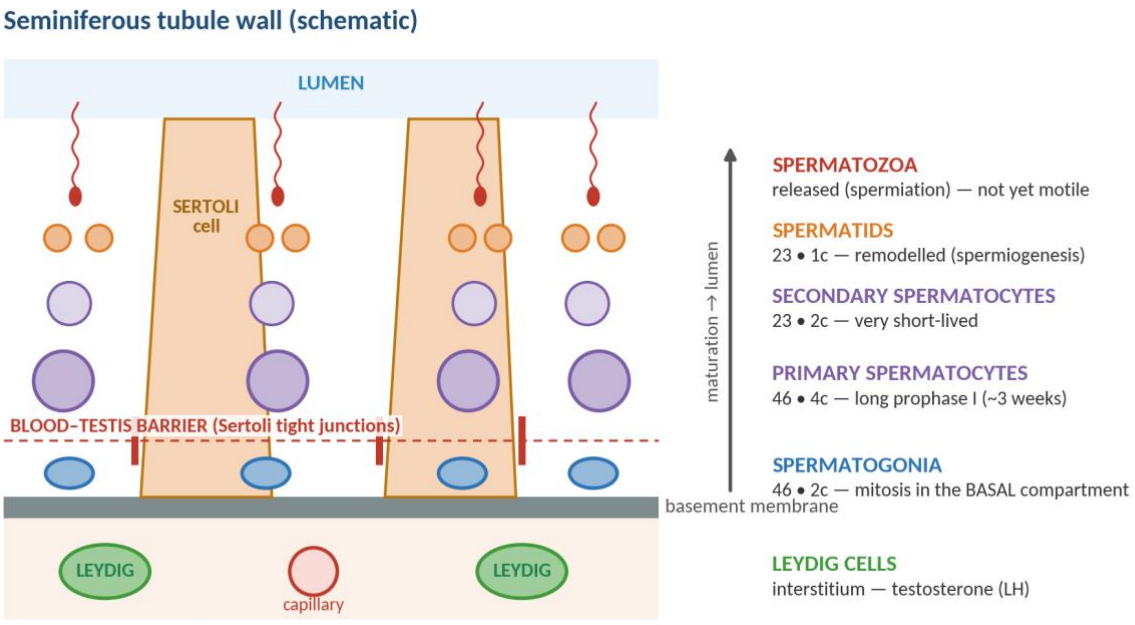


Figure 1. The tubule wall, from basement membrane to lumen.

SERTOLI CELLS

- Tall cells from basement membrane to lumen
- **Tight junctions → blood–testis barrier**: basal compartment (spermatogonia) vs adluminal (meiotic + haploid cells) — immune privilege
- **The only testicular cells with FSH receptors**
- Secrete **ABP**, **inhibin B**, activin, **AMH** (fetal); phagocytose residual bodies

LEYDIG CELLS

- In the **interstitium**, between tubules
- **LH → testosterone**
- Intra-testicular testosterone ~**100×** blood level — essential for spermatogenesis

3 The Three Phases

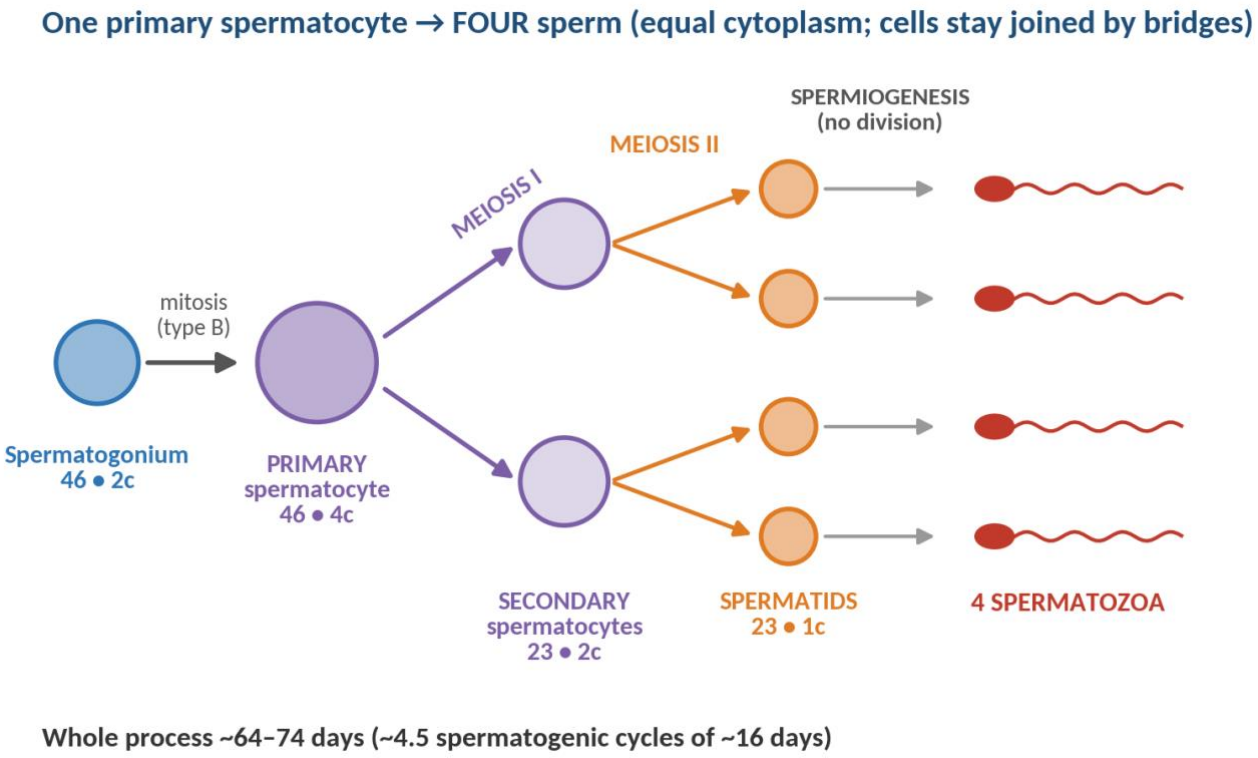


Figure 2. One primary spermatocyte makes four sperm.

Cell	Chromosomes	DNA	Notes
Spermatogonium (A dark, A pale, B)	46	2c	A dark = reserve stem cells; A pale = renewing; B = committed
Primary spermatocyte	46	4c	Crosses the BTB; long prophase I (~22 days) — crossing-over
Secondary spermatocyte	23	2c	Short-lived — straight into meiosis II
Spermatid	23	1c	Round, then remodelled
Spermatozoon	23	1c	Released into the lumen (spermiation)

- Daughter cells stay linked by **cytoplasmic bridges**, so a clone develops in step.

4 Spermiogenesis and the Spermatozoon

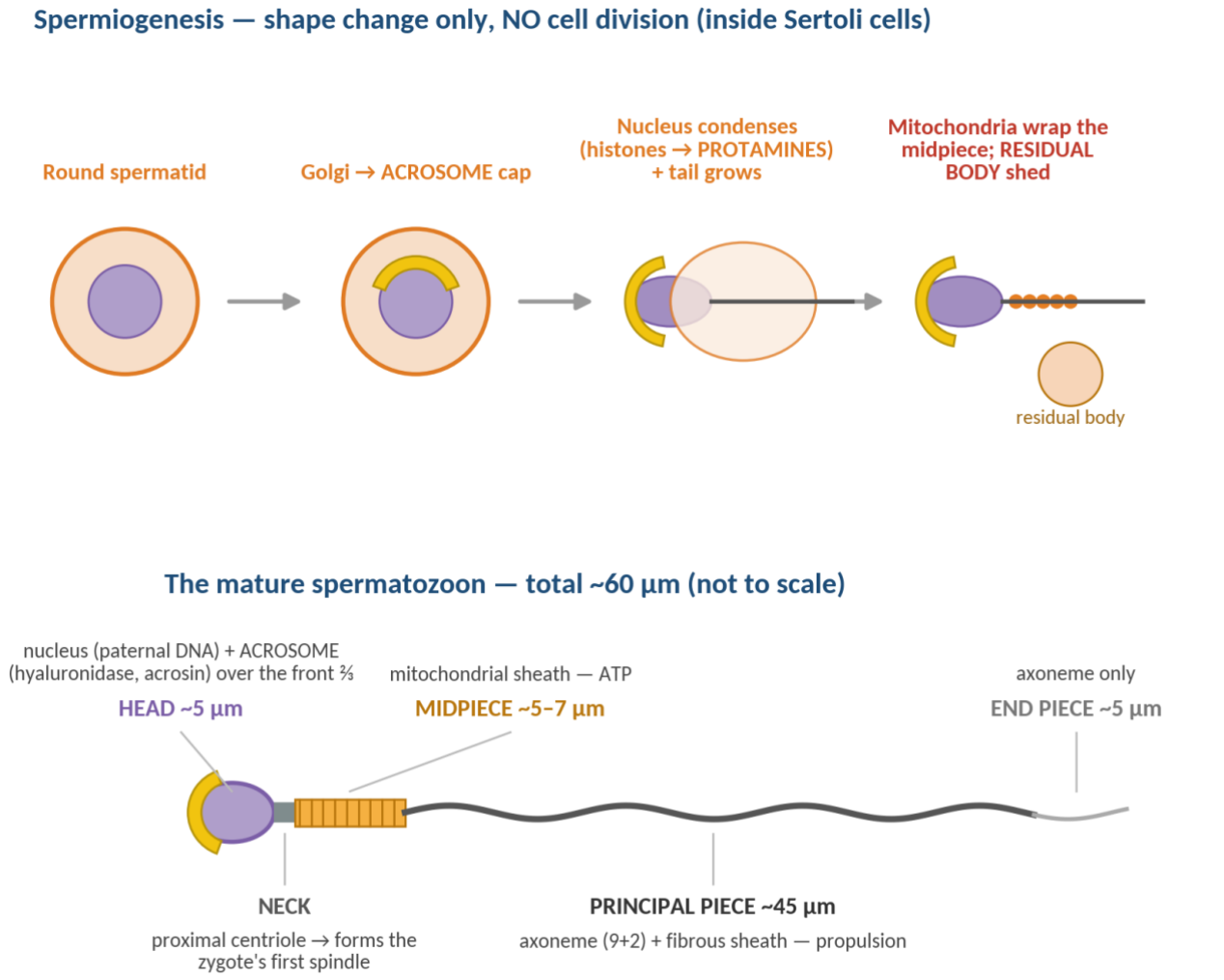


Figure 3. Remodelling the spermatid, and the finished sperm.

Change	Detail
Acrosome	Golgi vesicles form a cap over the front of the nucleus — hyaluronidase, acrosin
Nuclear condensation	Histones replaced by protamines; DNA packed very tightly; nucleus elongates
Flagellum	From the distal centriole — axoneme with 9+2 microtubules
Mitochondrial sheath	Wraps the midpiece — ATP for motility
Cytoplasm shed	As the residual body, eaten by Sertoli cells

MNEMONIC / MEMORY HOOK

'A New Flagellum Makes Change' — Acrosome, Nuclear condensation, Flagellum, Mitochondrial sheath, Cytoplasm shed.

5 Maturation, Capacitation and the Acrosome Reaction

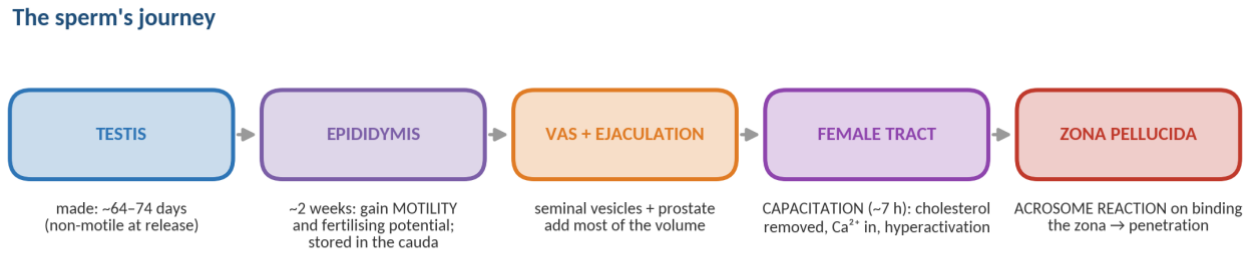


Figure 4. From testis to zona pellucida.

- **Spermiation** releases non-motile sperm → rete testis → efferent ductules → **epididymis** (~2 weeks: motility and fertilising potential; stored in the cauda) → vas.
- **Capacitation** (female tract, ~7 h): cholesterol and surface glycoproteins removed, Ca^{2+} and bicarbonate in, cAMP/PKA activation → **hyperactivated motility**.
- **Acrosome reaction** on binding the zona pellucida (classically via **ZP3**; human data point to **ZP2** as the main sperm-binding protein) → enzymes released → zona penetration.

6 Hormonal Control

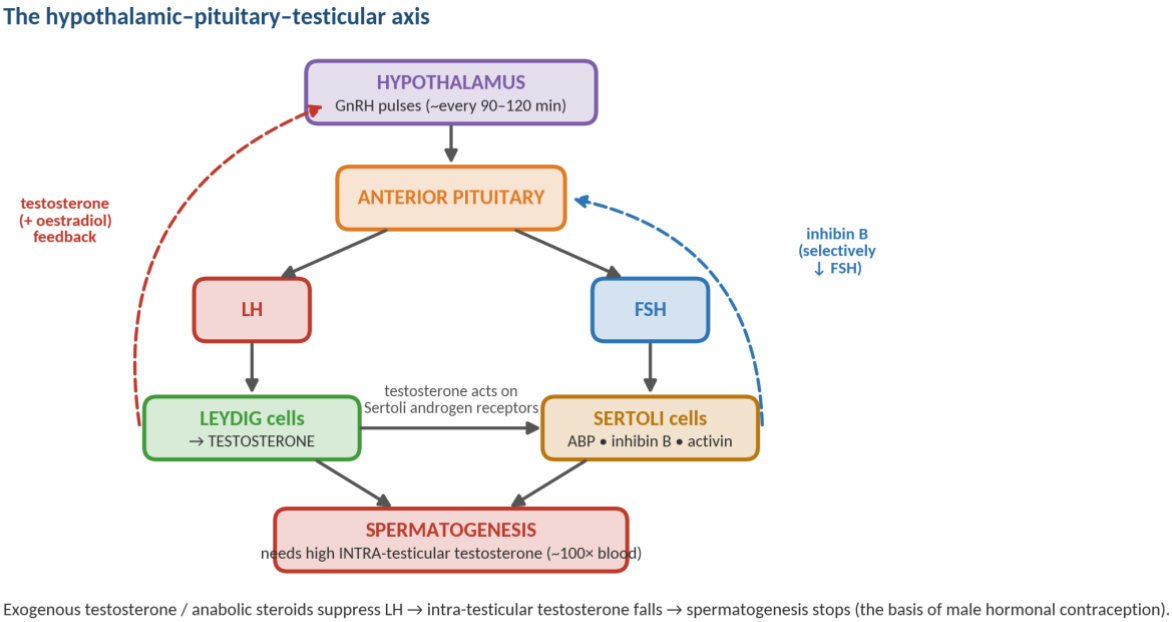


Figure 5. The testicular axis — two cells, two gonadotrophins.

> **MNEMONIC / MEMORY HOOK**
>
> **L for Leydig, L for LH; S for Sertoli, S for 'Sperm-support' (FSH).** Inhibin B from Sertoli feeds back on FSH only.

- **Retinoic acid (vitamin A)** is needed for spermatogonial differentiation. The **spermatogenic cycle** is ~16 days; ~4.5 cycles = 64–74 days. In humans, stages are arranged in a helical 'wave', so several appear in one tubule cross-section.

7 Spermatogenesis vs Oogenesis

Feature	Spermatogenesis	Oogenesis
Starts	Puberty	Fetal life (~12 weeks)
Pattern	Continuous, lifelong	Discontinuous — long arrests
Gametes per precursor	4 sperm	1 ovum + polar bodies
Cytoplasm	Equal	Very unequal
Output	~10^{12} over a lifetime	~400–500 ovulations
Arrests	Only a long prophase I	Diplotene (years), metaphase II (to fertilisation)
Age effect	Gradual; new point mutations rise	Steep fall in number and quality; aneuploidy rises

8 Semen Analysis

WHO 2021 — lower reference limits (5th centile)	
Volume	≥ 1.4 mL
Total sperm number	≥ 39 million / ejaculate
Concentration	≥ 16 million / mL
Total motility	≥ 42%
Progressive motility	≥ 30%
Normal morphology	≥ 4%
Vitality	≥ 54%
pH	≥ 7.2
Leucocytes	< 1 million / mL

Red = the three most examined. Below a limit ≠ infertile — repeat after ~3 months (one full cycle).

Figure 6. WHO 2021 lower reference limits.

9 What Impairs Spermatogenesis

Category	Examples
Heat	Testis needs to be 2–3 °C below core: cryptorchidism, varicocele, tight clothing (pampiniform counter-current exchange)
Drugs	Anabolic steroids / testosterone, chemotherapy, sulfasalazine, ketoconazole, opioids, cimetidine, alcohol
Toxins	Pesticides, heavy metals, radiation
Endocrine	Hypogonadotrophic hypogonadism (Kallmann), hyperprolactinaemia, thyroid disease

Category	Examples
Genetic	Klinefelter (47,XXY), Y microdeletions (AZFa/b/c), CFTR (CBAVD)
Infection / systemic	Mumps orchitis, STIs; obesity, diabetes, smoking, chronic illness

CRYPTORCHIDISM + VARICOCELE

- Undescended testis: heat damage; bilateral → infertility; ↑ **testicular cancer**
- **Orchidopexy at 6–12 months** (by 18 months at the latest) lowers but doesn't remove the risks
- Varicocele: **left ≫ right**; ↓ count and motility; repair helps selected men

GENETIC CAUSES

- **Klinefelter**: small firm testes, azoospermia (~90%), gynaecomastia — sperm sometimes found at **micro-TESE** for ICSI
- **CBAVD** in nearly all men with CF and some carriers — surgical sperm retrieval + ICSI; **screen the partner for CFTR**
- **Y microdeletions** — AZFa/b worst; passed to sons

★ PEARL

Testosterone therapy or anabolic steroids suppress LH and FSH → intra-testicular testosterone falls → **azoospermia** — the same principle behind male hormonal contraception (reversible over months).

Paternal age raises new point mutations (achondroplasia, Apert syndrome) — the counterpart of maternal-age aneuploidy.

10 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

64–74 d Whole process	**~16 d** One spermatogenic cycle	**~22 d** Prophase I	**4** Sperm per primary spermatocyte
~60 µm Sperm length	**~7 h** Capacitation	**2–3 °C** Testis below core	**~100×** Intra-testicular testosterone

HIGH-YIELD CHECKLIST

- ☐ Continuous from puberty; 64–74 days; ~100–300 million a day.
- ☐ Mitosis (spermatogonia) → meiosis (spermatocytes → spermatids) → spermiogenesis.
- ☐ Primary spermatocyte 46/4c; secondary 23/2c; spermatid 23/1c.
- ☐ Sertoli: blood–testis barrier, only FSH-target cells, ABP, inhibin B.
- ☐ Leydig: LH → testosterone; intra-testicular level ~100× blood.
- ☐ Spermiogenesis: acrosome, protamines, flagellum (9+2), mitochondrial sheath, residual body.
- ☐ Motility gained in the epididymis; capacitation in the female tract (~7 h).
- ☐ Acrosome reaction on zona binding.
- ☐ WHO 2021: 16 million/mL, 30% progressive, 4% normal forms (and 1.4 mL, 39 million total).
- ☐ Heat, drugs (anabolic steroids), Klinefelter, Y microdeletions, CFTR, varicocele, cryptorchidism.

Self-assessment — cover the right-hand column

Question	Answer
Main functions of the Sertoli cell?	Blood–testis barrier, germ-cell support, ABP, inhibin B, phagocytosis; FSH target
The key events of spermiogenesis?	Acrosome, nuclear condensation, flagellum, mitochondrial sheath, cytoplasm shed
FSH and LH targets in the testis?	FSH → Sertoli; LH → Leydig (testosterone)
WHO 2021 concentration / progressive motility / morphology?	16 million/mL • 30% • 4%
What is capacitation and where?	Membrane changes giving hyperactivation — female tract, ~7 h
Where do sperm gain motility?	Epididymis
Why does anabolic steroid use cause azoospermia?	LH/FSH suppressed → intra-testicular testosterone falls
Cause of CBAVD?	CFTR mutations
Paternal-age disorders?	New point mutations — achondroplasia, Apert syndrome
Sperm per primary spermatocyte vs ova per primary oocyte?	4 vs 1

11 References

- World Health Organization. Laboratory Manual for the Examination and Processing of Human Semen. 6th ed. 2021.
- Sadler TW. Langman's Medical Embryology. 14th ed. 2019.
- NICE CG156. Fertility problems: assessment and treatment. 2013 (updated 2017).