# HUBS3511 — Human Reproduction and Pregnancy

UNIVERSITY OF NEWCASTLE · BIOMEDICAL SCIENCES

**MEMORY AID SHEET**
Sem 1 2026 · **SIDE 1 OF 2**
Make & cycle · modules 1–3

**SIDE 1/2** MAKE A BABY · Male system & spermatogenesis · Female system, oogenesis & follicles · HPG axis & feedback · The menstrual / ovarian cycle

**RESTRICTED OPEN BOOK · 1× A4 TYPED AID**

Compiled by **AskSia** · mapped to the HUBS3511 syllabus · asksia.ai/cheatsheet/uon-hubs3511

## 0 · Exam Blueprint — READ FIRST

★ The course arc is Pringle's "make a baby → grow a baby → deliver a baby." Side 1 = **make & cycle**; side 2 = **conceive → deliver**.

**Assessment:** Assignment 1 educational resource (group) **40%** · 5× online tests **10%** · **Formal Exam 50%**. **Exam shape:** 120 min · **80 marks = 30 MCQ (30) + 19 short-answer (50)**, Zoom-invigilated. Short-answer carries most marks ⇒ this sheet privileges mechanisms, feedback loops & sequences. Possible ~10-min Zoom viva on your rationale.

**HOOK →** *The exam is **RESTRICTED OPEN BOOK**: one A4 double-sided sheet of handwritten OR TYPED notes (a "Memory Aid sheet") + a non-programmable calculator. This typed 2-side A4 IS that permitted sheet. Confirm on your current unit outline.*

## 1 · Male System — ANATOMY + GLANDS

**Scrotum** keeps testes 2–3 °C below core (needed for spermatogenesis). **Dartos** (smooth, wrinkles skin) + **cremaster** (skeletal, raises testis) thermoregulate. Heat ↓ sperm (fever, varicocele, cryptorchidism).

**Sperm pathway (memorise):** seminiferous tubules → rete testis → efferent ductules → epididymis (mature + store) → vas deferens → ejaculatory duct → urethra.

**Glands → semen:** seminal vesicles (~60–70%; fructose, prostaglandins, alkaline) · prostate (citrate, PSA) · bulbourethral (pre-ejaculate mucus).

**TRAP:** sperm are *made* in tubules but mature & gain motility in the epididymis, not the testis. **Vasectomy = cut vas deferens** (production continues, no exit).

## 2 · Sertoli vs Leydig — HIGH-YIELD

| | SERTOLI | LEYDIG |
|---|---|---|
| Where | inside tubule | between tubules |
| Driven by | **FSH** | **LH** |
| Makes | ABP, inhibin, AMH | **testosterone** |
| Role | nurse cells; blood–testis barrier | androgen source |

**Mnemonic:** FSH→Sertoli (Support); LH→Leydig. Blood–testis barrier (Sertoli tight junctions) hides haploid sperm from the immune system. **ABP** keeps local testosterone high for spermatogenesis.

## 2b · Semen — THE EJACULATE

Sperm + seminal plasma. ~**1.5–5 mL**, ~**200 million sperm** per ejaculate; only a few hundred reach the ampulla. Lost to vaginal acidity, leukocytes, wrong tube and the journey.

Plasma = fructose (energy), prostaglandins (stimulate female-tract motility), **alkaline** buffer (protects against vaginal acid), coagulation/liquefaction enzymes.

Low count/motility or abnormal morphology = common male-factor infertility — addressed by IUI, IVF or **ICSI**.

## 2c · Sex Determination — MODULE 1

**Bipotential gonad** (~wk 6) branches on SRY (Y chromosome). **SRY present** → testis → Sertoli (AMH) + Leydig (testosterone → DHT) → Wolffian duct persists, Müllerian regresses → male.

**SRY absent** → ovary, no AMH → Müllerian persists (uterus, tubes) → female = the default pathway.

## 3 · Spermatogenesis — 2N → N · 4 SPERM

In the seminiferous tubule wall, continuous from puberty, ~64–74 days. Cells move **periphery → lumen** as they mature.

1. **Spermatogonium (2n)** → mitosis → keeps stem pool + **primary spermatocyte (2n)**
2. Primary spermatocyte → **meiosis I** → 2× **secondary spermatocyte (n)**
3. Secondary spermatocyte → **meiosis II** → 2× **spermatid (n)**
4. Net 1 → 4 spermatids (4 functional sperm)

**Spermiogenesis** = final remodelling of round spermatid → spermatozoon: builds the **acrosome** (enzyme cap), condenses the nucleus, grows the **flagellum** + **mitochondrial midpiece**, sheds cytoplasm. No cell division.

**TRAP:** spermatogenesis = whole process; spermiogenesis = only the maturation step.

**Mature sperm parts:** *head* (condensed haploid nucleus + acrosome) · *midpiece* (mitochondria → ATP for the tail) · *flagellum* (propulsion). Meiosis I = reduction (2n→n, homologues separate); meiosis II separates sister chromatids.

## 4 · Female System — TUBE + UTERUS

**Ovary:** cortex (follicles = reserve) + medulla; makes oestrogen, progesterone, inhibin. **Tube:** fimbriae → infundibulum → ampulla (fertilisation site) → isthmus → uterus.

**Uterus wall:** perimetrium → **myometrium** (labour muscle) → **endometrium** = functional layer (sheds) + basal layer (regenerates).

**TRAP:** fertilisation in the ampulla, not the uterus. Implantation in the endometrial functional layer. Ectopic = implantation outside the uterus (usually the tube).

**Mammary gland:** alveoli (milk-secreting) → lobules → lactiferous ducts → sinus → nipple; myoepithelial cells wrap the alveoli for ejection. Oestrogen grows ducts, progesterone grows alveoli.

The endometrium has a **functional layer** (the part that cycles, thickens and sheds) over a permanent **basal layer** that regenerates it each month from its stem cells.

## 5 · Oogenesis — ARRESTS · POLAR BODIES

Begins in fetal life, finishes only at fertilisation.

1. **Oogonium (2n)** → mitosis (fetal) → **primary oocyte (2n)** starts meiosis I then ARRESTS at prophase I before birth (finite reserve)
2. Each cycle the **LH surge** → completes meiosis I → **secondary oocyte (n) + 1st polar body**
3. Secondary oocyte starts meiosis II then ARRESTS at metaphase II — this is ovulated
4. Meiosis II completes **only if fertilised** → ovum + 2nd polar body

Net 1 oogonium → 1 ovum (+ up to 3 polar bodies; cytoplasm conserved). Polar bodies take the discarded chromosomes.

**Why arrest?** Conserving cytoplasm gives the ovum its nutrient/organelle store; the long prophase-I arrest is also why older oocytes mis-segregate → ↑aneuploidy with maternal age.

**Two LH-triggered events:** the cycle's LH surge completes meiosis I (→ secondary oocyte); only *fertilisation* completes meiosis II — so the ovulated cell is always paused at metaphase II.

## 5b · Sperm vs Egg — CLASSIC COMPARE

| | SPERM | OOGENESIS |
|---|---|---|
| Starts | puberty (lifelong) | fetal life |
| Per precursor | **4** | **1 ovum** |
| Cytoplasm | equal | unequal |
| Arrests | none | proph. I + meta. II |
| Lifetime # | billions | ~400–500 |

Both make haploid (n) gametes; differences are *timing, number, symmetry, arrests.*

## 6 · Folliculogenesis — MEMORISE THE ORDER

1. **Primordial** — oocyte + flat granulosa (resting reserve)
2. **Primary** — cuboidal granulosa; **zona pellucida** forms
3. **Secondary** — many granulosa layers + **theca** cells
4. **Antral (tertiary)** — fluid **antrum** appears
5. **Graafian** — mature, bulging → ovulation
6. **Corpus luteum** — luteinised remnant → progesterone + oestrogen
7. **Corpus albicans** — scar if no pregnancy → hormones fall → menses

**Two-cell, two-gonadotropin model:** LH → theca → androgens → diffuse to granulosa, where FSH → aromatase → oestrogen. Granulosa inhibin (⊖ FSH) selects ONE **dominant follicle**; rest undergo **atresia**.

**TRAP:** corpus luteum secretes mainly progesterone; **rescued by hCG** in pregnancy, else → corpus albicans.

**Timing nuance:** early follicle growth (months) is gonadotropin-*independent*; only the final ~2 weeks are FSH/LH-driven. The zona pellucida (laid down at the primary stage) is the same coat later bound by sperm at fertilisation.

**Atresia:** the dominant follicle's inhibin + oestrogen lower FSH, starving the other recruited follicles, which die by atresia — a built-in mechanism that usually limits ovulation to one egg per cycle.

## 7 · HPG Axis — 3 NODES

**Hypothalamus** → GnRH (pulsatile) → **anterior pituitary** → FSH + LH → **gonads** → steroids + inhibin.

**Classes:** GnRH/FSH/LH/prolactin/oxytocin = *peptide* (membrane receptors, fast).
Oestrogen/progesterone/testosterone = *steroid* (intracellular receptors, slow).

**TRAP:** GnRH must be pulsatile — continuous GnRH *downregulates* the pituitary (basis of GnRH-agonist drugs).

```
HPG CASCADE (♀)
Hypothalamus ─GnRH→ Pituitary
─FSH/LH→ Ovary → E / P / inhibin
⊖ back on both nodes (default)
```

GnRH pulse *frequency* also tunes output: fast pulses favour LH, slow pulses favour FSH — the hypothalamus shapes the cycle by changing its rhythm, not just its amount.

## 7b · The Feedback Switch — ⊖ ⇄ ⊕

The *same* hormone (oestrogen) is inhibitory or stimulatory by its level + duration:

- **Most of cycle:** low/moderate E → ⊖ → GnRH/LH damped
- **Mid-cycle:** sustained HIGH E → ⊕ → GnRH/LH amplified → LH SURGE

This sign-flip makes ovulation a discrete, once-per-cycle event. **Both** the level *and* the duration of the oestrogen signal must cross threshold to flip the sign.

## 8 · Feedback & the LH Surge — THE CONCEPT

**Default = negative feedback:** rising steroids ⊖ suppress GnRH + FSH/LH; inhibin ⊖ FSH selectively. Keeps the system stable, prevents over-recruitment.

**The female-only switch:** sustained HIGH oestrogen near mid-cycle flips to ⊕ **positive feedback** → massive **LH surge** (+ smaller FSH rise).

**LH surge →** ovulation (~within 18 h) · drives the oocyte to complete meiosis I → metaphase-II arrest · luteinises the follicle → corpus luteum.

**TRAP:** it is HIGH & sustained oestrogen that triggers the surge — *low/moderate* oestrogen is inhibitory. Males have NO surge (tonic, negative-feedback only, testosterone ~constant; inhibin still ⊖ FSH).

**The full mid-cycle chain:** dominant follicle → oestrogen climbs past a threshold & stays high → ⊖ flips to ⊕ → GnRH/LH amplified → LH surge → follicle ruptures (ovulation) → the emptied follicle luteinises → progesterone rises and re-imposes ⊖, preventing a second surge.

## 9 · Male HPG Axis — NO SURGE

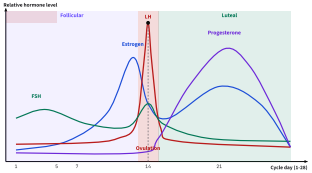
Hypothalamus → GnRH → pituitary → LH→Leydig→testosterone; FSH→Sertoli→spermatogenesis + inhibin + ABP.

**All feedback negative:** testosterone ⊖ on both; inhibin ⊖ FSH only. **No positive feedback, no LH surge** ⇒ continuous, stable output (contrast with the cyclical female axis).

Testosterone is held roughly constant (small ultradian pulses); spermatogenesis runs continuously. The female axis instead *builds toward* a single monthly surge.

**One-line contrast:** ♂ = tonic, ⊖ only, continuous gametes; ♀ = cyclical, ⊖ *plus* one ⊕ surge, one gamete per cycle. Same hormones (GnRH, FSH, LH, inhibin) — different feedback architecture.

## 10 · Cycle Hormone Curve — FLAGSHIP FIGURE




Estrogen peaks *before* the day-14 LH spike (it is the trigger). **Progesterone is ~zero pre-ovulation, dome-peaks in the luteal phase; E + P crash by day 28 → menses.**

**Read it off:** FSH (green) rises early then dips; oestrogen (blue) peaks ~d12–13; **LH (red) spikes at d14**; progesterone (purple) only climbs after ovulation. The estrogen peak *precedes* and *causes* the LH spike. A common short-answer is simply "label the four curves and the surge."

**Four-curve cheat:** if no pregnancy, the corpus luteum regresses (~d26) → E + P both crash → spiral-artery spasm → menses (d1 of the next cycle). If pregnancy, hCG rescues the corpus luteum → progesterone stays high → no menses.

**Colour key:** blue = oestrogen, red = LH, green = FSH, purple = progesterone. The single tall red spike at day 14 is the diagnostic feature — narrower and taller than FSH's small mid-cycle bump.

## 11 · Ovarian Cycle — ~28 DAYS

**Follicular (d1–13):** FSH↑ recruits follicles → oestrogen↑; inhibin restricts recruitment; one dominant follicle selected.

**Ovulation (~d14):** oestrogen peak → LH surge → Graafian follicle ruptures, releases the secondary oocyte.

**Luteal (d15–28):** corpus luteum → **progesterone** (+ oestrogen); no pregnancy → regresses (~d26) → P/E fall → menses.

**TRAP:** luteal phase length is fixed (~14 d) — cycle-length variation is in the *follicular* phase.

The corpus luteum has a built-in ~14-day lifespan unless rescued by hCG; that fixed timer is why progesterone falls on schedule and menses arrives ~14 d after ovulation.

## 12 · Uterine (Menstrual) Cycle — ENDOMETRIUM

| PHASE / DAY | DRIVER | ENDOMETRIUM |
|---|---|---|
| **Menstrual** 1–5 | P↓ (CL regress) | spiral-artery spasm → functional layer shed |
| **Proliferative** 6–14 | **oestrogen** | regrows, glands lengthen (= follicular) |
| **Secretory** 15–28 | **progesterone** | glycogen, vascular, receptive (= luteal) |

**Integrated:** FSH→follicles+E · E→proliferative + (high & sustained) the LH surge · LH surge→ovulation · P→secretory + maintains lining + ⊖ feedback · P falls → menstruation.

**TRAP:** progesterone peaks in the *luteal/secretory* phase (NOT ovulation); oestrogen peaks *just before* ovulation. Falling progesterone (not oestrogen alone) causes menses. Peak endometrial receptivity ~7 days post-ovulation.

## 13 · Puberty & the Switch — MODULE 3

Childhood HPG is suppressed; **puberty** = reawakening of pulsatile GnRH (kisspeptin-driven) → rising FSH/LH → gonadal steroids → secondary sex characteristics, growth spurt, menarche/spermarche.

**TRAP:** the *capacity* to reproduce (menarche/first ovulation, viable sperm) lags the first visible milestones — early puberty signs ≠ full fertility.

Adrenarche (adrenal androgens) and gonadarche (HPG reactivation) drive the visible changes; leptin signals adequate energy stores, linking body fat to the timing of puberty.

## 13b · Cycle Timing Maths — CALCULATOR OK

Luteal phase is fixed (~14 d), so ovulation ≈ cycle length − 14:

| CYCLE | OVULATION ≈ |
|---|---|
| 28 d | day 14 |
| 32 d | day 18 |
| 24 d | day 10 |

Longer cycles ⇒ later ovulation because the *follicular* phase lengthens, not the luteal one. Fertile window ≈ the 5 days before + day of ovulation (sperm survive ~3–5 d, oocyte ~24 h).

**Ovulation signs:** a urinary **LH-surge test** predicts ovulation ~1 day ahead; basal body temperature *rises* ~0.3–0.5 °C *after* ovulation (progesterone is thermogenic) — so BBT confirms, it does not predict. Cervical mucus turns clear & stretchy near ovulation (oestrogen effect).

## 14 · Hormone Source → Action — SIDE-1 BELT

| HORMONE | SOURCE | ACTION |
|---|---|---|
| GnRH | hypothalamus | pulsatile → FSH/LH |
| FSH | ant. pituitary | ♀ follicle+aromatase; ♂ Sertoli |
| LH | ant. pituitary | ♀ surge→ovulation+CL; ♂ Leydig→T |
| Oestrogen | granulosa | proliferative; LH-surge trigger |
| Progest. | corpus luteum | secretory; quiescence |
| Testost. | Leydig | spermatogenesis; ♂ traits |
| Inhibin | granulosa/Sertoli | ⊖ FSH only |
| hCG | syncytiotroph. | rescues CL; preg. test |
| Oxytocin | post. pituitary | labour ⊕; milk ejection |
| Prolactin | ant. pituitary | milk synthesis |

## 15 · Steroid vs Peptide — WHY IT MATTERS

**Peptide** (GnRH, FSH, LH, oxytocin, prolactin, hCG, inhibin): water-soluble, surface receptors, 2nd messengers (cAMP), fast & brief; stored in vesicles.

**Steroid** (oestrogen, progesterone, testosterone): lipid-soluble from cholesterol, intracellular receptors → alter gene transcription, slow & long-lasting; carried bound to plasma proteins.

**Exam use:** steroid lag explains why the proliferative/secretory endometrium responds *over days*, while the LH surge (peptide) acts within hours to trigger ovulation.

It also explains drug design: synthetic *steroids* (the pill) silently reset feedback over weeks; a *peptide* hCG "trigger" in IVF mimics the LH surge within hours.

**Receptor logic:** peptide hormones need a surface receptor on the target cell, so a tissue without that receptor ignores the signal; steroids diffuse into *any* cell but only act where the matching nuclear receptor + co-factors exist — selectivity comes from receptor expression, not hormone distribution.

This is why oestrogen acts on the endometrium, breast and bone alike (all express its receptor) while a peptide like FSH only hits gonadal cells carrying the FSH receptor.

## 16 · Side-1 Trap List — ONE GLANCE

1. FSH→Sertoli (Support); LH→Leydig. Inhibin ⊖ FSH only.
2. Spermatogenesis = **4 sperm**; oogenesis = **1 ovum** + polar bodies. Arrests: **prophase I** then **metaphase II**.
3. **HIGH sustained oestrogen = ⊕ → LH surge → ovulation.** Low oestrogen = ⊖.
4. Two-cell model: **theca→androgen (LH), granulosa→oestrogen (FSH)**.
5. Fertilisation in the **ampulla.** Progesterone peaks **luteal**, not ovulation.
6. **Falling progesterone** drives menstruation. Luteal phase fixed ~14 d.
7. GnRH must be **pulsatile**; continuous = pituitary shutdown.
8. Males: **no LH surge**, tonic axis.
9. Folliculogenesis order: primordial → primary → secondary → antral → Graafian → corpus luteum → albicans.
10. Sperm pathway: tubules → epididymis (mature) → vas → ejaculatory duct → urethra.

**SIA →** *Short-answers reward the mechanism + direction of feedback. Always name the hormone, its source, its target, and whether the arrow is ⊕ or ⊖.*

SIDE 2/2 GROW & DELIVER · Fertilisation & implantation · Placenta & pregnancy hormones · Maternal adaptations · Parturition & lactation · Fetal circulation · Contraception & ART

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## 17 · Capacitation & Fertilisation — IN THE AMPULLA

**Epididymal maturation** (in testis→duct): sperm gain motility, condensed DNA, zona-binding ability.
**Capacitation** happens in the female tract: cholesterol/inhibitory proteins removed → ↑membrane fluidity, ↑$Ca^{2+}$/cAMP → **hyperactivated motility**. Only capacitated sperm fertilise.
**Fertilisation sequence:**

1. **Cumulus penetration** by hyperactivated sperm
2. **Zona binding** to ZP glycoproteins (classically **ZP3**)
3. **Acrosome reaction** — releases acrosin/hyaluronidase to digest the zona
4. **Membrane fusion** with the oolemma

Fusion → oocyte completes meiosis II → maternal + paternal pronuclei → fuse → 2-cell zygote.
**Mitochondria are maternally inherited** (paternal destroyed).
**Sequence why it matters:** capacitation enables hyperactivation; hyperactivation powers cumulus penetration; only zona contact triggers the acrosome reaction (so it cannot fire prematurely) — each step gates the next, securing one sperm into one receptive egg. Fertilisation also restores diploidy via pronuclear fusion.

## 18 · Blocks to Polyspermy — MONOSPERMY

**Fast block** — transient oolemma depolarisation (seconds). **Slow block (cortical / zona reaction)** — $Ca^{2+}$ wave → cortical granules harden the zona + alter ZP receptors → no further sperm bind. Polyspermy → lethal triploidy.
**Zona roles:** species-specific binding · polyspermy block · embryo protection · implantation timing.
**Why monospermy matters:** two sperm sets → **triploid** (3n), which is lethal/non-viable. The cortical (zona) reaction is the durable guarantee; the fast block just buys seconds.
The $Ca^{2+}$ wave that triggers the cortical reaction also **activates the egg** — restarting meiosis II and beginning development. ICSI works because injecting the sperm reproduces this $Ca^{2+}$ activation directly.

## 19 · Pre-Implantation — TIMELINE

Zygote (d1) → cleavage (smaller cells, no growth) → d2 2-cell → d3 4–8-cell → **d4 morula** (solid) → **d5 blastocyst** (blastocoel + ICM + trophoblast) → **hatches** from zona (d5–6) before implanting.
**Blastocyst:** inner cell mass → embryo; trophoblast → placenta. **TRAP:** morula = solid; blastocyst = cavity + ICM/trophoblast split. Must hatch before implanting.
**Anatomical track:** ovary → ampulla (fertilisation) → oviduct (cleavage) → uterus (arrives ~blastocyst stage). Cilia + smooth muscle move it along; tube blockage (e.g. post-chlamydia) → ectopic risk.
**Compaction (~d4):** blastomeres maximise contact and polarise → this is the first cell-fate decision, splitting outer cells (→ trophectoderm/placenta) from inner cells (→ ICM/embryo). Totipotency is lost as cells specialise.
**Twinning:** two ovulated eggs → *dizygotic* (fraternal); one zygote splitting → *monozygotic* (identical) — timing of the split sets shared membranes.
**Hatching:** the blastocyst enzymatically thins and escapes the zona pellucida (~d5–6); only the now-exposed trophectoderm can contact and adhere to the endometrium.

## 20 · Implantation — ~DAY 6–7 · 3 STAGES

Into the endometrial **functional layer** during the **secretory phase** (progesterone-primed, receptive, pinopods present).

1. **Apposition / adplantation** — loose contact; ICM faces the endometrium
2. **Adhesion** — stable attachment via adhesion molecules; no longer dislodged
3. **Invasion** — **syncytiotrophoblast** breaches epithelium + basement membrane into stroma

Trophoblast splits: inner **cytotrophoblast** + outer multinucleate **syncytiotrophoblast** (invades AND makes hCG). **Decidualisation** = stromal cells → nutrient-rich, immune-tolerant decidua (progesterone-supported).
**TRAP:** order = Apposition → Adhesion → Invasion.
**Implantation window:** implantation needs BOTH a competent hatched blastocyst AND a receptive endometrium (secretory, progesterone-primed, pinopods) — a mistimed window is a cause of early loss/failed IVF transfer.
Normal site = posterior/superior uterine wall. **Placenta praevia** = low implantation over the cervix (bleeding risk); deep/abnormal invasion = **placenta accreta**.

## 21 · Placenta Structure — MODULE 8

Fetomaternal organ; functional unit = **chorionic villus** (fetal tissue bathed by maternal blood in the intervillous space). Haemochorial — maternal blood directly bathes the villi.
**Maternal–fetal barrier (out→in):** syncytiotrophoblast → cytotrophoblast → basal lamina → villous stroma → fetal capillary endothelium.
**EVT & spiral arteries:** extravillous trophoblast remodels maternal spiral arteries into wide, low-resistance, high-flow vessels. Failed remodelling → preeclampsia / IUGR.
**TRAP:** maternal & fetal blood **do NOT mix** — exchange is across the barrier only.
The barrier *thins* as pregnancy advances (cytotrophoblast becomes discontinuous) → shorter diffusion distance for late-gestation $O_2$/nutrient demand. **Hofbauer cells** in the villus stroma are placental macrophages. Umbilical cord = **2 arteries** (deoxygenated, fetus→placenta) + **1 vein** (oxygenated) in Wharton's jelly.

## 22 · Placental Transport — MATCH THE MODE

| SUBSTANCE | MECHANISM |
|---|---|
| $O_2$, $CO_2$, water, urea | **simple diffusion** |
| Glucose | facilitated (GLUT) |
| Amino acids, $Ca^{2+}$/Fe | **active** (against gradient) |
| IgG | receptor endocytosis |

**TRAP:** amino acids are *active* ⇒ fetal AA can exceed maternal. Maternal IgG crosses (newborn passive immunity); IgM does not. Many drugs/alcohol/viruses cross.
**Other roles:** waste removal (urea, creatinine), an endocrine organ (§23), and an immune interface that must tolerate the semi-allogeneic fetus (progesterone is immunomodulatory/anti-inflammatory).
**Gradient rule:** diffusion ($O_2$, $CO_2$, glucose) always runs *down* a gradient; only active transport (amino acids, $Ca^{2+}$, Fe) can move solute *up* a gradient, using ATP — which is why fetal levels of those can exceed maternal.

## 23 · Pregnancy Hormones — PLACENTAL ENDOCRINE

| HORMONE | SOURCE / ACTION |
|---|---|
| hCG | syncytiotrophoblast (peak wk 8–10); **rescues corpus luteum**; pregnancy test |
| **Progest.** | CL early → **placenta wk 6–9**; uterine quiescence |
| Oestrogen | fetoplacental (estriol needs **fetal adrenal**); ↑flow, labour priming |
| **hPL** | syncytiotroph.; **maternal insulin resistance** → glucose to fetus |
| Relaxin | softens cervix/pelvis |

**Luteal–placental shift (~wk 6–9):** early progesterone from the hCG-rescued corpus luteum; then the **placenta takes over** (CL no longer essential).
**TRAP:** hCG keeps the *corpus luteum* alive (not the placenta directly). hPL causes the insulin resistance behind **gestational diabetes**. Low estriol can signal fetal compromise.
**Estriol needs both:** the fetal adrenal makes DHEAS, the placenta aromatises it → estriol is a read-out of a healthy *fetoplacental unit*, which is why it falls with fetal compromise.
**Progesterone = "pro-gestation":** relaxes the myometrium, supports the decidua, blocks lactation until birth, and is anti-inflammatory/immunomodulatory — its functional withdrawal is what later permits labour.

## 24 · Maternal Adaptations — MODULE 9

- **CV:** blood volume ↑30–50% (plasma ↑ > RBC ↑ → dilutional anaemia); CO ↑30–50% (early ↑HR, later ↑SV); ↓SVR → BP *falls*, lowest mid-pregnancy
- **Resp:** ↑tidal volume (progesterone) → mild **respiratory alkalosis** (↓$PaCO_2$ aids fetal $CO_2$ offload)
- **Renal:** ↑GFR/RPF ~50% → ↓creatinine/urea; mild glucosuria
- **Metabolic:** insulin resistance (hPL) spares glucose for fetus

**TRAP:** pregnancy anaemia is dilutional = normal, not pathology. A failure of BP to fall, or rising BP, flags **preeclampsia**.

```
CARDIAC OUTPUT
CO = HR × SV
↑ ~30–50% in pregnancy
(early via ↑HR, later via ↑SV)
```

## 24b · DOHaD — BARKER

An adverse in-utero environment programmes later disease (CVD, T2DM, obesity). **Thrifty phenotype:** a nutrient-restricted fetus adapts to scarcity; a postnatal **mismatch** with plenty → metabolic disease. Mediated by **epigenetic** change (DNA methylation), e.g. reduced nephron number.
**TRAP:** it is the *mismatch* that harms; **low birth weight** is the classic marker.
**Screening vs diagnostic:** screening (e.g. NIPT, combined first-trimester) estimates *risk* — judged by sensitivity/specificity/false-positive rate; diagnostic (CVS, amniocentesis) is definitive but invasive (miscarriage risk). A positive screen needs a confirmatory diagnostic.
**Calculator note:** sensitivity = true positives / all affected; specificity = true negatives / all unaffected; a false positive is a high-risk screen in an unaffected pregnancy — high sensitivity catches cases, high specificity avoids needless invasive tests.

## 25 · Onset of Labour — 4 DRIVERS

1. **Progesterone functional withdrawal** — its quiescence action falls near term → myometrial excitability ↑
2. **Oestrogen priming** — ↑oxytocin receptors + ↑gap junctions (coordinated contraction)
3. **Oxytocin positive feedback** (the loop, §26)
4. **Prostaglandins** — fetal membranes → cervical ripening + ↑contraction strength

**TRAP:** in humans it is a functional/relative progesterone withdrawal (not always a blood-level drop). Oestrogen *primes*, it does not directly contract. Contrast: many animals show an *absolute* progesterone fall before labour.
Triggers behind the functional withdrawal: inflammation, placental senescence, uterine distension and fetal/maternal stress (fetal cortisol via the HPA axis) — together they convert a quiescent uterus to a contractile one.

## 26 · Oxytocin ⊕ Loop — THE EXEMPLAR

Contraction → fetal head onto cervix → cervical stretch → brain → posterior pituitary releases OXYTOCIN → blood → stronger contraction → more stretch… Self-amplifying; **broken only by delivery** (the stop signal).
Oxytocin from posterior pituitary (made in hypothalamus). **Synthetic oxytocin (Syntocinon)** = uterotonic to induce/augment labour & prevent PPH. THE textbook positive-feedback example.
**Contrast:** most homeostasis is *negative* feedback (returns to set-point); this ⊕ loop deliberately runs *away* from set-point to completion — like the LH surge and the clotting cascade.
The afferent limb (cervical stretch → hypothalamus → posterior pituitary) is the **Ferguson reflex**; oxytocin is the efferent signal that closes the loop on the myometrium.

## 27 · Stages of Labour — 3 STAGES

- **1 · Dilation** — onset → full cervical dilation (10 cm); longest
- **2 · Expulsion** — full dilation → delivery of baby
- **3 · Placental** — delivery of placenta (oxytocin contraction limits bleeding)

**TRAP:** cervix fully dilated at **10 cm**. Stage-3 failure → retained placenta / **PPH** (postpartum haemorrhage, often uterine atony). Stage 1 = latent (slow, to ~6 cm) then active (faster).

## 28 · Lactation — TWO-HORMONE SPLIT

Pregnancy: oestrogen (ducts) + progesterone (alveoli) + prolactin prepare the breast, but high progesterone blocks milk synthesis. After birth **progesterone falls** → brake released.
Prolactin (ant. pit.) MAKES milk (sustained by suckling → ↓dopamine → ↑prolactin). Oxytocin (post. pit.) EJECTS milk (let-down: contracts myoepithelial cells). **Don't swap them.**
Let-down can be *conditioned* (baby crying) and *inhibited by stress*. **TRAP:** retained placental fragments keep progesterone up → delay lactogenesis. Colostrum (IgA-rich) precedes mature milk.
High prolactin during breastfeeding suppresses GnRH → **lactational amenorrhoea** (a natural, partial fertility brake). Suckling drives both hormones — the more the infant feeds, the more milk is made and ejected (a supply-and-demand loop).

## 29 · Fetal Circulation — 3 SHUNTS

**Why:** lungs fluid-filled, high pulmonary resistance; placenta is the $O_2$ source → bypass lungs + liver.

1. Placenta → **umbilical vein (oxygenated!)** → DUCTUS VENOSUS (bypasses **liver**) → IVC → right atrium
2. FORAMEN OVALE (RA → LA, bypasses **lungs**) → LV → aorta → brain (best-oxygenated)
3. Pulmonary artery → DUCTUS ARTERIOSUS (PA → aorta, bypasses **lungs**) → body → umbilical arteries → placenta

Most-oxygenated blood is preferentially streamed (via the foramen ovale) to the left heart → aorta → brain & coronaries, while less-oxygenated blood is shunted through the ductus arteriosus to the lower body and back to the placenta.
**At birth:** first breath → lungs inflate → PVR drops; LA pressure ↑ → foramen ovale closes (fossa ovalis); ↑$O_2$ → ductus arteriosus closes (lig. arteriosum); ductus venosus closes (lig. venosum).
**TRAP:** ductus venosus → liver; foramen ovale + ductus arteriosus → lungs. Umbilical VEIN = oxygenated (reverse of usual). Failures: PFO, PDA.

## 30 · Fetal Haemoglobin — HBF

**HbF** has higher $O_2$ affinity than adult HbA → a left-shifted dissociation curve → at the low placental $PO_2$ it **pulls $O_2$ off maternal Hb** across the placenta.
HbF is replaced by HbA over the first ~6 months of life. At the placental working $PO_2$ (~25–30 mmHg) HbF sits at higher saturation than HbA — the gradient that drives $O_2$ transfer to the fetus.
**Why left-shift:** HbF binds 2,3-BPG weakly, so it holds $O_2$ more tightly. Combined with a higher fetal Hb concentration, this maximises $O_2$ uptake from the relatively hypoxic maternal blood.

## 30b · Birth Transition — NEONATE · MODULE 11

First breath → lungs inflate → PVR drops; cord clamp → SVR rises → pressures reverse → shunts close. Other transitions: thermoregulation begins (brown fat), independent glucose handling, gut/liver take over (jaundice if immature).
**TRAP:** persistent shunts = **PFO / PDA**; ductus arteriosus is kept open by prostaglandins ($PGE_2$) — indomethacin closes it. Closure order: ductus venosus (minutes) → foramen ovale (functional, with the pressure flip) → ductus arteriosus (hours–days). Remnants: fossa ovalis, lig. arteriosum, lig. venosum.

## 31 · Reproductive Ageing — MODULE 6

**Female:** ovarian reserve + oocyte quality fall → ↑aneuploidy with maternal age (non-disjunction in long-arrested oocytes). **Menopause** = follicle depletion → ↓oestrogen/inhibin → loss of ⊖ → ↑FSH/LH (high FSH = marker).
**Male:** more gradual decline in testosterone & sperm quality; paternal age raises some new (de novo) mutations. No abrupt "andropause" equivalent of menopause.
**TRAP:** postmenopausal FSH is HIGH (counterintuitive) — no inhibin/oestrogen to give negative feedback. Trisomy 21 risk rises sharply with maternal age via meiotic non-disjunction.
**Reserve markers:** AMH (from small follicles) and antral follicle count estimate remaining reserve and predict IVF response; both fall with age. Menopause = ~12 months without menses.

## 32 · Contraception — MODULE 3

- **Hormonal** (pill, POP, implant, injection, hormonal IUD) — ⊖ feedback suppresses FSH/LH → no LH surge → no ovulation; thickens cervical mucus; thins endometrium
- **Barrier** — condoms (only these reduce STIs), diaphragm
- **IUD** — copper (spermicidal/inflammatory) or hormonal
- **Emergency** — levonorgestrel delays ovulation
- **Sterilisation** — tubal ligation; vasectomy (cut vas)
- **Emerging male** — testosterone ± progestogen suppress spermatogenesis (⊖ feedback)

**Common thread:** most hormonal methods exploit the same physiology this sheet covers — feed back negatively to block the LH surge, so no ovulation occurs. Only **condoms** also protect against STIs.

## 33 · ART / IVF — MODULE 6

**IVF steps:** (1) ovarian stimulation (FSH grows many follicles) + GnRH agonist/antagonist to block a premature surge; (2) hCG "trigger" mimics the LH surge → final maturation; (3) oocyte retrieval; (4) IVF; (5) culture; (6) embryo transfer + luteal progesterone support.
**ICSI** — single sperm injected; for **male-factor** infertility.
**PGT/PGD** — genetic testing pre-transfer.
**TRAP:** the hCG trigger *substitutes for the natural LH surge*. ICSI is for male-factor, not routine.
**IVM** matures immature oocytes in vitro (avoids high-dose stimulation). **IUI** = prepared sperm placed in the uterus (mild cases). Luteal progesterone support replaces the corpus luteum the cycle would have made.

## 34 · Complications & STIs — MODULE 5/10

**Preeclampsia** ← failed EVT spiral-artery remodelling → placental ischaemia (HTN + proteinuria >20 wk). **IUGR**, gestational diabetes (hPL), miscarriage (often chromosomal), placenta praevia vs accreta, preterm labour, PPH.
**Drugs:** tocolytics STOP contractions; uterotonics CAUSE them. Targeted drug delivery (e.g. to the placenta/uterus) aims to treat the mother or fetus while sparing the other.
**STIs:** bacterial (chlamydia, gonorrhoea, syphilis) = **curable** (antibiotics); viral (HIV, HSV, HPV→cervical Ca, HepB) = managed, not cured. Chlamydia = silent cause of **PID → tubal infertility & ectopic risk**; HPV vaccine prevents.

## 35 · Side-2 Trap List — ONE GLANCE

1. **Capacitation** in the female tract, not before.
2. Implantation **Apposition→Adhesion→Invasion**; **syncytiotrophoblast** invades + makes hCG.
3. **hCG rescues the corpus luteum**; luteal–placental shift wk 6–9.
4. 3 shunts: ductus venosus→**liver**; foramen ovale + ductus arteriosus→**lungs**. **Umbilical vein = oxygenated.**
5. **Prolactin makes, oxytocin ejects** milk. Oxytocin loop = ⊕ feedback.
6. Pregnancy anaemia = **dilutional/normal**; postmenopausal **FSH high.**

**SIA →** *The big short-answer earners: draw/state the oxytocin ⊕ loop, name all 3 shunts + what each bypasses, and explain the luteal–placental shift. Write the mechanism, not just the label.*