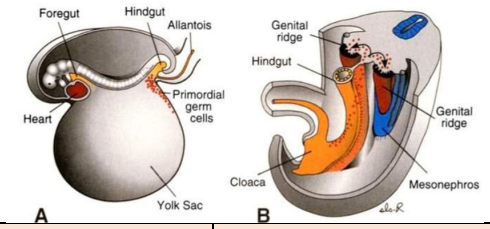
REPRODUCTIVE SYSTEM

REPRODUCTIVE EMBRYOLOGY

<table>
<tr><th></th><th colspan="2">Female</th><th colspan="2">Male</th></tr>
<tr><td>Indifferent stage
[Wk 6-7]</td><td colspan="4">• Indifferent Gonads are derived from BOTH germ cells & primitive sex cords:
○ Genital/Gonadal ridge [mesothelial layer of the peritoneum derived from germ cells of endoderm in Week 4]
○ primitive sex cords [proliferation of epithelium of the genital ridges]
*NB: Genital ridge (i.e. gonads) connected to scrotum/labia via gubernaculum (a ligamentous structure derived from mesenchyme)
 
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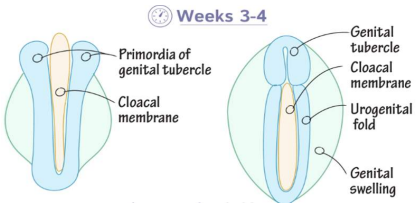
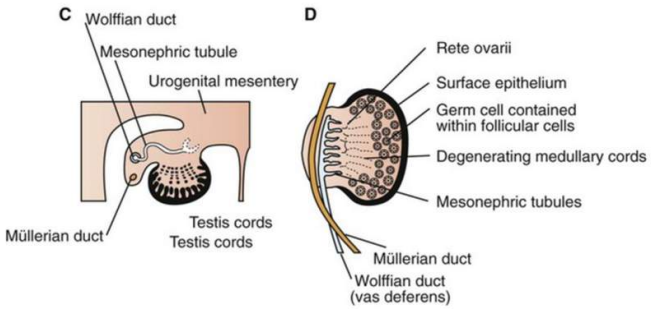
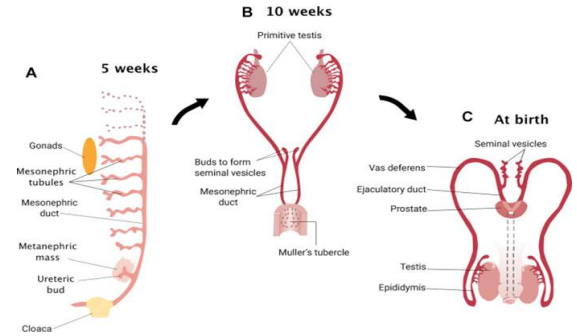
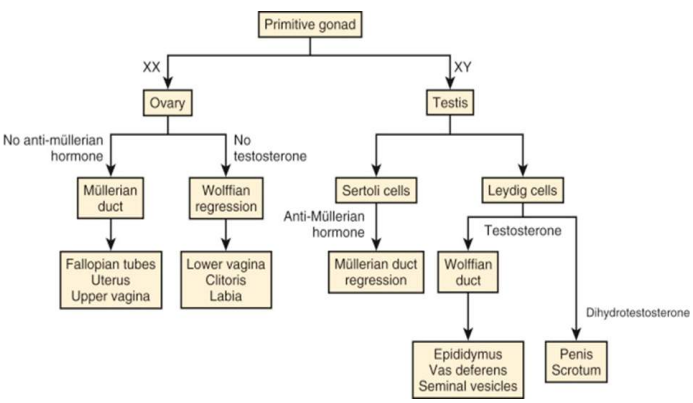
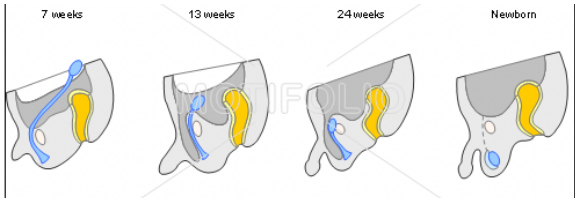
<tr><td>Embryology</td><td>Internal Genitalia</td><td><u>External</u> Genitalia</td><td>Internal Genitalia</td><td><u>External</u> Genitalia</td></tr>
<tr><td>Un-differentiated stage</td><td>• No Y chr. = No SRY gene
• No Leydig cells = No testosterone ➔ primitive sex cords degenerate = NO testic cords formed
• <u>No</u> Sertoli cells = <u>NO</u> anti-mullerian hormone → paramesonopheric ducts
• Gonadal epithelium proliferate ➔ becomes cortical cords → surround germ cells with epithelial follicular cells → primordial follicle</td><td><u>Mesenchymal cells</u> migrate to cloacal membrane ➔ forms cloacal folds:
• Fusion of folds cranially = genital tubercle
• Fusion of folds caudally = urethral folds (anterior) and anal folds (posterior)
• Either side of folds = Genital swellings</td><td>• SRY gene = triggers primitive sex cord development to form testis cords surrounded by tunica albuginea
• Testis cords = 2 cell types = Sertoli cells & Leydig cells</td><td>SAME
➢ Proliferation of ectoderm and mesoderm around closed membrane forms genital tubercle, genital swelling and congenital fold
 
</td></tr>
<tr><td>Differentiated stage</td><td><u>Anti-mullerian hormone</u>
• paramesonopheric ducts = fallopian tubes & uterus, cervix and upper 1/3 of vagina
• Proximal part = separature tube
• Distal part – uterus fusion

NB: urogenital sinus ➔ sinovaginal bulbs ➔ lower 2/3 vagina</td><td><u>Oestrogen causes:</u>
• Genital tubercle elongates ➔ clitoris
• Urethral folds (labia minora) & genital swellings (labia majora) do <u>NOT</u> fuse
• Urogenital groove remains open ➔ vestibule</td><td>1. Sertoli cells (germ) → epithelial cells → Secrete anti-Mullerian hormone to degenerate Paramesonephric ducts (becomes appendix testis) → At puberty: cords acquire lumen → become seminiferous
2. Leydig cells → mesoderm cells → produce TT to induce mesonephric ducts differentiation ➔ epididymis, vas deferens and seminal vesicles</td><td>Testes secrete androgen (DHT) to:
• Elongate genital tubercle ➔ phallus
• Pull Urethral folds ➔ urethral groove ➔ fold over ➔ penile urethra [4TH MONTH]
• Genital swellings ➔ scrotal swellings, moving caudally to eventually form the scrotum</td></tr>
<tr><td></td><td colspan="2"> 
</td><td colspan="2"> 

Proximal mesonephric duct = highly convoluted epididymis
Urogenital sinus = prostrate gland + bulbourethral glands</td></tr>
<tr><td>Descent of gonads</td><td colspan="2">• Ovaries migrate caudally but to lesser extent than testes ➔ reaches just within the true pelvis
• Remnant of gubernaculum = ovarian ligament + round ligament of the uterus
 
</td><td colspan="2">• Testes migrate caudally as foetus grows
• 28th week: Testes enter inguinal canal ➔ reach scrotum by 33rd week [retains testicular arterial supply from lumbar aorta]
• Remnant of gubernaculum = Scrotal ligament
ANOMALIES
• Hypospadius = external urethral orifice on ventral surface of penis/glans
• Cryptorchidism = failure of testes to descend into scrotum leading to ectopic testes [due to unusual descent route]
• Ectopic testes – undescended testes away from normal descent pattern
 
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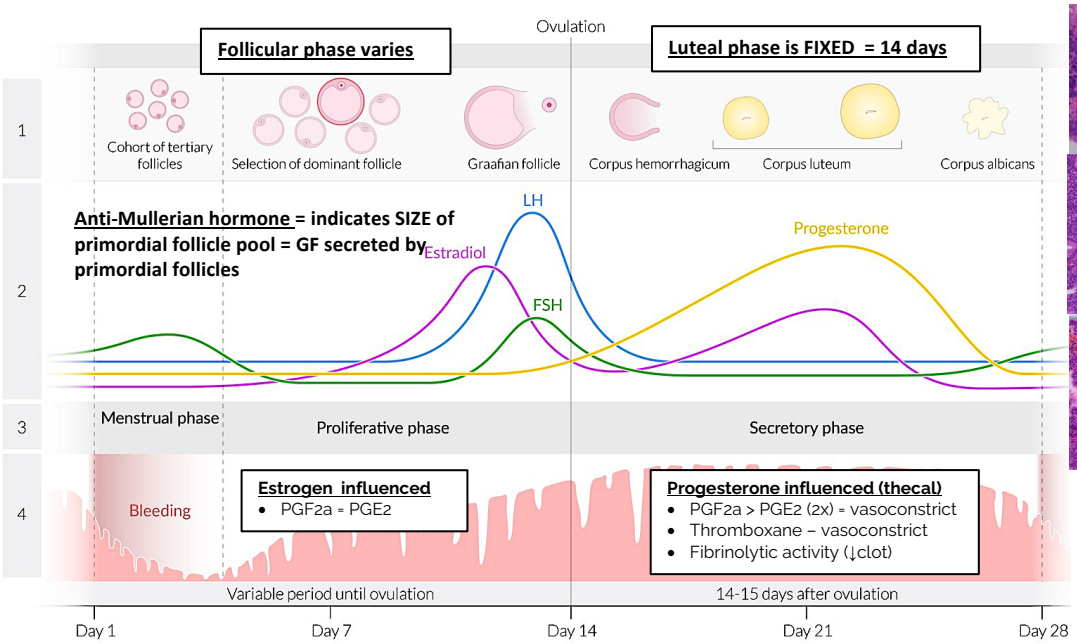
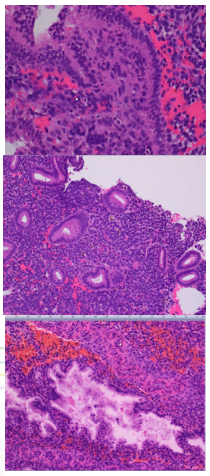
NORMAL MENSTRUAL CYCLE (21-35 days)





MENSES PHASE
Loss of star-shaped glands
Stromal (slough + haemorrhage)

PROLIF PHASE
Test tube glands
Mitotic figures

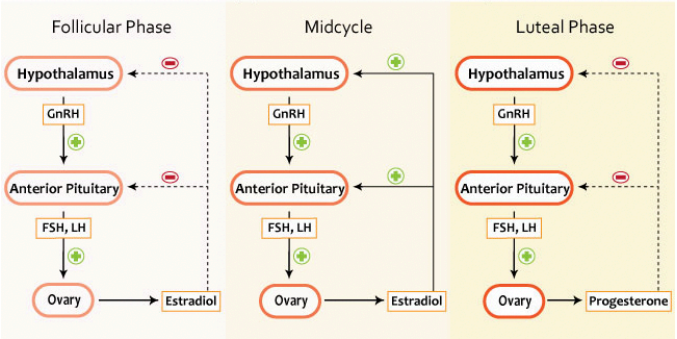
SECRET PHASE
Star shaped corkscrew gland dilated
Coiled arteries

TOP medications)
- **Misoprostol** – synthetic PG – induce uterine contractions
- **Mifepristone** = synthetic anti-PG - ↓embryo implantation
- **Prostacyclin (PGI2)** = arachidonic acid metabolite = relax uterine muscle tone

Stages	Day / Length	Hormones	Event
Phase 1: follicular (proliferative)	0-13 (Variable) (Older = shorter - fewer eggs, PCOS = longer as no dominant follicle to suppress others)	↑FSH	• **1st day of cycle = 1st day of period** • **Folliculogenesis** = primordial follicles develop into a **single mature, dominant Graafian follicle** [*limited # of follicles at birth] Primordial → primary → secondary → tertiary "antral" follicles → Graafian follicles
		↑Estrogen	• Estrogen causes endometrial proliferation = thicker endometrium
Phase 2: mid-cycle or ovulation	14 [LH surge day 9-16]	**HPA +ve feedback**	• **↑ 17β-oestradiol ↑↑ FSH & ↑↑ LH ➔ ovulation**
		↑↑ FSH & LH	• Breakdown wall of graafian follicle → ruptures → releases *secondary oocyte* into peritoneal cavity • Picked up by *fimbriae* of Fallopian tube → *infundibulum* → *ampulla* via *ciliary* movement of tubal epithelium on fallopian tube
Phase 3: luteal (secretory) phase	Day 15-28 Fixed at 14 days [**ovulation to start of menstruation**]	**↑ LH = ↑ progesterone**	**1)** **↑↑ LH → (+)** theca cells → ↑ progesterone (major) drive development of corpus luteum **2)** Corpus luteum (*ruptured Graafian follicle (i.e. granulosa and theca cells)*) ➔ also synthesizes/secretes17β-oestradiol • makes endometrium more glandular support embryo implantation • increases hypothalamic-set point to raise basal body temperature
Phase 4: menses of pregnancy	ovulation day + 14 days = menstruation	**Menses**	• **Corpus luteum regresses** → replaced by fibrotic scar (corpus albicans) ○ Spiral arteries contract to reduce blood loss during menstruation ○ **regression** = abrupt loss of progesterone and 17β- oestradiol • No fertilisation = endometrial lining sloughs ➔ menstrual bleeding
		Pregnancy	• **Fertilisation ➔ syncytiotrophoblasts secrete** hCG ➔ preserves corpus luteum ○ Synctiotrophoblasts produce villi to increase surface area around maternal uterine blood vessels ○ Thin membrane of cytotrophoblasts allows diffusion and removal of nutrients, wastes, gas → gradually develops into placenta • corpus luteum continues to produce/secrete progesterone and 17β-eostradiol • After 8 weeks: Placenta takes over to produce **PG, E2**

Hormone	Oestrogen	Progesterone
Cells	Granulosa cells	Theca cells
Origin	Ovaries	Corpus luteum (Ovary) / Placenta (5-10/40)
Role	Develop Female 2° sex characteristics (breast, vulva, vagina)	Maintain pregnancy ➢ Drive corpus luteum development
Fallopian tube	• Proliferation • Secretion of sugar rich fluid	• Reduce # of cilia • Reduce secretions
Endometrial effect	• Angiogenesis in uterus • Endometrial proliferation	Thicken and maintain endometrium
Cervix	Thins cervical mucus	Thicken cervical mucus
Other	Stop milk production	• Stop milk production • ↑ basal body temp (peripheral vasodilation + increased metabolism) • ↑ tidal volume (relax diaphragm and intercostals)

Female Hypothalamus-Pituitary Axis



*Hormonal Changes During Puberty (**TANNER STAGING**)*

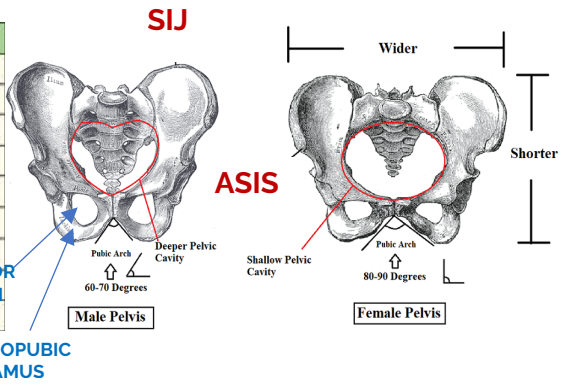
1) ***GH*** increases initially ➔ GROWTH spurt

2) HT secretes GnRH during sleep then during day → rising FSH/LH → rising estrogen and progresterone levels

3) FSH levels plateau (year before menarche)

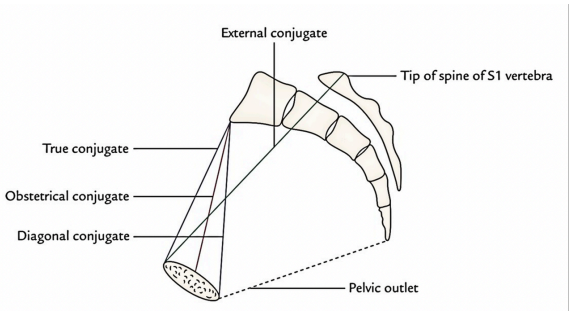
4) LH continue to rise and spike just before they induce menarche

Bony Pelvis	Male (♂)	Female (♀)
General structure	Thick and heavy	Thin and light
Greater pelvis (false pelvis)	Deep	Shallow
Lesser pelvis (true pelvis)	Narrow and deep, tapering	Wide and shallow, cylindrical
Pelvic inlet (superior pelvic aperture)	Heart-shaped, narrow	Oval and rounded; wide
Pelvic outlet (inferior pelvic aperture)	Comparatively small	Comparatively large
Pubic arch and subpubic angle	Narrow (<70°)	Wide (>80°)
Obturator foramen	Round	Oval
Acetabulum	Large	Small
Greater sciatic notch	Narrow (~70°); inverted V	Almost 90°



Clinical significance of the subpubic angle:

- Wider angle in females accommodates growing fetus in uterus during pregnancy
- Also makes childbirth easier to pull head through



What ligaments relax during pregnancy?

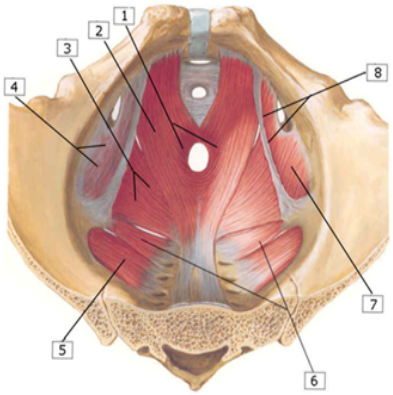
Mainly ligaments that expand pelvic space anterior-posteriorly

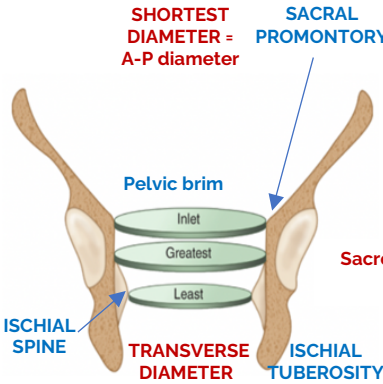
- Cardinal ligaments (transverse cervical ligament)
- Anterior/posterior sacral ligament
  - **Anterior** = pubocervical ligament
  - **Posterior** = uterosacral ligament
- Ligaments atrophy post-menopause ➔ greater risk of direct inguinal hernia or prolapse

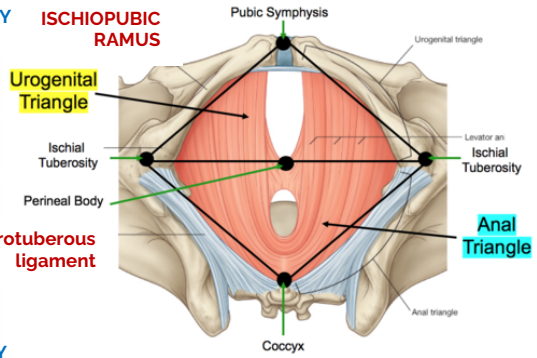
Determine if child can come out

Palpable (physically measures)

Pelvic floor & perineum and discuss their importance in clinical practice







Pelvic Outlet:

Levator ani (S2-S4 - keep poo of f the floor)

1. **Puboanalis/Puborectalis** ➔ prevent feacal incontinence
2. **Pubococcygeus** ➔ support pelvic floor
3. **Iliococcygeus** ➔ elevate pelvic viscera

4. **Obturator fascia**
5. **Piriformis muscle**
6. **Ischio-coccygeus muscle** → pull coccyx forward for defecation
7. **Obturator internus muscle**
8. **Tendinous arch of levator ani muscle**

Clinical importance of Perineum & pelvic diaphragm in childbirth

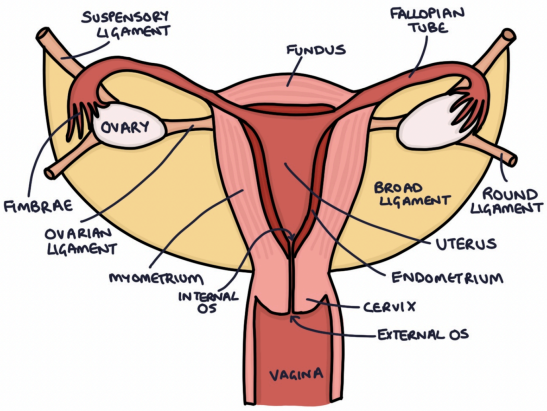
- **During childbirth**, the pelvic diaphragm should relax and stretch to thin out ➔ avoids excessive tearing of the perineum during delivery
- **Extra folds of skin** inside the vagina, **called ruggae,** ➔ allows extra stretching that will take place during delivery
- *Perineal stretch in last stage of parturition ➔ perineal tear
  - Affects pre-, post- and future pregnancies

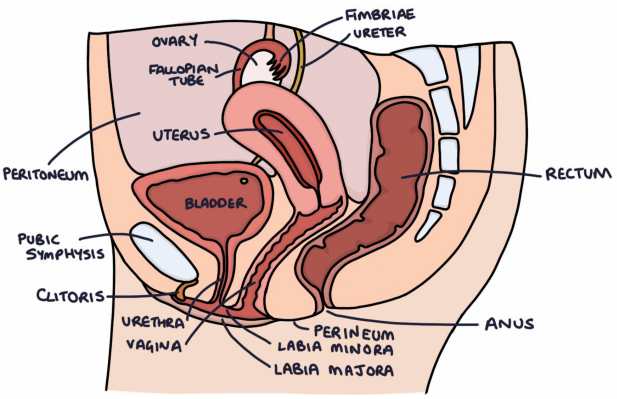
Laxity of pelvic diaphragm muscles post-childbirth + menopause can lead to uterine, bladder and rectal prolapse

➢ *Stress incontinence → laugh, cough and exercise*

	Description	Significance
Perineal body	central tendon of perineum that attaches perineal muscles to support pelvic floor	➔ damage leads to prolapse of pelvic viscera
Perineal membrane	dense fascia in perineum that divides **urogenital triangle** into superficial (inferior) and deep (superior) perineal pouches	Provide attachment for muscles of external genitalia
Pelvic diaphragm = pelvic floor	• muscle fibers of the levator ani, the coccygeus muscle → separates the **pelvic** cavity above from the **perineal** region (including **perineum**) below	• supports the pelvic organs and closes off the pelvic outlet, while allowing passage for the rectum, **vagina** and **urethra**
Urogenital triangle	root of penis + scrotum (M) or external genitalia (F)	
Anal triangle	Ischio-anal fossa (loose CT +fat)	space where **infection** can occur

FEMALE REPRODUCTIVE ANATOMY





Common Q's

Origin of L/R ovarian atery

- *Descending L2 aorta*

Drainage of L/4 ovarian vein

- *L renal vein or IVC*

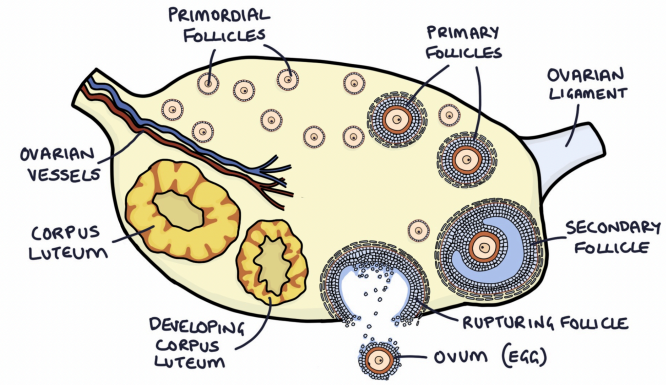
Locate ureter

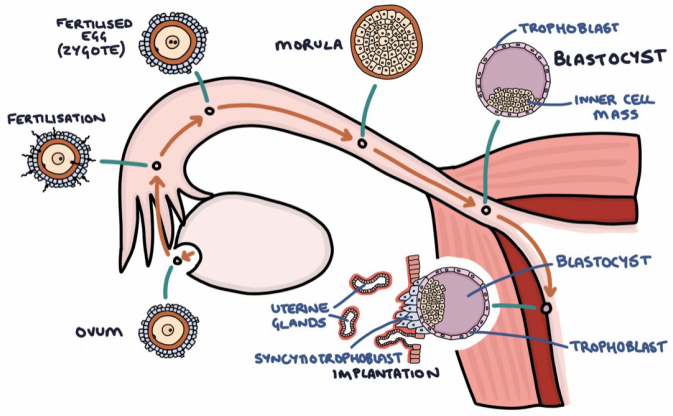
- *Pelvic brim*
- *Medial lead of broad ligament*
- *Under uterine artery*

Artery running under round ligament

- Sampson's artery

OVULATION, CONCEPTION AND IMPLANTATION

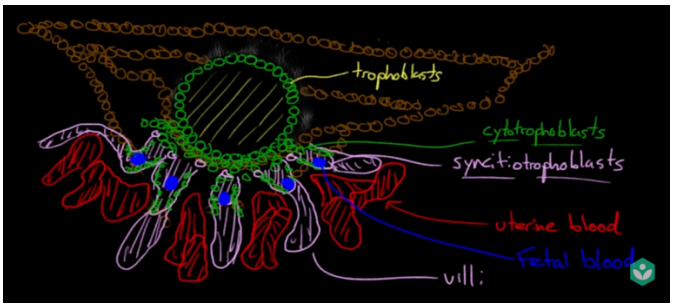


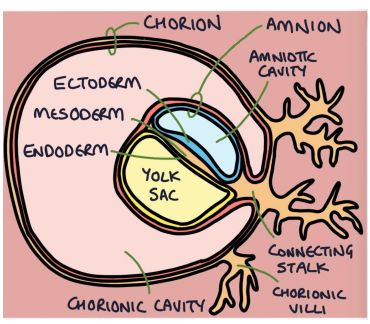


STAGE	DESCRIPTION
Primordial follicle	**3 layers:** ➢ Primary oocyte (centre) ➢ Zona pellucida ➢ Cuboidal shaped granulosa cells *Granulosa cells secrete material for the development of:* ➢ Theca interna = secrete androgens ➢ theca externa = smooth muscle
Secondary follicle	• Large primordial with fluid filled gaps b/w granulosa cells • Have FSH receptors
Antral follicle	• Single large fluid filled area (antrum) • Corona radiata = granulosa cells that surround zona pellucida and oocyte • One follicle becomes dominant
Ovulation	• Primary oocyte undergoes **meiosis (haploid cell) →** leftover chromosomes become polar body • **LH surge** → smooth muscle in theca externa contract → release follicle • Ovum picked up by fimbriae
Corpus luteum	Collapse follicle becomes corpus luteum **➔ corpus albicans (white scar tissue)** ➢ Granulosa cells + theca interna = luteal cells ➢ Luteal cells = secrete mainly progesterone **(highly responsive to HCG)**

Fertilisation and implantation

1. Haploid sperm fertilises haploid ovum **→ diploid zygote**
2. Zygote Cleavage → **morula** (ball of undiff. Cells)
3. Forms **Blastocyst** = embryoblasts (inner cell mass) with hollow cavity (blastocele) surrounded by trophoblasts
4. **Day 8-10 after ovulation** = blastocytes enters endometrium
    a. **Synctiotrophoblasts** (outer layer of trophoblasts) → produce villi projections into stroma to increase SA around maternal uterine blood vessels [**HIGH FLOW, LOW RESISTANCE**]
        i. If unable = pre-eclampsia, IUGR, placental abruption
    b. Stroma become **decidua → provides nutrients to trophoblasts**
    c. **Synctiotrophoblasts** = secrete B-HCG (maintain corpus luteum until placenta forms)
5. Thin membrane of *cytotrophoblasts* allows diffusion and removal of nutrients, wastes, gas → gradually develops into placenta



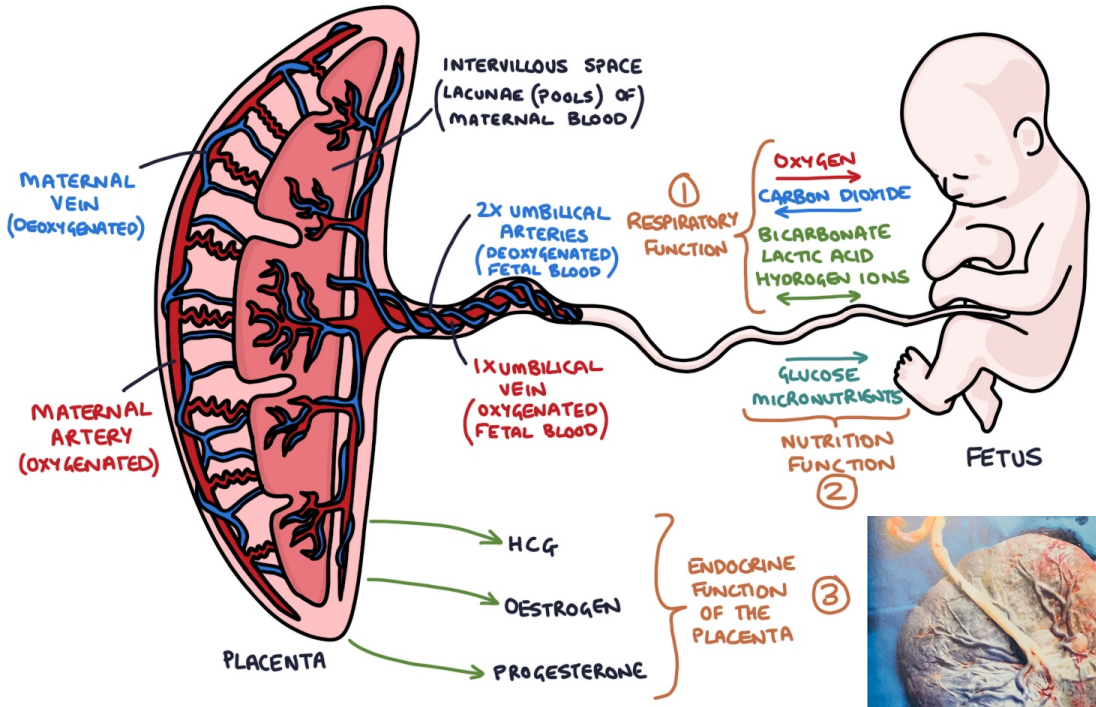


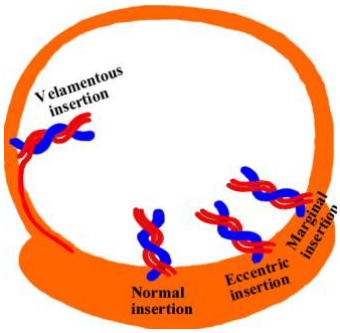
ENDODERM	MESODERM	ECTODERM
* GI TRACT	* HEART	* SKIN
* LUNGS	* MUSCLE	* HAIR
* LIVER	* BONE	* NAILS
* PANCREAS	* CONNECTIVE TISSUE	* TEETH
* THYROID	* BLOOD	* CENTRAL NERVOUS SYSTEM
* REPRODUCTIVE SYSTEM	* KIDNEYS	

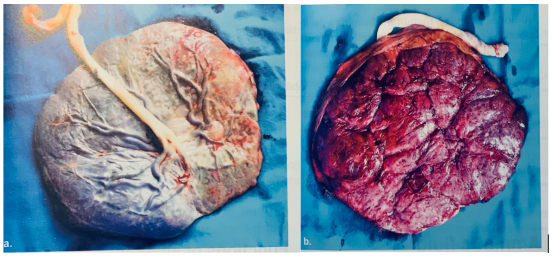
Embryo development

- *5/40 = **Gastrulation** in trilaminar disc (ecto, meso and endoderm)*
- *6/40 = fetal **heart** forms and beats*
- *6/40 = **spinal cord** and **muscles** develop)*
- *8/40 = all major organs develop*

DEVELOPMENT AND FUNCTION OF PLACENTA







- **Fetal portion (*chorion Frondosum*) | Maternal Surface (*Decidua basalis*)**
- **Umbilical cord (*centrally placed*)**

Placental and Umbilical Cord Development

1. Outer layer = ***syncytiotrophoblast***, grows into the ***endometrium*** with ***chorionic villi***, which contain fetal BV.
2. The chorionic villi nearest the connecting stalk of the developing embryo are the **most vascular** and contain ***mesoderm*** ➔ this area known as ***chorion frondosum***
3. The cells in the ***chorion frondosum*** proliferate and become the placenta.
4. Connecting ***stalk*** becomes the ***umbilical cord***. Placental development is usually complete by 10 weeks gestation.

Development of the Lacunae

1. Trophoblast invasion of the endometrium sends signals to the ***spiral arteries*** in that area to create **low vascular resistance and high blood flow**
2. Around 20/40 GA ➔ Increased blood flow causes BV to breakdown → creates pools of blood (lacunae)
3. Maternal blood flows from the ***uterine arteries***, into these ***lacunae***, and back out through the ***uterine veins***.
4. ***Lacunae*** surround the ***chorionic villi***, separated by the ***placental membrane*** – allow Xchange of nutrients and waste
    i. ***If high resistance or inadequate lacunae formation ➔ pre-eclampsia, IUGR, placental abruption***

Function	**Involvement**	**Clinical Significance**
Respiratory	HbF (higher affinity for O2) than HbA – attract oxygen off maternal Hb	Initial WOB post-partum
Nutrition	All nutrients/vitamins and minerals from mother	Drugs also diffuse
Excretion	Filter waste products (e.g. urea and creatinine) ➢ Xchange CO_2, H^+, HCO_3^- and lactic acid to maintain acid-base balance	
Endocrine	Secrete estrogen and progesterone to maintain endometrium at 5-10 weeks GA ➢ Estrogen = laxity of muscles/ligaments to allow pelvis to expand and soften cervix (↑ **lactiferous ducts = breast enlargement)** ➢ Progresterone = maintain pregnancy, relax uterine muscles (to prevent labour)	Higher B-HCG (molar pregnancies or twins) A/E of progesterone = LES weak (GOR), constipation and BV relaxed (hypoTN, headache, skin flush), raised basal body temp.
Immunity	Maternal antibodies can be transferred (e.g. antibodies against recurrent genital herpes)	IUTD, TORCH infection

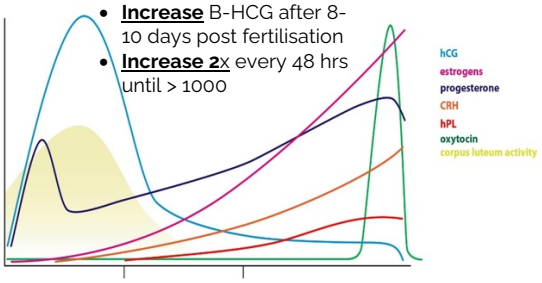
Pregnancy Physiological Changes → Sx + Mx (Hormone-dependent)

Hormone	Origin	Function
Oestrogen	Corpus luteum	• Growth of uterus, endometrium, breast • ↑ CO + prepare for delivery • ↑ **lactiferous ducts**
Progesterone	Corpus luteum	• ***Angiogenesis*** → maintain uterine lining • ↑ **lobules** = Breast growth + milk production • ***Smooth muscle relaxant*** = Inhibit uterine activity + GI motility = gastric upset / bloating
HCG	Placenta	• Maintain corpus luteum • ↓TSH, ↑T3/T4 (early pregnancy) → hypothyroid later
HPL	Placenta	• Regulate metabolism by stimulating IGF-1 production • ↑insulin ➔ insulin resistance (peaks @ 3rd trimester) • ↑BSL + lipolysis ➔ sufficient sugars for foetus

Oxytocin	Pituitary	• Stimulate uterine contraction
		• Trigger prostaglandin production := breakdown collage in cervix to dilate and efface during childbirth
		  ○ ***PGI2 = vasodilate*** = ↓BP during early pregnancy = prevent pre-eclampsia
		  ○ ***PGE2/F2a = vasoconstrict*** = ↓bleeding during childbirth

WHY CARE ABOUT B-HCG?

- **Increase** B-HCG after 8-10 days post fertilisation
- **Increase 2x** every 48 hrs until > 1000



E2 and PG sig. drop during birth!!

[hormone drop = "3-day blues" = mood swings]

Take serial *B-HCG or transvag USS

ectopic (until proven otherwise), *miscarriage, abnormal pregnancy, cancer (e.g. germ cell tumour of ovary- normal periods)*

NEURO SX

↑↑E2 = affects pain fibres

- *Headaches, migraines, N/V*
- *Paresthesia – carpal tunnel*

HORMONAL SYMPTOMS

High ACTH, A-MSH

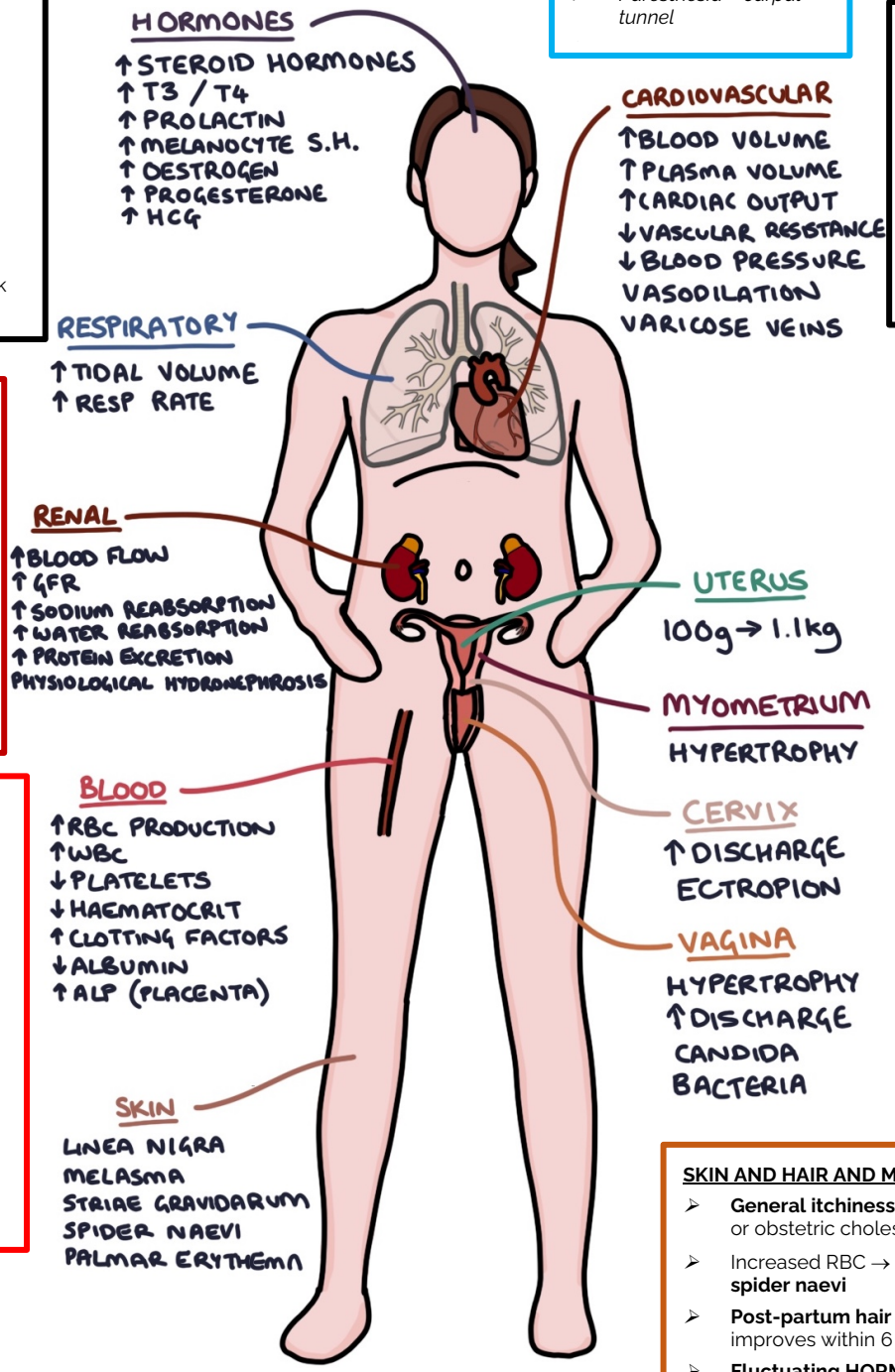
- *Linear nigra and mleasma*

Elevated T3/T4

- Palpitations, SOB

Elevated steroid (cortisol and aldosterone)

- Improves autoimmune conditions
- ++ infection and diabetes risk



CARDIOVASCULAR SX

Peripheral vasodilation

- *Flushing / hot sweats)*
- *Varicose veins*

Increased SV/HR (CO)

- Palpitations, SOB

Increased TV/RR

- **Tachypnoea** (maintain O2 demand)

RENAL SYMPTOMS

+GFR, Blood flow

- *Polyuria/Nocturia*
- *UTI risk*
- *Low urea/CR = normal*

Increased protein excretion

- Frothy urine
- hypoalbuminemia

Dilated ureters/collecting system

- R) sided hydronephrosis

GASTRO SX

↑↑PG = ↓Peristalsis

- *GORD, Constipation = haemorrhoids*
- *Rx: small meals, PPI*

E2 +PG

- Hyperemesis gravidarum

BLOOD SYMPTOMS

Increased RBC production

- *Low HCT – Anaemia (fatigue, SOB, palps)*
- *Higher Fe, folate, B12 req.*

Increased clotting factors (fibrinogen, F7, F8, F10)

- VTE (DVT and PE)

Low albumin

- Proteinuria

Other changes

- High ESR/d-dimer
- Normal ca levels (but increased Ca absorp)

GYNAECOLOGICAL SX

Growing fetus

- *Weight gain*
- *Abdo distension - Straia gravidarum (stretch marks)*

Increased Estrogen

- Cervical discharge
- Cervical ectropion
- Candida infection

SKIN AND HAIR AND MOOD CHANGES

- **General itchiness (PRURITUS) ➔** normal or obstetric cholestasis
- Increased RBC → **palmar erythema and spider naevi**
- **Post-partum hair loss** = normal and improves within 6 weeks
- **Fluctuating HORMONES = IRRITABLE, INSOMNIA, TEARFUL, POOR CONC.**