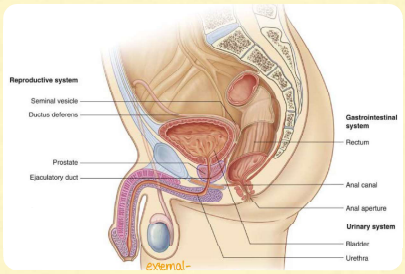
Reproductive System

Male Reproductive System

The Testes

- made up of tightly coiled tubes called the **seminiferous tubules**. These tubules are made up of **Sertoli** cells which is where spermatogensis (35 degrees) and sperm maturation occurs. The mature sperm are then released into the tubule lumen to go to the epididymis
- Surrounding these tubules is the interstitum called the **tunica albuginea**. This contains cells called **Leydig** cells which produce testosterone (which is a lipid so these cells contain lots of SER and lipid droplets).
- The seminiferous tubules continue into the efferent ductules (where excess fluid is lost to give concentrated sperm), then becomes the epididymis (where sperm further mature) and then finally the vas deferens (surrounding muscle contracts in ejaculation)
- The outside of the testes have a peritoneal membrane called the tunica vaginalis. **Hydrocoele** is a condition where this membrane becomes fluid filled and swollen. If shining a light on this swelling it will trans-illuminate
- The arterial blood supply is via the abdominal artery. (Gonadal artery)
- The venous drainage differs on the left and right. On the right the testicular vein drains directly into the IVC but on the left it drains into the left renal artery before the IVC. The **pampimiform** venous plexus is a net shaped system which comes together to form the testicular vein - the advantage of this is that it creates a larger surface area to exchange heart from the passing artery to keep the testes cool.
- The lymphatic drainage of the testes goes up into the abdominal cavity to the para-aortic nodes. Therefore, for testicular cancer a mass will not be felt but will be seen on a MRI around the nodes of the heart. This is different to the scrotal drainage which goes to the inguinal region, so swelling in the groin would suggest scrotal cancer.
- There may be many reasons for a **swelling of the testes** including; infection, inflammation, testicular torsion, hydrocoele, haematocoele (where damage to the testicular artery or vein causes blood to accumulate in the tunica vaginalis), vericoele (dilation of the pampimiform venous plexus which then goes to the testicular vein. This happens on the left as the vein goes to the renal artery before the IVC making it more congested. It shouldn't occur on the right therefore this would imply a mass or occlusion of the IVC.
- **Testicular torsion** occurs when the spermatic cords becomes twisted. This occludes the veins giving an increase in pressure which will eventually occlude the arteries. After 12 hours the testicle is unsalvageable. Surgery is required to untwist the cord and sew the testes to the scrotum. This is more common with a bell clapper shaped corpus vaginalis.

Anatomy



Spermatic Cord

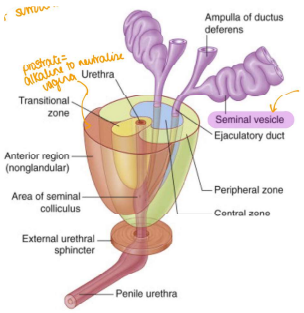
made up of 3s:

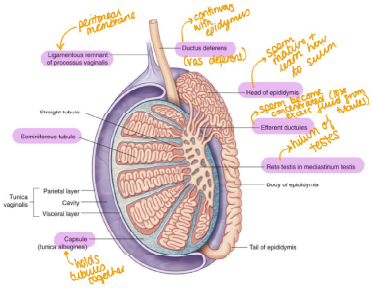
- 3 fascia layers (internal, cremasteric, external)
- 3 arteries (testicular, to the vas, cremasteric)
- 3 veins (testicular, to the vas, cremasteric)
- 3 nerves (ilioinguinal, cremasteric, sympathetic)
- Also contains the vas deferens
- The cremasteric artery, vein and nerve supply the cremasteric muscle which pull up the testes.

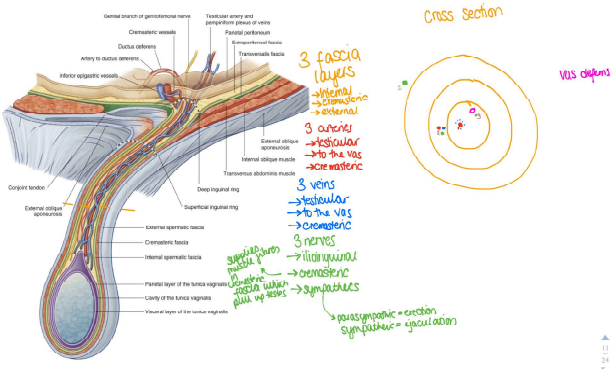
Layers of the Scrotum

S - skin
D - dartos fascia and muscle
E - external spermatic fascia (derived from the external oblique muscle)
C - cremasteric fascia and muscle (derived from the internal oblique muscle)
I - internal spermatic fascia (derived from the transverse abdominal muscle)
T - tunica vaginalis
T - tunica albuginea

The fascia is derived from muscles in the abdominal wall which surrounded the testes are is moved down through the abdomen to it position.







Prostrate

- the prostrate is a collection of glands which fully surrounds the urethra
- The *function* is the prevent urine escaping (as it surrounds the urethra) and also to produce an alkaline solution to neutralise the acidity of the vagina.
- In Benin Prostatic Hypertropy the **transitional zone** of the prostrate grows, compressing the urethra giving urinary problems
- In prostrate cancer the **peripheral zone** grows, but as this is next to the rectum there is no urinary problems and can be felt on rectal examination
- The vas deferens also goes through the prostrate, however just before it does the ejaculatory duct join it, bringing a fructose rich solution produced by the seminal vesicle. This fluid makes up 65% of the ejaculate, 25% comes from the prostrate and only 10% from the testes themselves.

The Penis

- the cross section of the penis shows a pair of **corpus cavernosum.** There is also a **corpus spongiosum** surrounding the urethra
- The erectile tissue is the corpus cavernosum and the soongiosum would stop urethral flow.
- The tunica albuginea is the interstitum surrounding the corpus cavernosum and the corpus spongiosum. It is made up of 2 layers of collagen fibres at 90 degrees of eachother to allow for the erection.
- The blood supply to the penis comes from the internal iliac artery. The smaller vessels after this can become blocked by atherosclerosis giving erectile problems.
- Vasodilation of the vessels in the penis though the parasympathetic nervous system results in erection. The sympathetic NS causes vasoconstriction to terminate the erection
- The sympathetic NS initiates ejaculation
- Half of the actually penis tissue is actually anchored to the pelvic bone

Female Reproductive System

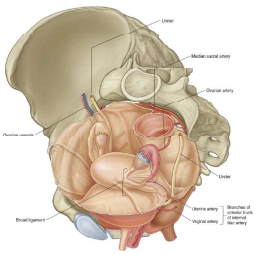
The Cervix
- if the woman has not had a baby, the external os will be visible as a small hole
- If the women has had a baby the external os will be seen as a slit
- There may be inflammation of the external os due to an increase in oestrogen e.g. the pill which will open up the transitional zone - now exposed to HPV

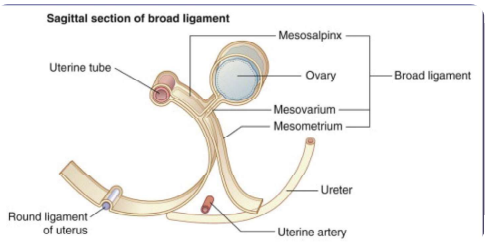
The Uterus and Vagina
- during pregnancy the *uterus* will expand up (pushing on the stomach giving acid reflux), push down (on the bladder increasing the frequency to urinate) and push backwards (onto the large intestine giving constipation).
- The *vagina* is Full of glycogen as this is what the lactobacillus in he uterus use in respiration - creating also lactic acid giving the vagina its acidic environment. - this tightly regulates the pH and flora. This is due to the presence of oestrogen so with age less glycogen is produced so less respiration altering the pH

Pouches
- **Retro-uterine pouch** (pouch of Douglas - found between uterus and rectum) is important as there may be fluid build up here in infection or possibly blood e.g. from a rupture of an ectopic pregnancy. You would feel shoulder tip pain as the blood from the rupture travels up through the paracolic gutters and irritates the diaphragm which is supplied by the phrenic nerve which covers the C3,4,5 dermatomes.
- **Visceral-uterine pouch** is found between the bladder and uterus but less clinically relevant

Peritoneum
- the Fallopian tubes open into the peritoneal cavity

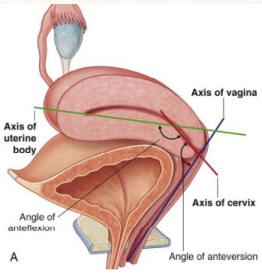
There are peritoneal ligaments which cover the female reproductive tract
- **broad ligament** - parts of the peritoneal membrane which cover different areas: the **mesometrium** covers the uterus body, the **mesosalpinx** covers the Fallopian tube and the **mesovarium** covers the ovary.
- **Suspensary ligament** to the ovary - a folding of the peritoneal membrane, covering blood vessels and nerves to the uterus.
- **Round ligament** and the **ligament to the ovary** - are continuous ad remnants of the gubernaculum (what pulls the gonads down in embryonic development)

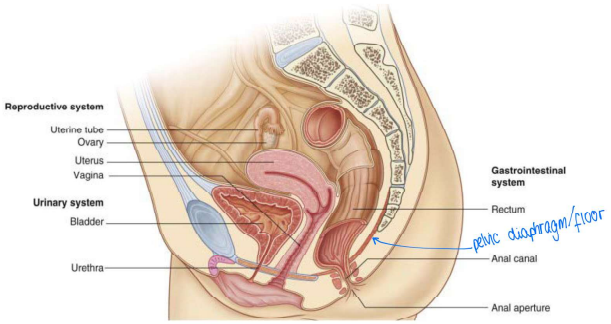




Blood Supply
- is through the **uterine artery** (from the internal iliac artery) and the **ovarian artery** (from the abdominal aorta). These often anatomise to give a rich blood supply.
- Also have the pampiniform venous plexus
- The left vein drains to the left renal artery then the IVC. The right vein drains directly to the IVC.
- The ureter travels under the uterine artery - this is important in hysterectomy not to damage the ureter when removing the uterus
- The **lymph nodes** drain to the para-aortic sinuses
- For the cervix they drain to the internal/external iliac and sacral lymph nodes

Position of the Uterus
- usually the position is **anteverted** and **anteflexed** - this is maintained by the round ligament
- If it were not like this then the uterus would push back down and out of the cervix and vagina. Not good.
- Both the angle of anteflexion and anteversion should be less than 180 degrees.



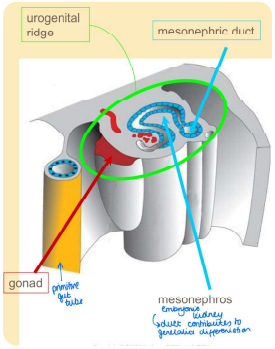


Fallopian Tubes
- the egg will leave the ovary by bursting through the peritoneal membrane. It will then be in the peritoneal cavity and must make its way to the fimbrae of the Fallopian tubes.
- The fimbrae have fingers and grooves to help the egg travel into the tube - if not the egg can float elsewhere in the peritoneal cavity
- The egg then goes through the infundibulum, ampulla (fertilisation occurs and most common site for ectopic pregnancies) and isthmus - through the help of ciliated cells wafting the egg along
- The arrangement of the Fallopian tubes means that infection can spread from the Fallopian tubes (e.g. an STI) and into the peritoneal cavity.
- Contain 2 different types of cells; **peg cells** (secrete factors to nourish and maintain the egg) and **ciliated cells**

Cancers and Pathology
- During ovulation the egg must burst through the ovary and parietal peritoneal membrane and into the peritoneal cavity. Repeated trauma of the egg bursting through the ovary traumatises the ovary so that **ovarian cancers** may develop
- In **cervical cancer** the columnar epithelia of the cervix is exposed into the vagina as what is known as the transitional zone. This exposed area is not used to the acidic environments of the vagina unlike the stratified squamous epithelia which usually line it. Therefore, *metaplasia* occurs giving rise to cervical cancer.
- **Ovarian cysts** can occur which are fluid filled lesions. They can cause pain (due to stretching of the peritoneum, rupturing, direct pressure and torsion). Such cysts should not be popped in case they may contain cancerous cells which could spread.
- **Ectopic pregnancies** are felt as severe pain on the side of implantation. This could be confused with appendicitis on the right so always take a pregnancy test for lower right abdominal pain. If an ectopic pregnancy ruptures the uterine and ovarian arteries can bleed to abuse a haemorrhage.
- **Endometriosis** - where endometrial tissue which is normally found lining the inside of the uterus is found elsewhere (possibly pouch of Douglas)

Embryonic Development

OUTLINE
- start with primordial germ cells whose karyotypes will determine grow the gonad will develop
- if the SRY gene from the Y chromosome is present then testes will develop, along with he rest of the male duct system (vas deferens and epididymis)
- If there is no SRY gene (i.e XX) then the gonads will develop into ovaries with their corresponding duct system (uterus, tubes, vagina)
- Following this the external genitalia will develop (either the penis/scrotum or the vulva)



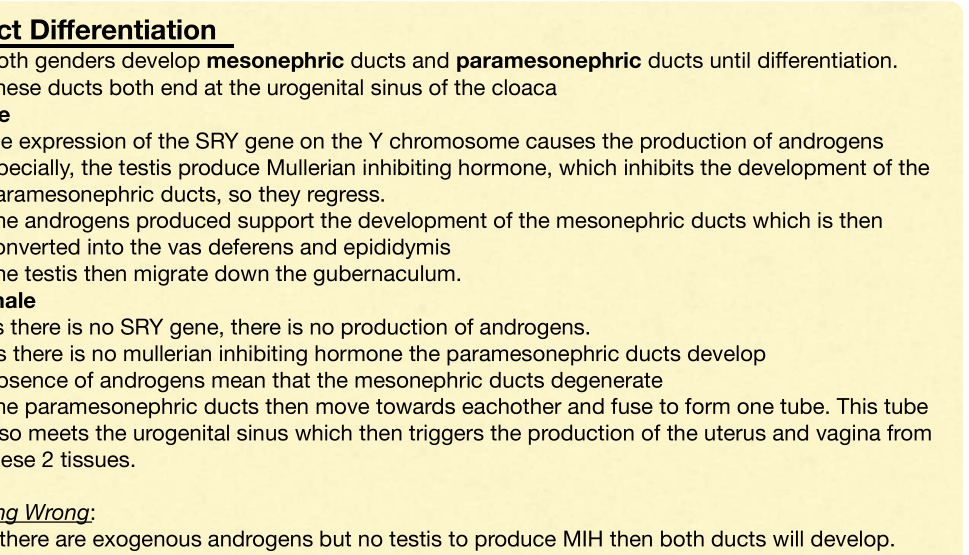
Urogenital and GI tract Development
- the 3 systems all develop from the hindgut (tube produced from the folding of the yolk sac),specifically the dilated end of the hindgut known as the **cloaca**.
- The cloaca has no surrounding mesoderm - which is good as there is therefore no blood supply to the cloacal membrane so that it can determinate to produce an orifice.
- The **Urogential ridge** is an area of intermediate mesoderm which produces both the kidneys and gonads. This means that the gonads are produced by both intermediate mesoderm and primordial germ cells
- The primordial germ cells come from the allantois into the wall of the yolk sac and migrate along the retroperitoneal to the urogenital ridge.

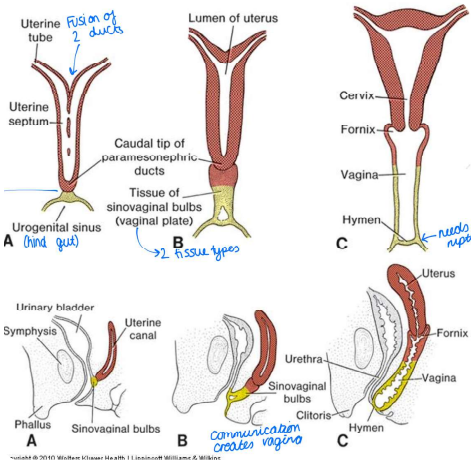
Duct Differentiation
- Both genders develop **mesonephric** ducts and **paramesonephric** ducts until differentiation. These ducts both end at the urogenital sinus of the cloaca

Male
- the expression of the SRY gene on the Y chromosome causes the production of androgens
- Specially, the testis produce Mullerian inhibiting hormone, which inhibits the development of the paramesonephric ducts, so they regress.
- The androgens produced support the development of the mesonephric ducts which is then converted into the vas deferens and epididymis
- The testis then migrate down the gubernaculum.

Female
- as there is no SRY gene, there is no production of androgens.
- As there is no mullerian inhibiting hormone the paramesonephric ducts develop
- Absence of androgens mean that the mesonephric ducts degenerate
- The paramesonephric ducts then move towards eachother and fuse to form one tube. This tube also meets the urogenital sinus which then triggers the production of the uterus and vagina from these 2 tissues.

Going Wrong:
- if there are exogenous androgens but no testis to produce MIH then both ducts will develop.
- In Androgen sensitivity syndrome the testosterone receptors dont work so both ducts degenerate (as MIH is still present)





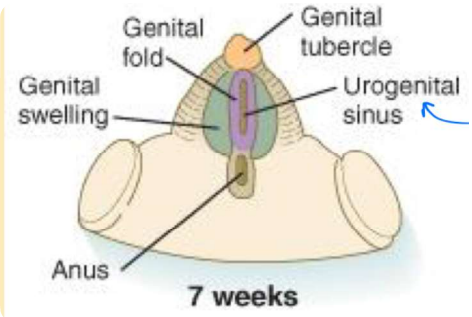
External Genitalia Production
There are some basic components found in both genders: genital tubercle, genital folds and genital swellings

Male:
- the Genital tubercle elongates
- Genital folds fuse to form the spongy urethra
- Driven by the androgen, **dihydrotestosterone**

Female:
- no fusion in the female
- The genital swelling grows to develop into the labia majora and labia minora
- The genital tubercle develops into the clitoris

Descent
Male
- The testis are retroperitoneal
- They descend down the gubernaculum (a ligament attaching the gonad to the future scrotum)
- Takes layers of the muscle wall with it

Female
- the ovary also descends down the gubernaculum, however it doesn't descend as far down and so has some remnants remaining of the gubernaculum which become the round ligament and ligament to the ovary



Puberty and the HPG Axis

Puberty

- **Definition**: a stage of human development when sexual maturation and growth are completed and result in the ability to reproduce
- Girls begin and end puberty before boys
- The pineal gland influences puberty through the secretion of melatonin
- Their is a critical weight in girls in which puberty can occur (47kg). This is because Leptin will sense the amount of adipose to signal whether this is adequate for reproductive life
- Puberty is also dependant upon nutrition as well as body weight.
- The **Tanner scale** can be used to assess which point in puberty a child is in
- **Precocious puberty** - this is when puberty occurs early (at 8 years old). This may occur because of congenital adrenal hyperplasia, hydrocephalus, Brain injury, pineal tumour, meningitis (interferes with pulsations of GnRH). This results in the child being short as epiphyseal growth plates fuse sooner. Treatment involved GnRH analogs to block pituitary hormones.
- Delayed puberty can also occur - if LH and FSH hormones are normal however, there could be a blockage preventing menstruation, or that the ovaries aren't responding to oestrogen. If LH and FSH are low it could be to do with weight to malnutrition. Look at FSH/LH levels against androgen/oestrogen levels to see if its a gonadal or pituitary problem.

Girls:

- between the ages of 9-13 puberty begins with breast bud development and pubic hair growth (testosterone)
- Adrenarche then begin which involves a growth spurt and the onset of menstrual
- Menarche ends puberty with adult pubic hair and breasts.
- **Aromatase** is an enzyme found which will convert testosterone into oestrogen
- The oestrogen will close epiphyseal growth plates following the growth spurt (this occurs earlier in girls) as well as maintaining bone mass

Boys:

- puberty begin between 10-14 with testicular development (said to have started puberty when testicular volume is 4ml)
- Pubic hair growth and spermatogensis (therefore, wont have sperm at the start of puberty) then follow
- Finally he will have a growth spurt (12 months after the start of puberty) and develop adult genitalia and pubic hair.
- Initially both boys and girls will have the same amount of testosterone and oestrogen (as they are need by both sexes), however puberty changes the amount the sexes produce.

Hypothalamus-Pituitary-Gonadal Axis

In order for puberty to occur the HPG axis must be switched on - This is done by a gradual increase of **GnRH** (Gonadotrophin releasing hormone)

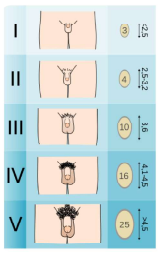
- GnRH is released in pulses from the **hypothalamus** by neurocrine secretion
- GnRH release is controlled by **Leptin** and **Photoperiod** - these act on the hypothalamus to switch on the pulsating release. Leptin (which is also released in a pulsating pattern) will determine when there is enough adipose fat to sustain reproductive life - in girls they must be a minimum of 47kg until this can happen. If weight falls after puberty, Leptin levels will also fall causing a cease in reproductive life.
- The GnRH then travels in the blood to the anterior pituitary gland
- The anterior pituitary gland will then produce **Luteinising hormone** (LH) and **Follicle-stimulating hormone** (FSH) from Gonadotrophs

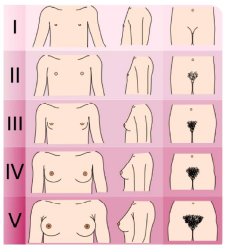
reminder the anterior pituitary produces 6 different hormones in total - look at MEH.

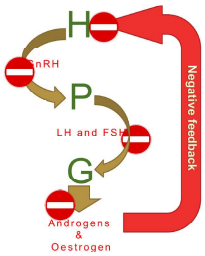
- pulsation avoids down regulation of GnRH receptor
- LH and FSH are not only pituitary hormones required in puberty. Growth hormone produced at the anterior pituitary is needed for he growth spurt.

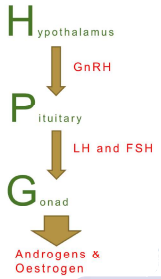
Control of the Axis

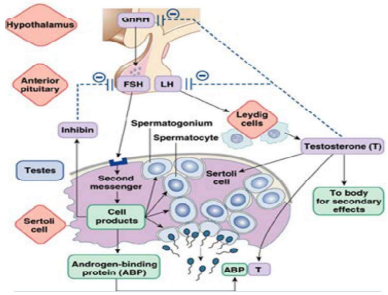
- the HPG axis is controlled through positive and negative feedback
- The androgens and oestrogen produced by the gonads have a negative feedback effect on the hypothalamus - this prevents GnRH being produced and so ultimately decreases the production of gonadal hormones. When these levels are low again there is no longer any negative feedback so their production can increase.
- It is also controlled by the release of GnRH - as the hormone is released in a pulsating pattern so intensity and frequency of GnRH can vary to control the axis.
- There seems to be a natural rise in the pulsating of LH during sleep (which is why they have a lot of testosterone in the mornings)





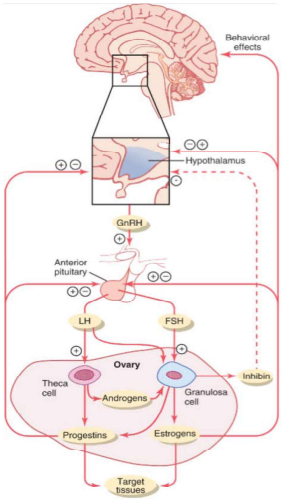






HPG in Females

- FSH target ovarian cells known as **granulose cells** to produce oestrogen
- LH targets the ovarian cells known as **Theca interna cells** to produce androgens
- These cells will stimulate sex hormone production of oestrogen, progesterone and inhibin
- The negative feedback loops however, differ from the males: normal oestrogen levels give negative feedback of GnRH production. However, high levels of oestrogen give a positive feedback response leading to a LH surge.
- Progesterone will prevent the positive feedback from oestrogen and will also increase the negative feedback effect of normal oestrogen levels.
- Inhibin is secreted by granulose cells in the corpus lectures to inhibit FSH



HPG in Males

- LH stimulates **Leydig Cells** in the testis to produce *testosterone* - this is affected by the circadian cycle (more LH at night) and environment).
- Leydig cells are found in the interstitial space between the seminiferous tubules
- Also in the testes are **Sertoli Cells,** which are stimulated by FSH - these are found lining the seminiferous tubules (along with spermatogenic cells) and allow maturation of sperm cells and secrete **inhibin**.
- Inhibin causes a negative feedback loop on FSH.
- The Sertoli cells have tight junctions between them - this gives a blood barrier, which is good as sperm as classified as non self (foreign antigens) so would be destroyed by the bodies immune system

Gametogenesis

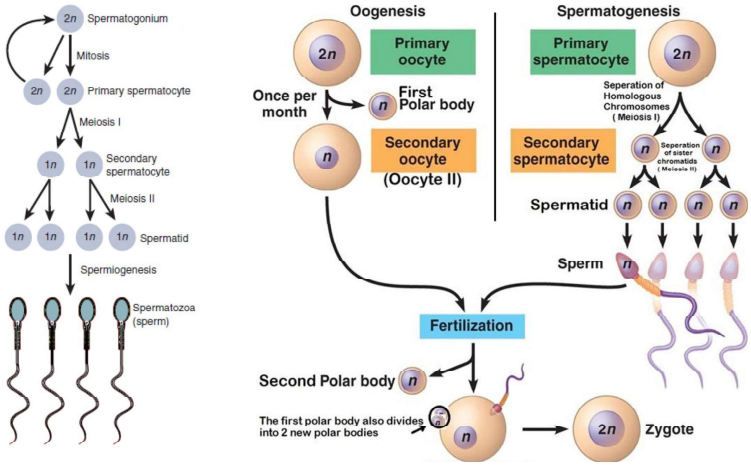
Primordial Germ cells migrate from the wall of the yolk sac towards the gonad, with the female cells collecting in the cortex of the gonads and the male in the medulla, where they will then proliferate by mitosis followed by meiosis (to give a haploid population). The meiosis that occurs is either known as Oogenesis or Spermatogenesis

Spermatogensis

- occurs in the seminiferous tubules in the gapes between the Sertoli cells
- Spermatogonium are the germ cells which undergo mitosis to increase in number.
- This results in primary spermatocytes which then divide by meiosis to give 4 spermatids
- The spermatids then undergo **Spermiogenesis** (differentiation into spermatozoa): this involves being released into the lumen of the tubule (**spermiation**), remodelling through the lumen where they are still non-motile (Sertoli secretions and peristaltic contractions move them to epididymis)
- The **Spermatogenic cycle** is the time taken for the reappearance of the same stage of spermatogenesis at the same part of the tubule - there needs to be different stages of the cycle going on at all times in order for the male to always be fertile
- The **Spermatogenic wave** is the distance between the same stage in the tubule
- Semen is made up of secretions from the seminal vesicles, prostrate, vas deferens and bulbourethral glands.
- **Sperm capacitation** is the final stage for fully functioning sperm - this is where the glycoproteins and cholesterol are removed from the sperm membrane which allows the sperm to bind to the zona pellucida.

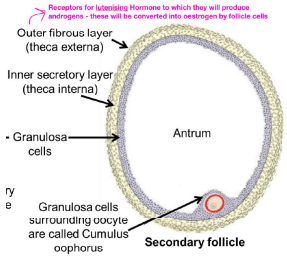
Meiosis

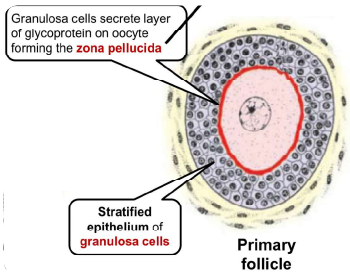
- reduces the chromosome number to 23 and ensures every gamete is unique
- Reproduces 4 daughter cells from 2 divisions (however in oogenesis only 1 daughter cell is produced with 3 polar bodies)
- Genetic variation arises from crossing over at chiasmata during prophase 1 to give recombinant DNA, independent assortment of bivalents and chromatids at the 2 metaphases



Ovulation

- the mature follicle becomes known as a Graafian follicle before its release from the ovary.
- In the ovary the leftover granulosa and the interna cells become vascularised and change in lutein cells to form the corpus luteum.
- The **corpus luteum** secretes oestrogen and progesterone to prepare for embryo implantation.
- The corpus luteum will die after 14 days if no fertilisation occurs forming a mass of scar tissue known as the **corpus albicans.**
- If fertilisation does occur then the corpus luteum doesn't degenerate due to the production of HCG hormone and in stead grows and secretes progesterone.





Oogenesis

- the germ cells collect in the cortex of the gonad and proliferate by mitosis to produce **oogonium.**
- Some oogonium undergo meiosis but arrest in prophase 1 (making them **primary oocytes**).
- Cell death occurs to many primary oocytes and oogonium
- The primary oocytes are surrounded by a layer of flare endothelial cells called follicular cells - this makes them a **primordial follicle.**
- there are then 3 stages of maturation that the primordial follicle undergoes:

1. **Preantral** - the surrounding epithelia change from a flat sheet to Cuboidal stratified layer of granulosa cells. These granulose cells secrete a glycoprotein to produce the zona pellucida
2. **Antral** - fluid filled spaces between the granulosa cells appear which come together to form the antrum. The follicle will have an outer fibrous layer (theca externa) which has LH receptors which allow androgen production which will be converted to oestrogen.
3. **Preovulatory** - LH surge induces this stage. Cell enters meiosis 2 but arrests in metaphase - meiosis 2 will only be completed on fertilisation. *During division in meiosis 1 2 daughter cells are released, but one gets all the cytoplasm (ova) and the other becomes a polar body).

Menstrual Cycle

HPG Axis - Feedback

- low levels of oestrogen cause a negative feedback response
- However, when the levels of oestrogen are high there is a positive feedback response (allowing for the LH surge)
- Oestrogen and progesterone together cause a negative feedback response

Hormones Recap

- **FSH** causes follicular development
- **LH** causes ovulation
- FSH and LH indirectly cause the release of oestrogen
- The *corpus luteum* produces oestrogen and progesterone
- Inhibin is produced which negatively feedbacks on FSH
- In **menopause**, the follicle cells are depleted and so the sex steroid hormones levels will gradually decrease. Initially however, the low amount of oestrogen will cause a negative feedback response and so the levels of FSH and LH will increase (FSH by more as the inhibin isnt being produced)
- Progesterone can act as a **contraceptive** due to it causing the mucus to become more sticky and thicker, this stops sperm from entering

Ovarian and Endometrial Cycle

The Menstrual Cycle is made up of 2 parts:

Ovarian cycle

- this has a follicle stage where the follicle is developing
- After ovulation there is a luteal stage, describing the corpus luteum left in the ovary

Endometrial Stage

- Has a proliferative stage and a secretory stage
- This is where the lining of the uterus changes depending on hormones
- If oestrogen is present it will proliferate and the presence of progesterone causes it to specialise
- It is the **functional layer** of the endometrium that is hormone responsive and will shed if no pregnancy occurs
- The **basal layer** of the endometrium is where the functional layer will grow from.
- The thickening occurs during the follicular stage where oestrogen causes the thickening of both the endometrium and myometrium. **Progesterone** will cause the thickening of the cervical mucus as well as causing the endometrium to specialise into a secretory form. The progesterone will also cause an increase in body temperature and metabolic changes

Endometriosis

- causes irritation of peritoneum giving adhesions
- These areas respond to oestrogen
- The GnRH must be released in a pulsatile pattern. If it was continuous then the GnRH receptors will become desensitised and so the FSH and LH production will stop - this can be used to treat endometriosis.
- As the plaques of endometrium growing outside the uterus have oestrogen and progesterone receptors we need to switch the axis off to prevent them responding to the ovarian hormones. A **GnRH agonist** will do this.
- However, this treatment is not too good for long term as low oestrogen levels can lead to **osteoporosis**.

Stages of the Cycle

Firstly, you have to prepare the gamete (ovarian cycle) and the endometrium (uterine cycle). Once the follicle is ready you then have ovulation. Next is the waiting phase, to see if fertilisation occurs. This is all controlled by gonadotrophin and ovarian steroids.

Preparation of the Gamete:

1. FSH increases and allows for development of the primordial follicle into the graafin follicle (mature). The FSH binds to the granulosa cells and allows the development of the theca interna. This is the first day of menstruation.
2. The mature follicle will start secreting oestrogen and inhibin secretion will begin.
3. The FSH was allowed to increase due to the lack of inhibin being produced up until this point.
4. There are low oestrogen levels which prevents the FSH and LH levels rising too much (**negative feedback)**
5. The oestrogen levels and inhibin levels will then begin to rise as the developed follicle can now secrete lots of oestrogen
6. This increase in oestrogen causes positive feedback giving a large **surge in LH**, but little FSH (due to **inhibin** also being produced)
7. Progesterone production will also begin as the granulosa cells now become responsive to LH

Ovulation

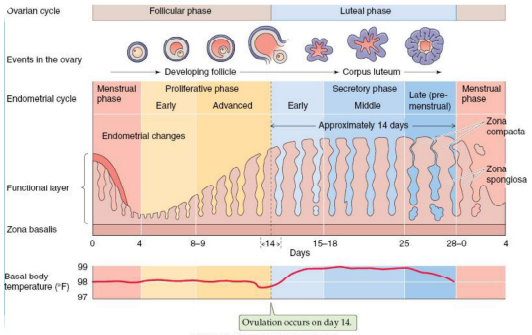
- the rise in LH causes the oocyte to complete Meiosis 1 and Meiosis 2 will start as well as ovulation
- This leaves a **corpus luteum** which produces oestrogen and progesterone as well as inhibin still
- This combination of hormones gives **negative feedback** so LH and FSH production are suppressed.

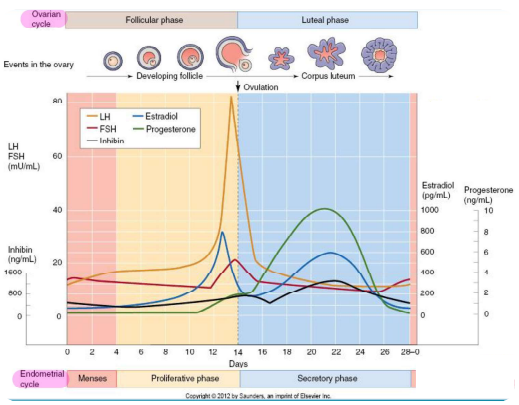
Luteal/Waiting Phase

- The corpus luteum is producing progesterone, oestrogen and inhibin.
- It will regress in 14 days if there is no further rise in LH - this causes a fall in ovarian and gonadal hormones so the cycle will reset unless fertilisation occurs

Fertilisation

- if fertilisation occurs the **syncytiotrophoblast** will produce **HcG** which will have the same effect as LH, maintaining negative feedback to ensure no more FSH is produced so that no new gametes mature
- The corpus luteum and placental HcG will provide hormones to support pregnancy until the placenta is capable enough to sustain this by itself





Problems

Amenorrhoea

- **primary** = failure to establish menstruation by 16 years old
- **Secondary** = stopping of a previously normal menstruation for over 6 months
- The main cause is pregnancy and menopause but can have other causes such as hormonal problems.

Oligomenorrhoea

- infrequent menstruation

Menorrhagia

- excessive menstrual blood loss
- Common causes include fibroids, polyps, endometrial Cancer, bleeding diathesis and drugs like warfarin
- **Fibroids** are benign tumours of the smooth muscle of the myometrium. These are hormone dependant and so can go away at menopause. They are thought the cause heavy bleeding to to a large surface area. Treatment involves **GnRH agonists** *see Endometriosis for details*

Dysmenorrhea

- pain during menstruation
- Primary is idiopathic
- Secondary due to endometriosis (constant stimulation causes adhesions which irritate the peritoneum causing pain) or obstructed menses.

Causes

- could be hormonal and due to the HPO axis
- Could be chromosomal such as **Turners syndrome** (XO karyotype gives problems with the ovary so that it would respond to GnRH, LH or FSH)
- Could be structural: fibroids, agenesis of genital tract, imperforate hymen (thin membrane covers vaginal entrance so blood can't escape and collects) or cervical stenosis
- Bleeding diathesis - if you have clotting Disorders yours more prone to bleeding
- Drugs
- Thyroid disease

Sex and Fertility

Maturation of Sperm

In the Epididymus

- before the sperm leaves the epididymus they can't move
- Maturation here allows the sperm to swim and gives them to potential to fertilise an egg
- This is dependant on androgens (testosterone)

In the Female Tract

- **capacitation** must occur to allow for fertilisation
- This involves the tail moving into a whip like action and loss of the acrosome
- The **acrosome** contains enzymes which are released when it is lost - these enzymes include hularonidase which degrades the corona radiata (granulosa cells surrounding the egg)
- The spermatocytes bunds to the **ZP3** glycoprotein on the zona pellucida, causing its digestion

Inside the Female Reproductive Tracts

Mucus

- the cervical mucus is thin and stretchy before ovulation
- The cervical mucus will thicken and become sticky and form a plug - this stops the flow of sperm - this occurs after ovulation

Fertilisation

- the semen is deposited at the external os of the cervix - they sperm then move to the ampulla of the Fallopian tube, where fertilisation will occur
- The sperm are transported by there own propulsion compared to the oocyte requiring cilia and peristalsis of the uterine tube
- Once the sperm penetrates a **cortical reaction** occurs (where cortical granules are emptied, changing the membrane of the oocyte so that no more sperm can penetrate)
- meiosis 2 then occurs and the pronuclei move together and begin to divide by mitosis
- This forms a morula which contains totipotent cells (can become any type of cell)

Implantation

- occurs at the superior, posterior uterine wall
- Can get *ectopic* pregnancies or *placenta praevia* (in front of internal os)

Semen

- made up of sperm and seminal plasma

Seminal Plasma

- it is a transport medium which provides nutrition and acts a buffer against the acidic vagina
- The **seminal vesicles** make up the 60% of the volume of the plasma - this is alkaline and contains fructose (allows for anaerobic respiration of sperm)
- The **prostrate gland** also contributes, producing a milky fluid, containing citric acid (gives calcium ions chelation which allows of the sperm to stop coagulation)
- **Bulbourethral glands** contribute a small amount of alkaline fluid

PARAMETER	VALUE
Volume of ejaculate	2–6 mL
Viscosity	Liquefaction in 1 hr
pH	7–8
Count	≥20 million/mL
Motility	≥50%
Morphology	60% normal

The Phases of The human Sex Response

Excitement phase

- this is where *psychogenic* (sight) and *tentile* (touch) stimuli cause an erection
- This causes the sympathetic nervous system to be inhibited
- The **parasympathetic nervous system** is initiated and signals are sent through the pelvic nerve (from lumbar sacral origins)
- This innervation causes the arteries in the corpus cavernous of the penis to dilate and the sinusoids there to relax - this increases blood flow, causing the corpus cavernosum to expand, push against its surrounding tunica albuginea and compress the veins
- The corpus spongiosum does also expand slightly but not by much as this would block the spongy urethra.
- The parasympathetic innervation causes these actions through the release of **Nitric Oxide**
- The nitric Oxide is released directly from nerves or formed from endothelial cells after the ACh binds to M3 receptors
- **Erectile Dysfunction** - can be caused by tears in the tunica albuginea, drugs (antihypertensives, antidepressants) - Viagra slows down the rate at which cGMP is degraded, causing an increase in NO which increases blood flow to the penis

Plateau Phase

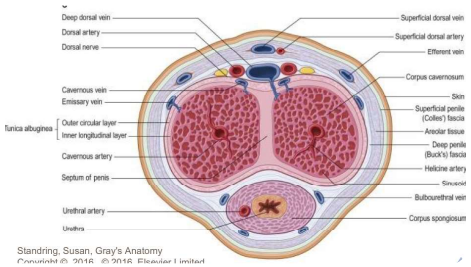
- this is the stage where either the threshold is reached and ejaculation occurs or it is not reached

Orgasm Phase

- ejaculation occurs
- This is now under **sympathetic control**
- It control emission and ejaculation
- **Emission** is the contraction of the smooth muscle in the prostrate, vas deferens and seminal vesicles to move semen into the prostatic urethra
- **Ejaculation** is the expulsion of semen, involving rhythmic striated muscle contractions
- Sympathetic antagonists will prevent the smooth muscle from contracting causing a *dry orgasm*

Resolution Phase

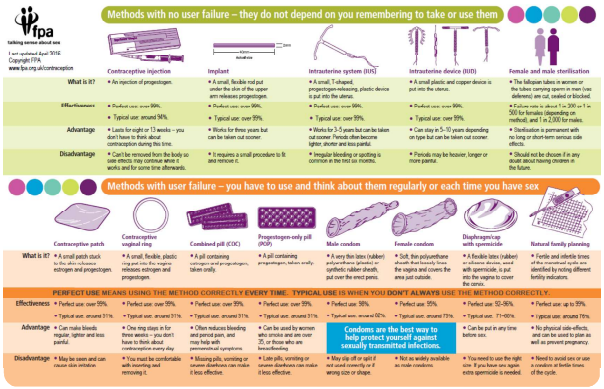
- *refractory stage* in males allows a return to haemodynamic norm. Females do not require a refractory period



Standing, Susan, Gray's Anatomy

Contraception

- methods to prevent pregnancy
- Natural includes abstinence, withdrawal, fertility awareness (e.g. temperature, cervical secretions) and lactation always amenorrhoea method (breastfeeding disrupts GnRH affecting HPG)
- Barriers include the condoms and protect from STIs
- There are many hormonal Control options - the **combined oestrogen and progesterone pill** (inhibits ovulation by preventing the LH surge, also prevents proliferation of endometrium and thickens mucus), the **high dose progesterone pill/implant** and the **low dose progesterone** pill (low doses does not affect the feedback mechanisms - purely thickens the mucus to stop sperm entering)
- Also the coil can be progesterone (**interuterine system**) - progesterone effects) or copper (**interuterine device** - copper is toxic to sperm)
- Or sterilisation



Infertility

Subfertility = failure of conception in a couple having regular, unprotected sex

- this can be *primary infertility* where they've never conceived before or *secondary infertility* where they've had previous pregnancies but can't conceive now

Main causes include

- **Male causes** - these could be endocrine (hypothalamus dysfunction, hyperprolactinaemia and diabetes), genetic, vasculature, obstructive, STIs, drugs
- **ovulatory disorders** - can be hypothalamic-pituitary failure (easily treated with GnRH), hypothalamic-pituitary-ovarian Dysfunction (such as polycystic ovary syndrome and hyperprolactinaemia (prolactin interferes with GnRH release - this is where the feedback mechanisms aren't working properly) and ovarian failure
- **Polycystic Ovary Disorder** = where you have too much androgens (thought to be caused by insulin resistance) so get a lack of pulsatile GnRH. This causes abnormal oestrogen secretion. This means that ovulation does not always occur due to inappropriate feedback signals due to different hormone levels. There is also an excess of LH. The increased oestrogen puts women at risk of endometrial malignancy. Patients present with weight gain, amenorrhoea, excess hair and infertility.
- **Uterine Disorders** include fibroids, pelvic inflammatory disease (causes adhesions), endometriosis or development Abnormalities (agenesis, didelphys - duplication, septate - fibrous band in the middle of a uterus or bicornuate - 2 uteri sharing 1 cervix and vagina.
- **tubal damage** - endometriosis, pelvic surgery or pelvic infections

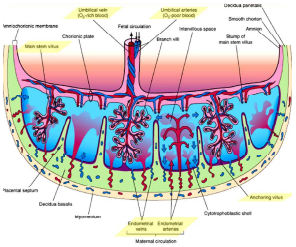
Fertility Treatments

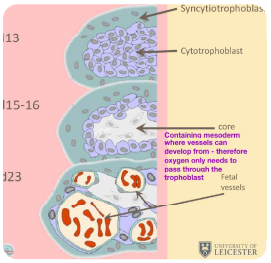
- **assisted reproduction techniques** - oocytes are fertilised in vitro and allowed to divide to give a morula. One cell of the morula is tested for genetic defects before being transferred into the women
- **Surgical treatment** to restore fertility
- **Medical treatment** to restore fertility - e.g. drugs like dopamine/bromocriptine

Pregnancy

Placenta Growth

- in the second week of embryonic development the outer cell mass of the embryo differentiates into the cytotrophoblast and syncytiotrophoblast
- The syncytiotrophoblast has specialised receptors to allow for the initial contact of the embryo with the endometrium and for the blastocyst to fully enter the endometrium - this will allow the embryo to gain access to the vasculature and glands in the endometrium
- Hatching from the zona pellucida must occur so that these receptors can make contact with the endometrium
- These 2 layers together are called the **chorionic membrane** and makes up the placenta
- The connecting stalk in the embryo will become the umbilical cord





Transport Across the Placenta

- simple diffusion allows small molecules to move down their concentration gradient (e.g. water, electrolytes, urea and gases)
- Facilitated diffusion is required for glucose transport
- Active transport is required for amino acids, iron and vitamins
- Passive immunity is achieved in the new born as IgG can pass through the placenta. However, this can be dangerous if the mother is Rh positive. Despite this, the mother is producing less immunoglobulins so that it doesn't attack the fetus at the placenta (decreasing the mothers immunity)

Implantation

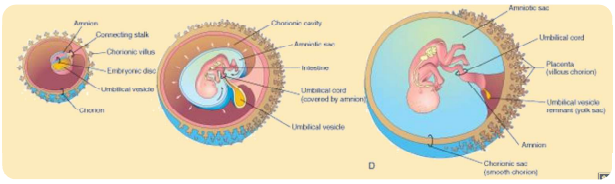
- occurs on day 6
- Occurs in the superior, posterior uterine wall
- Implantation is interstitial - meaning that the embryo must go into the Endometrial lining rather than the cavity - this means the endometrium must adapt to these changes.

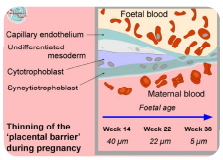
Implantation in the wrong place

- **ectopic pregnancy** = implantation occurs any where other than the uterine body. Most commonly this is the Fallopian tubes. This is a life threatening emergency
- **Placenta praevia** = implantation over the internal os. This can cause haemorrhage during birth

Incomplete Implantation

- **pre-eclampsia** = the eggs doesn't implant fully into the endometrium





Fetal Circulation

- there are 2 umbilical arteries bringing deoxygenated blood from the fetus to the placenta
- There is 1 umbilical vein bringing oxygenated blood from the placenta to the fetus

Decidua

- the endometrium must transform to become the decidua
- The decidua controls the invasion of the embryo into the endometrium
- Therefore, if there is no decidua then there is no control on implantation - this is why is ectopic pregnancies, the lack of decidua means the egg can invade the whole way through the structure of which it implanted
- The decidua reaction may also be sub-optimal meaning the egg can only partially implant into the endometrium - this causes pre-eclampsia

Changes in the Mother

Metabolism

- increased fat storage and so can respire using fatty acids
- Reduced insulin sensitivity and so more circulating glucose

Cardiovascular

- blood pressure will stay the same, however it can decrease slightly due to the vasodilation of progesterone causing sweating (as blood vessels are closer to skin) and some dizziness
- The growing baby can also compress the IVC to cause varicose veins
- The heart has to pump more blood - this causes hypertrophy. The heart also develops a murmur
- Hyperventilation to increase oxygen results in physiological respiratory alkalosis

Renal

- GFR will increase
- Pressure on bladder causes incontinence
- Progesterone causes dilation of ureter increasing the risk of UTIs

Calcium Metabolism

- placenta produces DHCC to help promote calcium absorption to help fetal bone development

Structure of the placenta

- the placenta is made up of the *chorionic membrane* (made from the cytotrophoblast and syncytiotrophoblast - this covers the whole egg)
- Over part of this membrane there is a area which has become specialised as it contains many villi - therefore the placenta is only part of this membrane (not all of it)
- all throughout the syncytiotrophoblast there is mesoderm so that fetal blood vessels can develop and so be close to the placental lining to exchange with the mothers blood
- The **villi** allows for maximum transport between mother and fetus by increasing the surface area
- The villi are constantly surrounded by maternal blood - however, the 2 bloods do not mix!
- At the placenta there are structures called **cotyledons** - these are made up of the villi from the fetus as well as tissue from the mother (so these structures contain tissue from both). This is where diffusion occurs.
- As the fetus develops the placenta membrane becomes **increasingly thinner -** this means there's a shorter diffusion distance, so maximises diffusion

Endocrine Function of the Placenta

The placenta produces protein and steroid hormones - these can influence the mothers metabolism

Steroid:

- **progesterone** and **oestrogen** are produced - this means that the corpus luteum can stop producing them.
- They maintain the pregnant state, as well as inhibin as this prevents FSH which would otherwise cause follicle maturation.
- Progesterone is a vasodilator - helps to increase blood flow to placenta
- Progesterone also increases appetite - this allows for more fat stores to be laid down which can be used in respiration by the mother and also used for transport to the fetus when its metabolic demands increase later in development.

Protein:

- **Human chorionic gonadotrophin** - this is produced in the first 2 months of pregnancy. It help to support the corpus luteum in hormone secretion until the placenta takes over. hCG is produced by the syncytiotrophoblast.
- **Human Chorionic Somatomammotrophin** - this increases insulin resistance in the mother - this means she cant take up glucose into her cells so there is a large amount of circulating glucose in her blood. This glucose can then diffuse across the placenta for the baby to use.
- hC tyrotrophin
- hC corticotrophin

Teratogensis

- **teratogens** are agents that pass through the placenta and can influence normal development
- Examples include thalidomide (causes limb defects), alcohol, warfarin, ACE inhibitors, anti-epileptic drugs and smoking
- *Smoking* prevents sufficient oxygen supply to the baby as carbon dioxide has a higher affinity for Hb than oxygen
- Teratogens will cause lethal effects in the first 2 weeks. However, the most sensitive period is the **embryonic period** (as organs and structures are being built)

Pathology

Trophoblast disease

- a **molar pregnancy** is when there is overgrowth of the chorionic membrane - this means it can implant further through the endometrium and even out through the other side to spread through the blood
- **Choriocarcinoma** is a malignancy of the chorionic membrane

Gestational Diabetes

- if the mother already has a raised glucose this means even more glucose will be transported across the placenta to the baby
- The baby will therefore use more glucose so will be much larger - this can cause asphyxia during birth so a C section is required. Means they may also out grow the placenta supply
- the glucose will also be stored in the liver as glycogen giving a fatty liver
- The pancreas must produce more insulin to control this glucose - therefore there is hyperplasia of the B cells
- The babies will have respiratory distress as they are being born earlier, so they didn't have time to produce surfactant
- Immediately after being born the babies will also be hypoglycaemic - as they previously relied on the mothers glucose which has been stripped from them

Anaemia in Pregnancy

- Normally, women will become slightly anaemic - this is because there is a larger *increase in blood plasma* than RBC mass (reducing the haematocrit). This is because the baby has a larger demand for nutrients which come from the plasma rather than oxygen from the RBCs.
- However, if the anaemia was already present or becomes severe then the baby is at risk of still birth, growth retardation
- Give iron supplements to help

Pre-eclampsia

- this is where the trophoblast doesn't invade fully into the endometrium (as the decidua doesn't transform fully). this means the needs of the fetus cant be met fully
- To compensate the blood flow from the mother to placenta increases to try and deliver more nutrients - this gives the mother a very **high blood pressure**
- The mother will also have proteins in the urine, pitting oedema, worsening liver and kidney functions
- As the condition worsens the mother will experience eye changes and changes in her reflexes
- Eye changes include double vision, blindness and blurred vision -this is due to ischaemia to the vessels in the back of the eye
- Reflexes become more active due to increased blood flow until eventually seizures result from this
- This can progress to **eclampsia** which is life threatening seizures

The Fetus

Maternal-Fetal Oxygen Exchange

- oxygen passes from maternal blood into the umbilical veins
- This diffusion requires a gradient to be maintained

There are several factors that help maintain this gradient

- the maternal blood has a slightly higher pO2 as the mother is hyperventilating. However, this increase isnt enough to produce the whole gradient
- **Fetal haemoglobin** - made up of 2 alpha and 2 beta subunits. This has a greater affinity for oxygen then HbA. So when oxygen diffuses across it is taken out of solution easily to maintain a low pO2 in the fetal blood.
- **Increased maternal 2,3-BPG -** this is found in the tissues and causes a decrease in affinity for oxygen. Therefore, the oxygen will be given up by the haemoglobin at the tissues/placenta increasing the pO2 there. This is occurs due to the hyperventilation creating a respiratory alkalosis in the mother - this gives less CO2 which works against the Bohr effect so 2,3-BPG is released to combat this.
- **Double Bohr Effect** - in the mother, CO2 passes from the fetal to the maternal blood, this causes the pH to decrease so the Hb has a lower affinity for oxygen due to the H+ so the oxygen dissociates increasing the pO2. At. The same time CO2 is lost in the fetal blood causing the pH to increase - this causes an increase in Hb for oxygen. (Bohr effect goes in the other way)

Amniotic Fluid

- the amniotic fluid give protection and helps with the development of the lungs
- For the first 8 weeks the amniotic fluid is produced by from maternal plasma diffusion
- By 9 weeks the fetal kidneys start to produce urine - this is released to produce amniotic fluid
- An amniocentesis is carried out to sample fetal cells to look at their karyotype

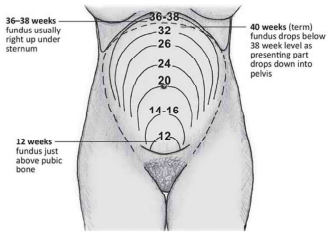
The fluid is recycled through 2 methods:

- it is either **inhaled** by the baby so that the lungs can start moving and helps develop the lungs
- Or it is **swallowed** by the baby into the GI tract where the fetus can then absorb water and electrolytes

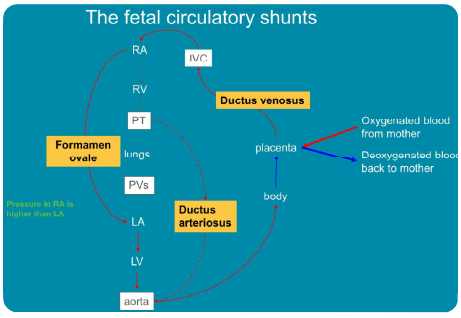
The remaining fluid not absorbed it combined with fetal bile secretion to form the debris called **Meconium**. This will be egested as the baby's first bowel movement after birth - until the baby is stressed this many be passed in uterus.

Birth Weights

- 3500g is average.
- Below 2500g suggests growth restriction, premature birth, if they are constitutionally small (have a small mother)
- Above 4500g is known as **macrosomia**. This could be due to gestational/normal diabetes



Gestational age	Fundal height landmark
12 weeks	Pubic Symphysis
24 weeks	Umbilicus
36 weeks	Xiphoid Process of Sternum
37–40 weeks	Regression of fundal height between 36–32 cm



Maternal-Fetal CO2 Exchange

- **progesterone** causes hyperventilation meaning more CO2 is expelled from the lungs
- This gives a lower pCO2, maintaining the diffusion gradient

Fetal Circulation

There are 3 shunts that occur in fetal Circulation:

1. **Ductus Venosus =** ensure blood bypasses the liver (as it comes from the placenta to the heart via the IVC) as its too metabolically active so will use up all the oxygen. Closed when the umbilical cord is clamped
2. **Ductus Arteriosus** = shunts blood from the pulmonary trunk to the aorta to bypass the lungs (however, a small amount will still go to the lungs for development). The lungs are not functional so doesn't need a blood supply. By allowing blood through the RV means it has something to pump against allowing the ventricle to develop
3. **Foramen Ovale** = shunts blood from the RA to LA as the lungs and right ventricle don't need supplying. This means the head and heart get the most blood supply. Closed when the pressure in the LA exceeds the RA

Fetal Hypoxia

- the fetus is adapted to manage small decreases in oxygen due to its large amount of HbF giving a high haematocrit
- The fetal heart rate will **slow down** in hypoxia to reduce oxygen demand
- The chemoreceptors detecting pO2 or increased pCO2 stimulate the ***vagus nerve*** to give bradycardia
- Normally the fetal heart rate is 110-160bpm
- If hypoxia persists the baby can be born with growth restriction *see more*, developmental issues.

Growth Restriction

- Malnutrition of the mother can lead to growth restriction of the fetus
- The restriction is either symmetrical or asymmetrical
- In symmetrical growth restriction all of the fetus is proportionally smaller
- In asymmetrical growth restriction the head is commonly spared and so bigger but the body is smaller. The body can also sometimes be bigger then the head

Bilirubin

- the mother takes care of fetal conjugation and excretion of bilirubin
- Therefore, at birth it takes time for the baby's liver to mature for this process, meaning at birth there is some physiological jaundice

Growth and Weight Changes of the Fetus

- there is a stable increase throughout the whole of the fetal life in **crown-rump length**
- The **weight** of the fetus doesn't increase much until the end of the embryonic stage, when all the systems are developed It especially increases toward the end when there is adipose deposition to help with nutrition and thermoregulation
- The body proportions change during development - the head grows first and then the trunk catches up - at week 9 the head counts for half of the crown-rump length

Ante-Natal Assessment

there are different methods for assessment:

- asking the mother about **fetal movements** at 20 weeks
- The **symphysis-fundal height** can be measured from the fundus of the uterus to above the pubic symphysis - after 20 weeks the height should match the age of the fetus in weeks. This is less accurate in obesity and with twins. The height could be larger/ smaller due to macrosomia and too much/little amniotic fluid. There are landmarks of fundal height for different ages
- **Ultrasound scan** - routinely carried out at 20 weeks as then the organs are developed and big enough to see so can look for Abnormalities.
- Doppler ultrasound assesses blood flow across the placenta
- The Crown Rump Length between weeks 7-13 is accurate for age assessment rather than last menstrual period
- Biparietal diameter - is the distance between the parietal bones of the fetal skull
- Abdominal Cirucmference
- Femur length

Fetal Body Systems Development

Respiratory:

- they develop from the foregut and are only separated when the tracheoesphageal septum appears.
- At weeks 8-16 is the Pseudoglandular stage where the bronchioles develop but there is no exchange
- At weeks 16-26 is the canaliculi sage where Respiratory bronchioles from but still no exchange
- From weeks 26-term the alveoli develop. There is differentiation of type 1 and 2 pneumocytes so **surfactant** begins to be produced by week 26, however, the majority of surfactant is produced at weak **34**
- Therefore, premature birth means not all surfactant may be produced leading to **respiratory distress syndrome** - this is often the case in conditions like pre-eclampsia so the mother must be given glucocorticoid treatment to increase surfactant production in the fetus.
- The fetus is only viable at 24 weeks when the alveoli have developed - this gives the abortion limit

CVS

- heart rate is achieved at 15 weeks
- Bradycardia associated with hypoxia

Urinary

- begins at week 10- so urine first produced then
- If there is too little amniotic fluid produced (**oliohydramnios**) this indicates renal problems e.g. in placental insufficiency, maternal hypertension, bladder outlet obstruction
- Too much amniotic fluid (**polyhydramnios**) can be due to fetal Abnormalities such as the CNS inability to swallow (so fluid not absorbed), blind ended oesophagus, if the tracheoesphageal septum isnt positioned correctly

Nervous System

- This is the first and last to develop so most vulnerable to disturbance
- Myelination of the brain begins at birth - that's why there increased infant mobility with age

Giving Birth

Definitions

Parturition = the transition from pregnancy to a non-pregnant state
Labour = the process by where the fetus is expelled from the uterus.
Delivery = the method of expulsion of the fetus

Hormonal Control in Labour

Starting Labour:

- Hormones are released to allow cervical ripening and to excite uterine musculature
- A rise in oestrogen and fall in progesterone occurs - This stimulates an increase in prostaglandins and oxytocin
- **Prostaglandins** triggers cervical ripening and cause contractions of the smooth muscle of the uterus. It is synthesised by the placenta and myometrium
- **Cervical ripening** is the break down of connective tissue in the cervix, giving a higher water/hyluaronic acid to fibrous tissue ratio. This allows the cervix to soften and shorten (effacement and dilation) - this occur a few weeks before giving birth.
- Cervical ripening is also controlled by **oestrogen** and **relaxin** as well as prostaglandins
- The presence of **progesterone** inhibits contractions - oestrogen increases gap junctions between smooth muscle cells to help in contractions with prostaglandins
- **Oxytocin** will initiate the uterine contractions. At 36 weeks there's more oxytocin receptors to respond to the pulsitile release of oxytocin from the posterior pituitary gland

Inducing Labour

- in order to induce labour you must stimulate prostaglandin release through the use of artificial prostaglandins
- Also can use synthetic oxytocin and anti-progesterone agents

Helping Labour

- Ceasrean section can be used if the mother/Baby is under risk
- You can use forceps or a vacuum extraction with vaginal delivery

Post Partum

- this is the period from delivery of the placenta to 6 weeks post natal - in this period changes occur in the mother to revert back to a pre-pregnant state
- Midwives must visit the mother after delivery and then health visitors must after this

Changes:

- low oestrogen levels cause changes in the lower genital tract such as reduction in size, poor lubrication, closure of internal os
- Bleeding also occur - firstly this is a heavy blood flow (lochia rubra) followed by a pink flow (lochia alba). This bleeding shouldn't contain clots.
- The pelvic ligaments lose their laxity
- White cell count may remain high despite no infection

Problems:

- **post partum haemorrhage** = 500ml of bleeding occurring immediately after birth (primary) or afterwards (secondary). Physiologically this is prevented by uterine contractions.
- **Mental health** - postpartum depression is common in women after birth
- **Thromboembolic disease** - the blood is more hypercoagulable during and after pregnancy
- If not all of the placenta is passed through the uterus may still feel firm
- **Sheehan's syndrome** = blood loss and hypovolaemia following birth. This can particularly affect the anterior pituitary gland as this has increased in size (due to an increased hormone production) giving a worse blood supply (to what was already bad due to the portal system). The posterior is not affected due to a better blood flow.
- Problems with he baby - *Erb's palsy* and *Klumpke's palsy* could occur due to traumatic birth *see MSK*

Labour

There are 3 phases of labour;

Stage 1

- this is the **creation of a birth canal** - the brith canal has a bony part (the pelvis) and a soft tissue part (cervix vagina and perineum). The perineum (levator ani) stretches greater during brith that is almost goes transparent
- The **latent stage** of labour stage 1 is when there is slow cervical dilation and softening (cervical ripening)
- The **active stage** of labour stage 1 is when there is a faster rate of contractions and full cervical dilation
- An epidural can be given to block the sensory afferent fibres from the uterus blocking pain from T9-S4

Stage 2

- this is where there are changes in uterine contractions to expel the baby through the birth canal
- The cervix is fully dilated at this point and the ligaments in the pelvis are relaxed (resulting in exaggerated lordosis)
- There are both passive and active methods to help for an easy expulsion
- **Passively** the baby reflexes its head sideways (transverse position) as it has the smallest diameter this way
- **Actively** the uterine contractions cause rotation of the head internally
- As the head crowns (stretches the perineum and muscle) and is pushed past the pubic symphysis it can rotate back to its normal position (restitution) - by feeling the fonatelles you can tell what position the babies head is in
- Once the head is through the shoulder rotate due to uterine contractions to give delivery of the anterior then posterior shoulder
- Movements overview: Neck flexion, rotation, extension then restitution. Shoulder delivery
- You can monitor the baby at this stage through doppler ultrasound, maternal temp, amniotic fluid colour.

Stage 3

- this is the **expulsion of the placenta** due to further uterine contractions
- This starts after the birth of the baby and usually lasts 5-15 minutes
- However, this process could involve a lot of bleeding if it wasn't for the **uterine contractions** which compress the vessels to prevent blood flow
- The placenta can then separate and come down

Uterine Contractions

- the myometrium muscles contractions, but then unlike how muscle normally relaxes, the myometrium does not return to its original size - instead it **retracts**
- This retraction gives a gradual shortening of the muscle fibres
- This reduces the space in the uterine cavity in order to push the baby out
- Contractions are made more frequently and forcefully due to prostaglandins and oxytocin

Lactation

- Sensory afferent nerve fibres detect **suckling** at the nipple - this sends a message to the brain to inhibit dopamine release - this allows the release of **prolactin** which causes the *production of breast milk*
- **Oxytocin** causes *contraction of the myoepithelial cells* surrounding the glands causing **milk secretion**. It also causes the dilation of the ducts to allow the ease of milk flow - this is the 'let down' reflex.
- Oxytocin is released to many stimuli including suckling, hearing a baby cry and seeing a baby. However, it is inhibited by **stress.**
- Progesterone, oestrogen, prolactin and growth hormones all contribute to the hypertrophy of the mammary glands and formation of new ones.

Components of Breast Milk:

- it has a high energy content and high lactose
- In early lactation there is a higher water content whereas later on it contains more fats and irons

Function:

It protects the baby through different mechanisms

- **lactoferrin** binds to iron preventing the iron dependant organism E.coli from proliferating
- Encourage develop of the **normal flora**
- Bacteriocidal enzymes present
- **Immunoglobin A** passed on from the peters patches into the mothers gut to give passive immunity

STIs and PID

Gonorrhoea
- caused by the gram negative diplococcus Neisseria gonorrhoea

Symptoms
- males - urethral/anal discharge, dysuria
- Females - usually asymptomatic. However, can get discharge, abdominal pain

Diagnosis
- gram stain, endocervical swab

Treatment
- IM ceftriaxone and oral azithromycin
- The azithromycin is used as it can be used to treat chlamydia which is a common co-infection, boosts the affects of ceftriaxone and prevents resistance to ceftriaxone
- **Co-infection** = these occur because the causative organisms often co-exist together and also because if the person if having risky sexual behaviour, they will be more likely to have another STI

Chlamydia
- caused by the bacterium Chlamydia trachomatis

Symptoms
- male - dysruia, urethritis (mild symptoms)
- Female - mostly asymptomatic, but can have increased discharge and intermenstrual bleeds
- Systemically can have conjunctivitis and a Pharyngeal infection

Diagnosis
- men - urine test
- Women - endocervical swabs
- doesn't have a cell wall so cant do a gram stain - instead serology, urine tests and PCR

Treatment
- doxycycline

Herpes Simplex Viruses 1 + 2
- HSV 1 is the usually cause of oral and labial herpes
- HSV 2 is more likely to cause recurrent symptoms

Symptoms - painful ulceration, dysuria and discharge, fever

Diagnosis -virus detection from vesicle fluid, serology

Treatment - antivirals (aciclovir)

Anogenital Warts
- these are benign lesions caused by the HPV virus
- Mostly caused by HPV types 6/11 which dont cause cervical cancer

Treatment - may need physical excision and prevent with vaccination

Bacterial Vaginosis
- this is caused by an imbalance of pH in the vagina e.g. from vaginal douching

Symptoms
- Fishy discharge

Treatment
- Metronidazole

Candidiasis
- this is caused by the fungi Candida albicans
- Oral contraceptive pill can increase risk

Symptoms
- vaginal discharge, itching, soreness

Diagnosis
- high vaginal smear

Treatment
- topical and oral antifungals (azoles)

Syphilis
- caused by Treponema pallidum

Symptoms
- primary stage = painless ulcer
- Secondary stage = 10 weeks after. Rash
- Latent stage where they are symptom free
- Tertiary stage = 40 years after can get systemic affects e.g. aortic regurgitation
- Pregnant women can pass this onto children = congenital syphilis

Diagnosis
- PCR and serology

Treatment
- early syphilis = benzathine penicillin. Other antibiotics are used for later stages

Presentation of STIs
Abnormal Discharge
- chlamydia
- gonorrhoea
- trichomonas vaginalis - frothy
- bacterial vaginosis - fishy smell, white, thin
- Candida albicans = thick white discharge

Ulceration
- herpes - painful ulceration
- syphilis - not painful

Skin Manifestations
- anogenital warts
- Scabies
- Pubic lice

Systemic Complications
- pelvic inflammatory disease
- Sexually acquired reactive arthritis

Testing For STIs
Men
- urine sample = for chlamydia
- Bloods
- Rectal samples especially for MSM
- Swab ulcers

Women
- endocervical swabs = for chlamydia, gonorrhoea
- High vaginal swabs = BV
- Bloods
- Urine sample
- Swab ulcers

Trichomonas Vaginalis
- Protozoa

Symptoms
- Frothy discharge, dysuria, strawberry cervix

Treatment - Metronidazole

Pelvic Inflammatory Disease
- This is the result of infection ascending from the endocervix causing endometritis (inflammation of the lining of the uterus), salpingits (inflammation of the Fallopian tubes) and ovarian abscesses
- As the infection ascends from the endocervix it causes infection - this damages the tubule epithelium and causes adhesions
- The infection passes from the uterus to the Fallopian tubes
- Inflammatory exudate can fill the tubes if adhesions block off the ends to form an abscess - this may present as a lump in the groin
- The infection may stay contained in the tubes or spread to the ovaries - from here it can spread into the peritoneal cavity (peritonitis) due to the lack of covering by peritoneal membrane

Symptoms:
- abdominal pain, pyrexia, abnormal discharge, vaginal bleeding
- Maybe asymptomatic for quite a while

Causes:
- STIs including chlamydia, gonorrhoea and bacterial vaginalis
- Copper coil - insertion could potentially move infections up

Investigations
- urine sample, pregnancy test, endocervical (for gonorrhoea and chlamydia) and high vaginalis swabs (BV), blood tests, HIV screening

Risk Factors
- these are the same for STIs and are if you are younger, dont use protection during sex, have multiple sexual partners and are of a lower socioeconomic class

Consequences:
- can cause future ectopic pregnancies - inflammation of the tubes and adhesions prevent movement so egg implants early in the tube
- Leads to infertility - due to adhesions
- Chronic pelvic pain - fixed retroverted uterus due to adhesions making it sick to abdominal wall
- Fitz-Hugh-Curtis syndrome - this gives RUQ pain and hepatitis as peritonitis spreads to liver - this is seen in chlamydia caused PIDs

Treatment;
- Ceftriaxone, doxycycline and metronidazole for 14 days
- Surgery may be required for adhesions and abscesses

Menopause

Menopause

- ***this is the end of menstruation for 12 months with no biological causes***
- The ovaries become *completely depleted of follicles* giving a decline in oestrogen but a rise in FSH and LH
- The age ranges between 45-55 years
- There are 4 categories of menopause:

Pre-menopausal

- this is the time prior to menopause
- Changes in the menstrual cycle occur such as - shorter follicular phase, early/absent ovulation, less oestrogen secreted, **rise in FSH/LH** (as the oestrogen level declines below a critical value the oestrogen can no longer inhibit the FSH and LH - FSH rises more due to no inhibin) and reduced fertility.

Peri-menopausal

- this is the transition phase (also called **climacteric**)
- There are physiological changes occurring which are associated with the end of reproductive life

Menopause

- this is the cessation of menstruation caused by failure of ovarian follicular development

Post Menopause

- this is the time after a women has completed 12 months without a period

Symptoms Treatment

Non-hormonal:

- dressing in lighter layers helps with hot flushes and night sweats
- Reduced fat/alcohol/caffeine/spicy food

HRT (hormone replacement therapy)

- can be given orally, as a vaginalis cream or transdermally - this helps limit osteoporosis
- this is an oestrogen replacement therapy
- must be taken with progesterone in those women who still have a uterus as oestrogen will cause endometrial proliferation and carcinoma, however, the progesterone has anti-proliferation effectives
- The increased estrogen increases the likelihood of breast cancer and DVTs/PEs as its hypercoaguable

Types of Menopause

Physiological

- normal decline in ovarian function resulting in reduced ovulation and eventual cessation of menstruation
- **Symptoms** = itchy, sweaty, sleepy, bloated, irritability, insomnia, forgetful and diminished sex interest
- The symptoms arise due to the oestrogen deficiency
- **Vascular changes** = hot flushes occur. These are transient rises in skin temperature and flushing.
- **Ovary Changes** = the ovaries become smaller, this is due to the decline in oestrogen. The ovaries produce androgens with the enzyme aromatase converting the androgens to oestrogen. Therefore, with menopause the increased FSH/LH ensures a continued androgen production despite having smaller ovaries.
- **General Appearance Changes** = the skin is less elastic due to loss of collagen, weight increases, hair becomes dry and voice is deeper
- **GI Changes** = motor activity decreases giving constipation, urethra and bladder lining become drier, thinner and less elastic (due to oestrogen decline) - this leads to urinary incontinence and an increased risk of UTIs
- **Uterus Changes** = becomes smaller and fibrotic due to atrophy of the muscles. The cervix will become smaller
- **Bone changes** = calcium moves out of bone leaving them weaker and more prone to fractures. This is because reduced oestrogen enhances osteoclasts ability
- **CVS Changes** = increased cholesterol, increase risk of heart disease and stroke, BP increases

Pathological

- the gradual or abrupt cessation of menstruation before 40 years

Dysfunctional Uterine Bleeding

- this can be seen as; spotting between cycles, heavy menstrual flow, mid-cycle bleed, unpredictable cycle lengths and durations
- This is because there is a continued oestrogen causing the endometrium to continue to thicken (hyperplasia)
- But as there is no corpus luteum there is no progesterone help cause shedding - this leads to ineffective shedding
- This results in an increased risk of carcinoma as there's unopposed oestrogen

Perineum

This is an anatomical region in found between the thighs. The diamond shape can be spilt in half to give an anterior and posterior triangle.

Pelvic Floor

- This is the floor boundary of the perineum region containing ligaments and muscles which support the organs found in the perineum

Function:

The function is to **support** the pelvic organs (vagina, uterus, bladder and rectum), maintain abdominal pressure (e.g. when coughing and sneezing), help facilitate defecation and micturition (by the muscles helping to become sphincters) and helps facilitate childbirth and help **continence.**

Muscles

- there are various muscles involved in the pelvic floor
- The **levator ani** muscles predominately make up the pelvic floor - these are the pubococcygeus, puborectalis and the iliococcygeus. They encircle the urethra, vagina and rectum
- The puborectalis ensures fecal continence.
- If pelvic floor support if lost then the external urethral sphincter will drop to give incontinence
- There are also perineal muscles of which there is a superficial layer (bulbospongiosus, external anal sphincter and transverse perineal) and deep layer (transverse perineal, external urethral sphincter)
- There is a fibrous patch of tissue called the **perineal body -** this acts as a site of attachment for the muscles, prevents tearing between the vagina and anal sphincter and suspends peritoneal viscera

Neurovascular Supply

- blood supply is through the pudendal arteries and veins
- Nerve supply is through the **pudendal nerve** (S2,3,4)

Bartholin's Glands

- these are found in the anterior perineum and produce a mucus like fluid to maintain a moist vagina
- These can become blocked forming cysts, which become inflamed/infected (**Bartholinitis**)

Episiotomy

- this is a medial-lateral incision along the **bulbocavernous** during childbirth
- This happens when it looks like the *perineal body may split* - if it does spilt consequences include prolapse (as viscera aren't held in as well by the weaker pelvic floor), dysfunction of the anal sphincters
- Needed for larger babies, shoulder distortion, if there's uncontrolled tearing of the perineum
- Complications can include haemorrhage, extension to anal sphincters, infection and pain

Pelvic Floor Dysfunction

Pelvic Floor Prolapse

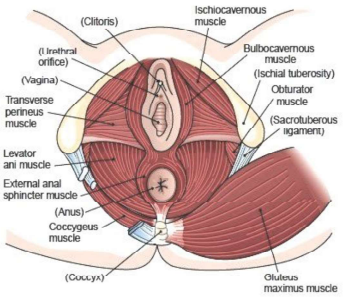
- This is the loss of support for the uterus, bladder, colon or rectum leading to prolapse of one or more of these organs into the vagina - they are normally held in place by ligaments and muscles
- This is not life threatening but decreases the quality of life
- Prolapses can be anterior onto the vagina (**cystocele -** bladder bulges onto vagina), posterior (**rectocele** - rectum bulges on vagina) or onto the **middle** of the vagina causing the uterus to prolapse and hang out of the vagina
- After a hysterectomy the top of the vagina may prolapse giving a **vaginal vault**
- During a posterior prolapse the rectum can push the uterus into the rectovaginal space/pouch of Douglas
- **Risk factors** include connective tissue disorders (marfans), giving birth (weakens muscles), having a large baby, difficult delivery, obesity
- Childbirth particularly increases the risk due to stretching of muscles and potential tearing of perineal body, there may also be puce all nerve damage
- **Symptoms** = feeling a lump, feeling of not emptying rectum, may have insert fingers in the vagina to reposition the rectum, discomfort, heaviness
- **Management** = surgery, pessaries (fits the prolapse back up)

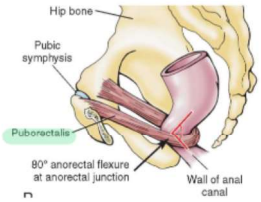
Urinary Incontinence

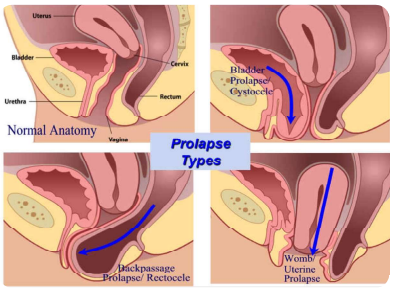
- dysfunction of the pelvic floor causes stress incontinence (urge us due to overactive bladder) - as the muscles normally contribute to make up the sphincter
- **Management** = pelvic floor muscle exercises, surgery

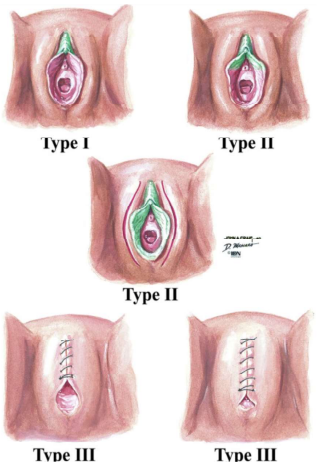
FGM

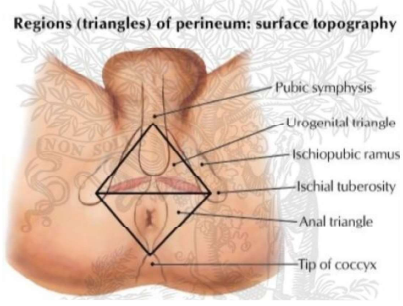
- these are procedures involving partial or total removal of the external female genitalia or any other injury the female genital organs
- Type 1 removes the clitoris, type 2 removes the clitoris, labia minora and labia majora, type 3 is the narrowing of the vaginal orifice through sealing the labia minora and type 4 is any other injury
- This can lead to haemorrhage, sever pain, sepsis, HIV and death
- Laters consequences include sexual difficulties, pain, keloid scar, urinary outflow obstruction, difficultly conceiving, PTSD
- There are obstetric consequences including haemorrhage, lacerations, difficult labour
- This is illegal in the UK and must be reported to the police if under 18

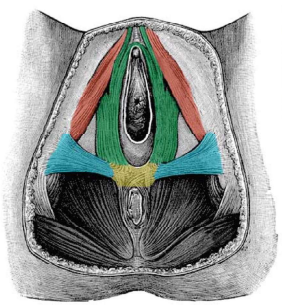


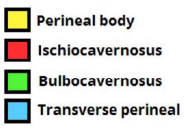












Cancers

Histologically you see dyskaryosis (abnormal nuclei), increased nucleus:cytoplasmic ratio, abnormal chromatin, mitotic figures

Cervical Cancer

This develops in the **transformation zone** of the cervix. This area develops during puberty when the endocervix (lined by columnar, glandular epithelium) become more exposed to the vagina so naturally undergoes metaplasia to squamous epithelia to withstand the acidic conditions better. However, this metaplasia means there more opportunity for neoplasia.
The cervix usually contains glands, which under the influence of progesterone produces the mucus plug

Risk Factors

- **HPV** 16 and 18 - these infect the metaplastic squamous cells in the transformation zone and produce the viral **protein E6 and E7**. These proteins inhibit the tumour suppressing proteins **p53 and pRB**, meaning more proliferation can occur and a reduction in the ability to repair damaged DNA. This is more likely to occur in immunosuppressed patients as lots of HPV infections are cleared by the immune system before a cancer can develop.
- Sexual intercourse, Multiple births/partners, Early 1st pregnancy, Smoking, Oral contraceptive pill

Screening

- a **Pap** (Papanikolaou) **test** is where cells from the transformation zone are scraped off and stained
- If abnormality if then detected a visual examination of the cervix can be done (**colposcopy**)

Prevention

HPV vaccination is offered to girls aged 12-13. Not offered to boys in the UK despite protecting against penile cancer and offering herd immunity to girls (as intercourse with penile cancer can cause cervical cancer)

Cervical Intraepithelial Neoplasia

- this is dysplasia of the squamous cells in the cervix (induced by HPV infection) but has not invaded the basement membrane
- This is the precursor to squamous cell cervical carcinoma
- **CIN I** = some dysplasia but mostly regresses
- **CIN II** = some more dysplasia
- **CIN III** = carcinoma in-situ. Lots of dyplasia but has not yet invaded the basement membrane
- treatment for this include a cone excision of the transformation area

Invasive Cervical Carcinoma

- most commonly squamous cell but can also be adenocarcinoma
- Can be exopyhtic (like polyps) or infiltrative (goes through basement membrane)
- Spreads to bladder, ureter, rectum, vagina and to para-aortic lymph nodes.
- Presents with screening abnormality, vaginalis bleeding.
- This is treated by cervical cone excision if small, hysterectomy, chemotherapy

Ovary

- Presentation depends if they are non-functional or functional (produce hormones)
- Non-functional effects include ascites (if implantation of cancer cells occurs on peritoneal surface), distension, pain
- **CA-125** tumour marker
- BRAC mutation associated - if detected can give prophylactic salpingo-oophrectomy
- Contraceptive pill is protective as it prevents trauma from ovulation and the scarring/ healing of the ovary afterwards where dysplasia can occur

Classification

Mullerian Epithelium Tumours

- of these types of tumours there are 3 histological appearances; serous, mucinous and endometrioid
- **Serous** ovarian tumours often spread to the penitent surfaces and cause ascites
- **Mucinous** tumours are large and cystic (fluid filled). These are usually benign and glandular.
- **Endometrioid** tumours resemble endometrial glandular tissue
- this includes endometriosis where there are deposits in the ovaries

Germ Cell Tumours

- these are mostly **teratomas** which are normally mature/benign but are rarely malignant or *monodermal*
- Benign teratomas are cystic and usually contain hair, sebaceous glands and teeth
- Monodermal teratomas are composed of thyroid tissue and if functional can cause hyperthyroidism
- There are malignant variations such as yolk sac tumours and choriocarcinomas

Sex Cord-Stromal Cell Tumours

- these arise from the endocrine areas of the ovaries
- These can be feminising if they contain granulosa/theca cells (causing precocious puberty or endometrial hyperplasia) or masculinising if they contain Leydig or Sertoli cells (causing breast atrophy, amenorrhoea, hair loss, infertility, voice changes, facial hair)

Metastasises to the Ovaries

- most commonly from primary mullerian tumours in the female reproductive tract
- **Kruckenberg tumour** = from the stomach

Vulval Tumours

- these are usually **squamous cell carcinomas**

Risk Factors:

- Younger women: **HPV**
- Older women: vulva irritation/inflammatory conditions including squamous cell hyperplasia and **Lichen sclerosis** (fibrosis of the superficial dermis causing chronic irritation giving squamous abnormalities)

Vulvar Intraepithelial Neoplasia (VIN)

- this is the precursor to vulval squamous cell carcinoma
- It is where there are atypical squamous cells in the epidermis of the vulva but they have not invaded through the basement membrane

Vulval Cell Carcinoma

- this spreads initially to the inguinal, pelvic, iliac and para-aortic lymph nodes
- Can then spread to the lungs and liver

Endometrium

Risk Factors

- endometrial hyperplasia is a common precursor caused by increased oestrogen (due to annovulation, obesity and exogenous oestrogen)
- In obesity the adipose tissue contain aromatase to convert androgens into oestrogen so there's more circulating oestrogen

Endometrial Adenocarinoma

- presents with vaginal bleeding
- Can be polyploid or infiltrative
- Can be 1 of 2 types; endometrioid or serous
- **Endometrioid Endometrial Adenocarcinoma** = the most common type usually from hyperplasia.
- **Serous Carcinoma** = more aggressive as cells can drop off, spread to other locations and still be viable so spreads easier.

Myometrium

- **Leiomyomas** (fibroids) are benign smooth muscle tumours which are white and well shaped.
- symptoms - heavy/painful periods, urinary frequency due to bladder compression and infertility
- Rarely become malignant to cause uterine leiomyosarcoma which metastasise to the lungs

Testicular Cancer

- tumour markers = alpha fetoprotein and HCG
- Risk: if the testes fail to descend- **Orchhiopexy** (surgery to fix this) decreases risk

There are 2 types:

1. **Germ cell Tumour**
   - these are **seminomas** or **non-seminomatous**
   - Non-seminomatous are usually a mix of yolk sac tumours, embryonal also carcinomas, choriocarcinomas and teratomas
   - Teratomas are malignant post puberty
   - Seminars spread to iliac and para-aortic nodes
   - Non spread to earlier
2. **Sex Cord-Stromal cell tumours**
   - these are most commonly Sertoli cell tumours or Leydig cell tumours