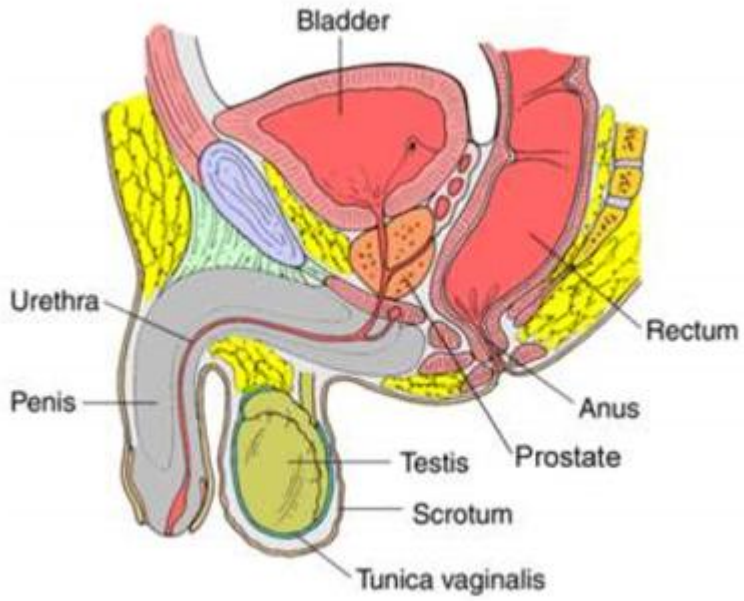
Pupil Notes Unit 2

Unit 2 is entitled 'Physiology and Health'. It is divided into two sections. Section 1 notes cover the following topics – Reproductive organs and hormonal control, Biology of fertility control and Ante- and postnatal screening. Section 2 covers the following – Structure of the cardiovascular system, the cardiovascular system in action and Cardiovascular disease, diabetes and obesity.

Section 1 Notes

Reproductive Organs, gametes and Fertilisation (chapter 8)

Testes and Ovaries



Gametes are formed from Germline Cells

The testes are the site of sperm (spermatozoa) production

The testes are also the site of manufacture of the male sex hormone testosterone

Sperm are formed from germline cells in tiny tubes called Seminiferous Tubules

Seminiferous tubules unite to form coiled tubes that connect to the Sperm Duct – free swimming sperm leave the testes in the sperm duct

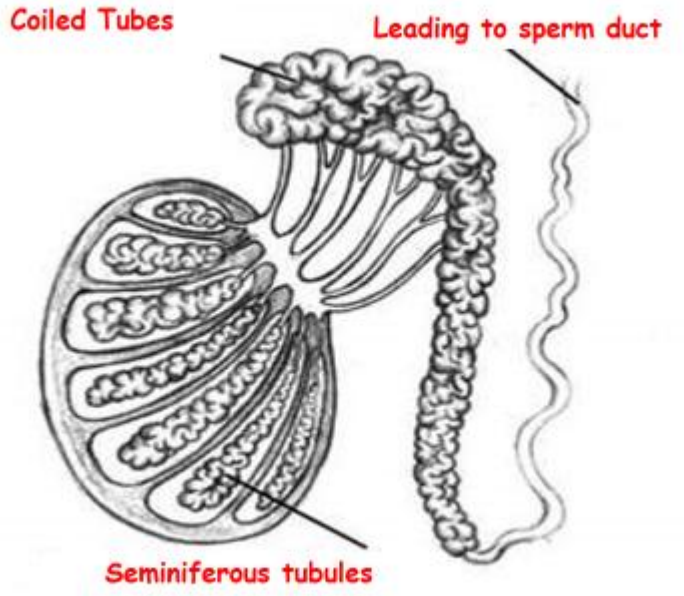
Interstitial Cells

Between the seminiferous tubules are cells called the Interstitial Cells

These cells produce the hormone Testosterone

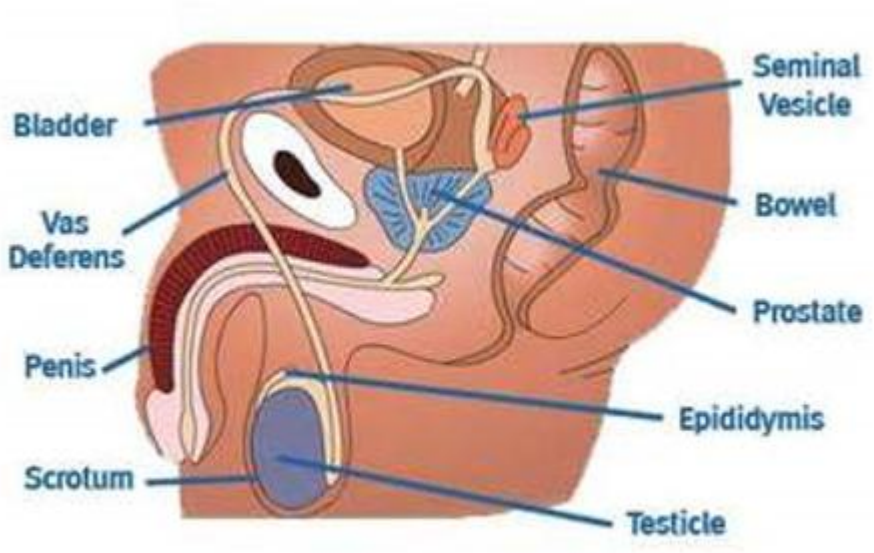
Testosterone passes directly into the blood stream

Fertilisation depends on the motility of the sperm - motility requires a fluid medium and a source of energy



Semen is the collective name given to the milky liquid release by males

Semen contains sperm plus the fluid from the Seminal Vesicles and the Prostate Gland



Seminal Vesicles and Prostate

Seminal Vesicles –

Secrete a liquid rich in fructose to provide energy for sperm motility

The liquid contains hormone-like compounds that stimulate contraction of the female reproductive tract

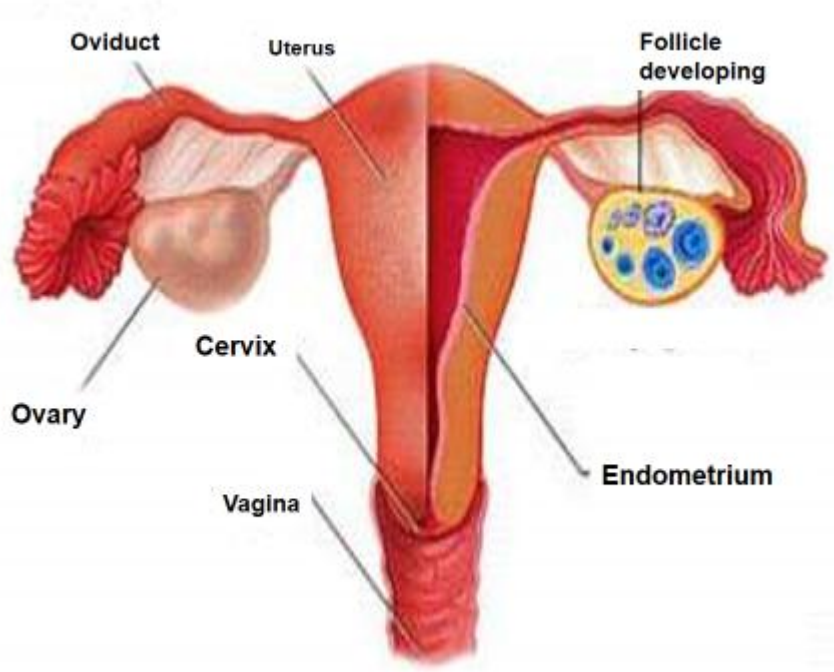
These contractions help the sperm to reach the oviduct (where fertilisation takes place) quicker than 'swimming' alone

The prostate gland secretes lubricating liquid containing enzymes

These enzymes maintain the fluid at optimum viscosity for sperm motility

Just before ovulation the cells lining the female cervix secrete a watery mucus

This watery mucus is easily penetrated by sperm



Eggs or Ova are formed from germline cells in the female ovaries

The ovaries contain immature eggs at various stages of development

Ovulation is when a mature ovum is released, from the ovary, into the oviduct

Fertilisation takes place in the oviduct if sperm are present - fertilised egg or zygote develops into an embryo

Hormones

Hormones are 'chemical messengers' produced by Endocrine Glands

Hormones are secreted into the bloodstream

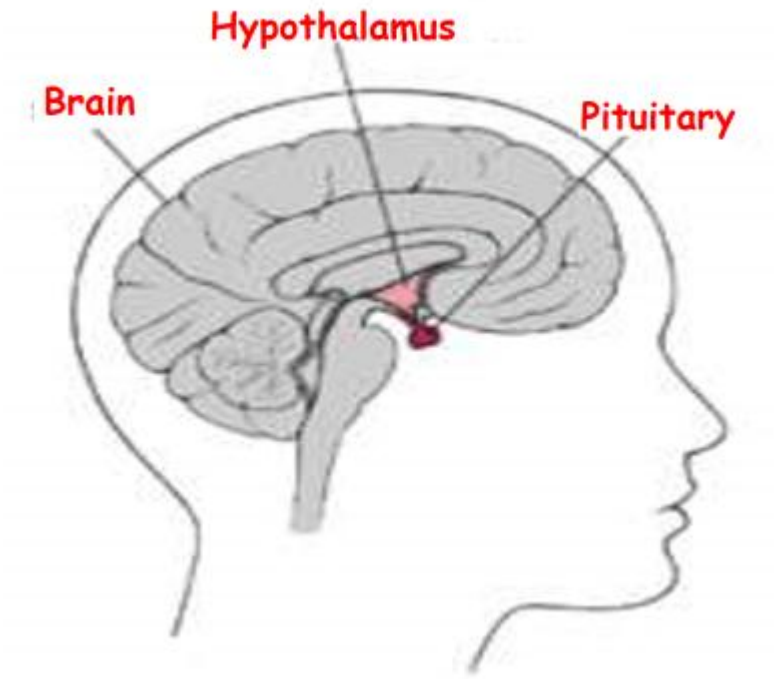
When they reach a 'target organ' they bring about a specific effect

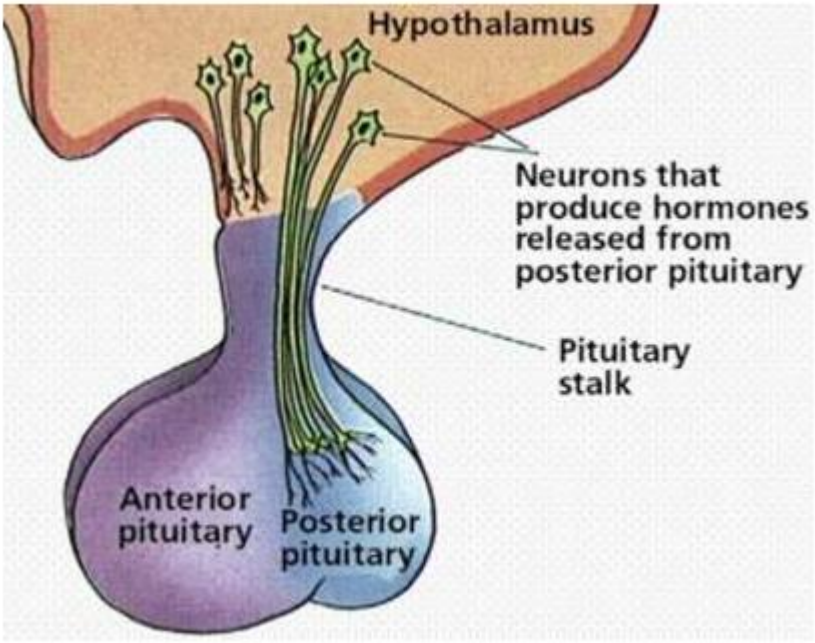
In reproduction, hormones control –

The onset of puberty

Sperm production

The menstrual cycle





At puberty the Hypothalamus secretes a releaser hormone whose target is the Pituitary Gland

The pituitary responds by producing <u>two</u> hormones

The first is FSH, follicle stimulating hormone

In males, the second is ICSH (interstitial cell-stimulating hormone)

In females, the second is LH (luteinising hormone)

Hormonal control of sperm production

FSH promotes sperm production in the seminiferous tubules

ICSH stimulates the interstitial cells to produce the hormone Testosterone

Testosterone –

Stimulates sperm production

Activates the Seminal Vesicles and Prostate Gland to produce secretions

Negative Feedback Control

As testosterone concentration builds up in the bloodstream it reaches a level that inhibits FSH and ICSH secretion

This leads to a decrease in testosterone concentration

As a result, the pituitary gland releases FSH and ICSH again

This type of self-regulating mechanism is called negative feedback

Pituitary hormones and Ovaries

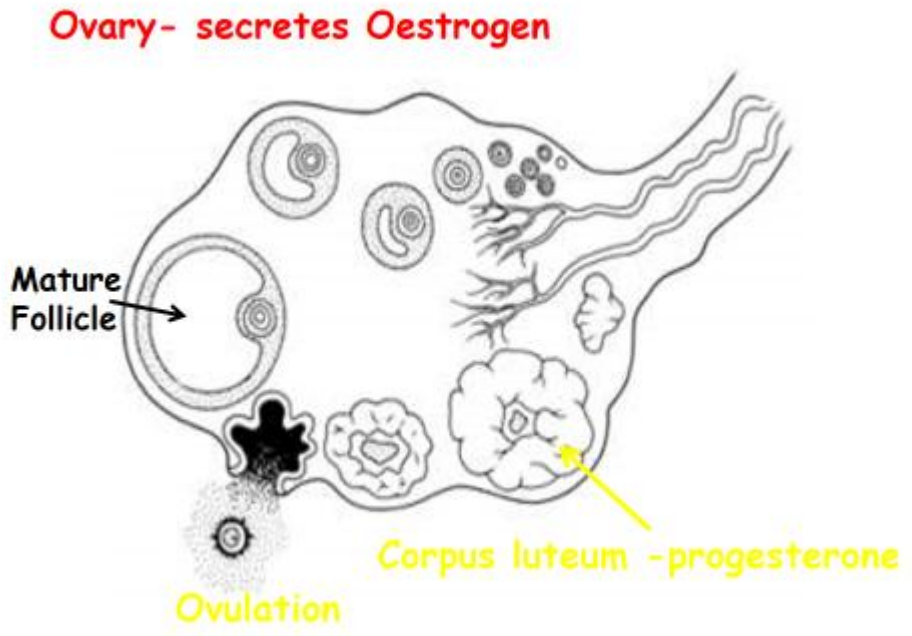
FSH stimulates the development and maturation of each follicle

It also stimulates the ovary to secrete the female sex hormone Oestrogen

LH triggers ovulation

It also brings about the development of the Corpus Luteum from the follicle

The corpus luteum then secretes the sex hormone Progesterone



Oestrogen stimulates the proliferation of the Endometrium, the inner layer of the uterus

This prepares the uterus for implantation of an embryo

High levels of oestrogen stimulates the cells lining the cervix to secrete a watery mucus easily penetrated by sperm

The highest concentration of oestrogen is just before ovulation (increases chance of fertilisation)

Oestrogen also stimulates the production of LH by the pituitary

Progesterone –

Promotes the further development and vascularisation of the endometrium, in preparation to receive a blastocyst

Progesterone inhibits the secretion of FSH and LH by the pituitary

Menstrual Cycle

Lasts approximately 28 days

The first day of the menstruation is regarded as day 1

The cycle takes place in two phases – the first or Follicular Phase and the second or Luteal Phase

Follicular Phase (day 1→14)

During the first half of the cycle the pituitary gland releases FSH

FSH has two effects

It causes a follicle to develop in the ovary

It stimulates the wall of the follicle and the tissues of the ovary to secrete the hormone oestrogen

The immediate effect of oestrogen is to bring about healing and repair of the uterine wall

In the course of the next 2 weeks the level of oestrogen in the body builds up

Peak levels of oestrogen stops the pituitary producing FSH and stimulates it to produce a surge in the secretion of LH

The surge in LH triggers ovulation

As stated previously, high oestrogen level affects the consistency of the cervical mucus -the mucus is more easily penetrated by sperm and leads to an increased chance of fertilisation

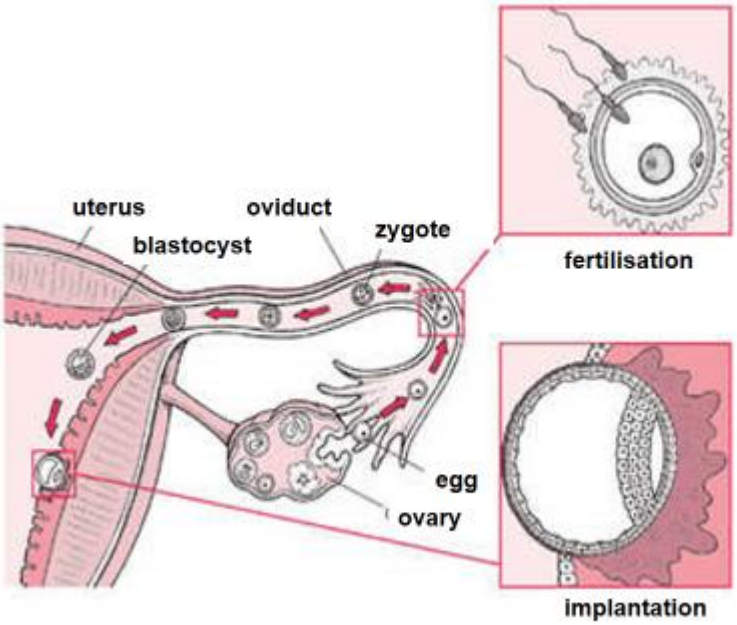
Luteal Phase (day14→28)

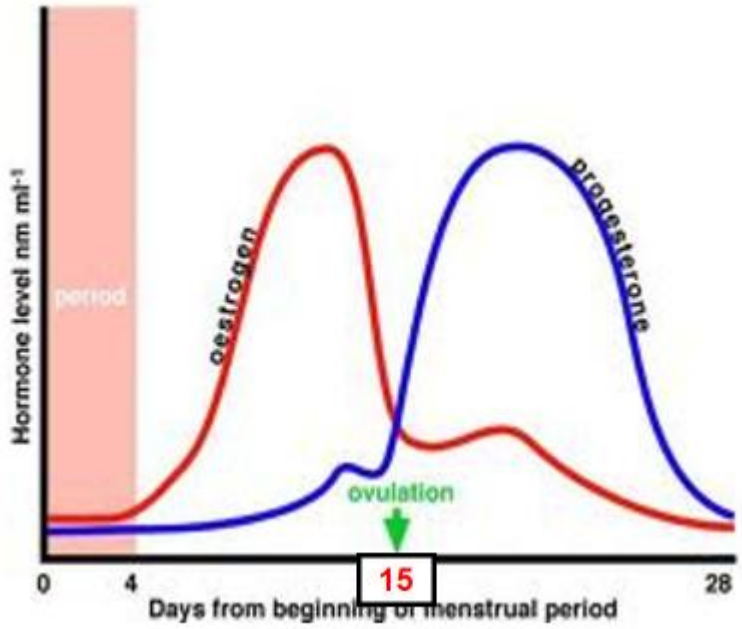
LH causes the follicle to change into the corpus luteum

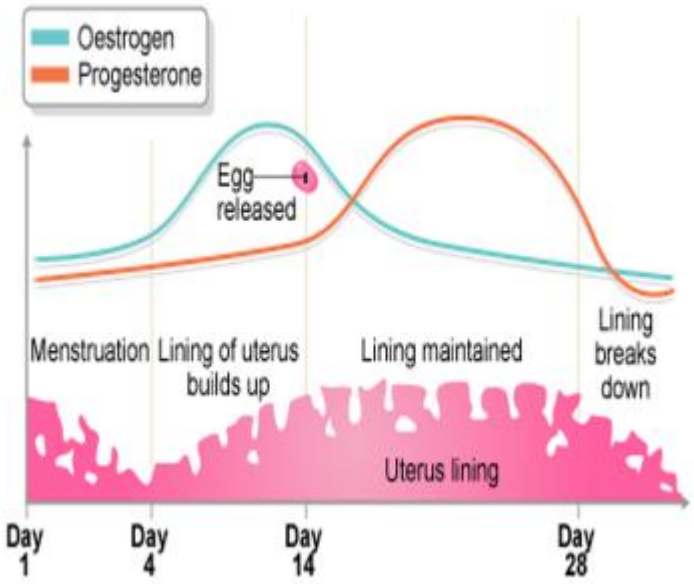
The corpus luteum secretes a hormone called progesterone

Progesterone (and oestrogen) cause the continued proliferation and vascularisation of the endometrium in preparation for receiving a blastocyst

During the next 10 days or so the concentration of progesterone inhibits the production of FSH and LH from the pituitary


uterus
oviduct
zygote
blastocyst
fertilisation
egg
ovary
implantation


Hormone level nm ml⁻¹
period
oestrogen
progesterone
ovulation
15
0
4
28
Days from beginning of menstrual period



Inhibition of FSH and LH

Inhibition of FSH and LH –

Prevents further follicles from developing

Stops the ovary producing oestrogen

Causes the corpus luteum to degenerate and cease producing progesterone

Sudden drop in oestrogen and progesterone causes menstruation to occur

Summary FSH and Oestrogen

FSH

Follicle develops

Ovary secretes oestrogen

Oestrogen

Heals and repairs lining

At high concentration, oestrogen inhibits FSH and stimulates pituitary to produce LH

Summary of LH and Progesterone

LH

Sudden surge of LH causes ovulation

LH changes follicle to corpus luteum

Corpus luteum secretes progesterone

Progesterone

Progesterone and oestrogen cause further proliferation and vascularisation

High progesterone inhibits FSH and LH

Ovary stops secreting oestrogen

Corpus luteum stops producing progesterone

No hormones to proliferate lining

Menstruation

After Fertilisation, HCG

The embryo secretes a hormone called Human Chorionic Gonadotrophin, HCG

This hormone has the same effect as LH

HCG maintains the corpus luteum

Corpus luteum continues to secrete progesterone and prevents menstruation

After 6 weeks the placenta takes on the job of secreting progesterone

HCG in urine is basis of pregnancy testing

Cells lining the cervix secrete mucus for lubricating the vagina

High levels of Oestrogen cause these cells to excrete watery mucus

High Oestrogen levels precedes ovulation

Thin mucus at this time increases the chance of fertilisation

High progesterone levels cause the cervical mucus to become viscous

In the event of pregnancy the mucus changes into a semi-solid 'plug'

This protects the fertilised egg/embryo from infection

At Ovulation –

Temperature rises by about 0.5C

Temperature remains at this high level during the luteal phase of the menstrual cycle

The biology of controlling fertility (chapter 9)

In human males, there is a relatively constant level of FSH and ICSH in the bloodstream

Therefore, a steady quantity of testosterone is secreted and a steady quantity of sperm produced

As a result, human males are continuously fertile

Cyclical fertility is in marked contrast with the continuous fertility in males

The interplay of pituitary and ovarian hormones results in the period of fertility being restricted to the 1-2 days following ovulation

The indicators 'Temperature' and 'Mucus' can be used by a woman to calculate her fertile period

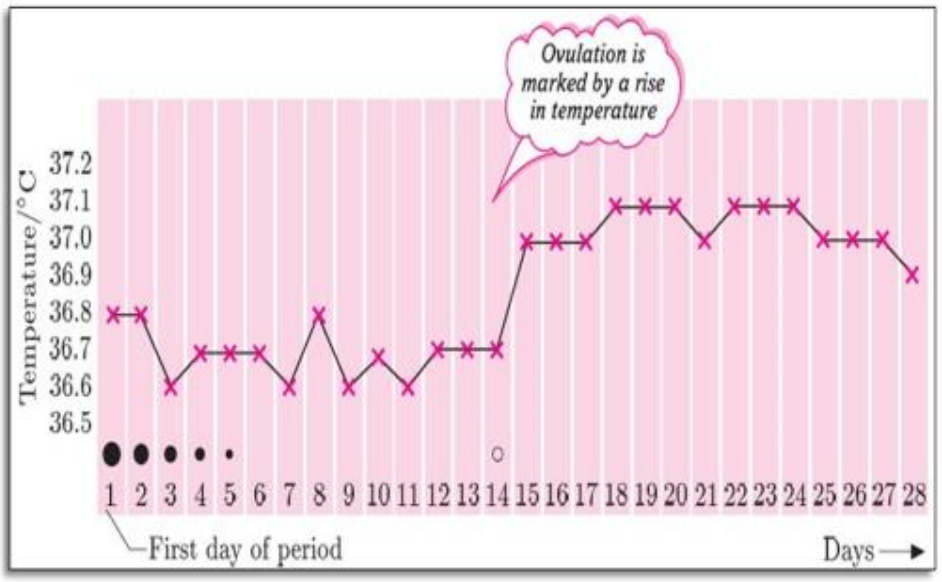
This is obviously of use to a couple who are wishing to conceive

Approximately 1 day after the LH surge which triggers ovulation, a woman's body temperature rises by 0.2-0.5 C

It remains at this elevated level for remainder of the luteal phase

Fertile period lasts for about 1-2 days

The infertile period is resumed after the 3rd daily recording of higher temperature



The cervical mucus secreted into the vagina during the fertile period is thin and watery

This allows easy access of sperm to the female reproductive system

After ovulation, progesterone causes the mucus to gradually increase in viscosity

Infertility treatments and Contraception are based on the Biology of fertility

Sometimes there is a failure of the pituitary gland to secrete adequate FSH or LH

Ovulation can be stimulated by

- Drugs that mimic the normal action of FSH and LH

- Drugs that prevent the negative feedback effect of oestrogen on FSH secretion

These drugs can be so effective that they bring about 'Super Ovulation' which can lead to multiple births

Super ovulation can be used to collect ova for IVF

Artificial Insemination

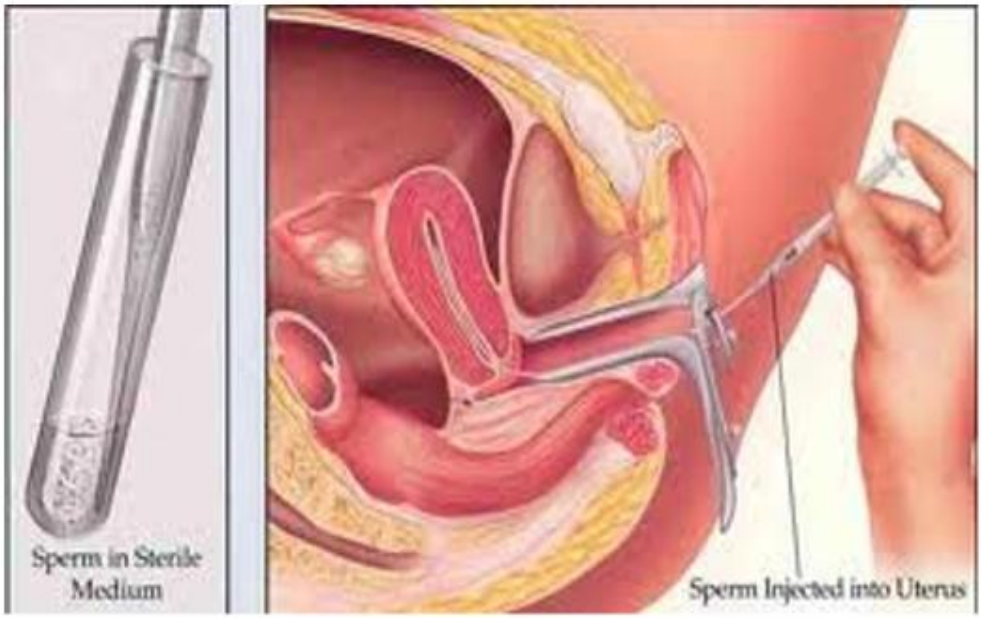
This involves the insertion of semen into the female tract by some means other than sexual intercourse

It is particularly useful where a male has a low sperm count

Several samples of semen are collected and each is preserved (freezing) until required

They are then defrosted and released together into the partner's cervical region during her fertile period

If a partner is sterile, artificial insemination can be used to insert the semen of a donor who has a normal sperm count into the female reproductive tract

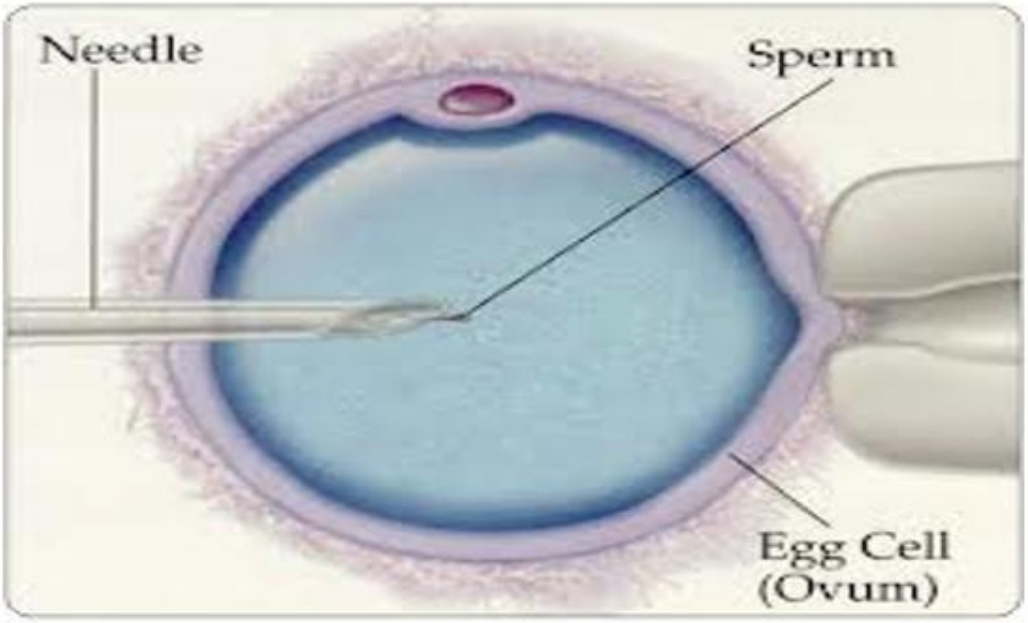


<u>Intracytoplasmic Sperm Injection (ICSI)</u>

This technique is employed when a man's sperm count is low

Or, many of the mature sperm are defective

The procedure involves drawing a healthy sperm into a needle and injecting the <u>head</u> of the sperm directly into an egg – to achieve fertilisation



IVF enables fertilisation, outside the body, in a culture dish

IVF overcomes the problem of infertility caused by a blockage of the oviducts

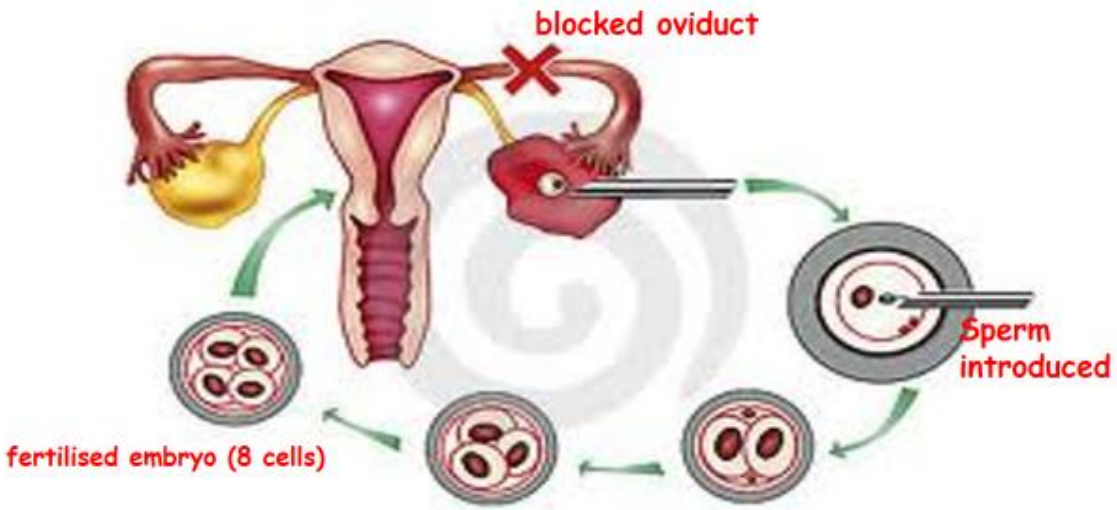
It takes place in the following 6 stages –

1. Woman is given hormone treatment to stimulate multiple ovulation

2. Surgical removal of the eggs from the ovary, using equipment like a syringe

3. Eggs are mixed with sperm in a culture dish, containing nutrients, to allow fertilisation to take place

Alternatively, sperm may be injected directly into the egg using ICSI



4. Fertilised eggs are incubated for 2-3 days to form embryos of at least 8 cells or more

Pre implantation screening can be employed at this stage to identify genetic disorders and chromosomal abnormalities

5. Two (or three) embryos are inserted into the uterus for implantation

6. Remaining embryos are frozen in case a second attempt is needed

Pre implantation Genetic Screening (PGS) and Pre implantation Genetic Diagnosis (PGD)

PGS is a **non**-specific approach

It checks the embryos for single gene disorders and common chromosomal abnormalities

PGD is a specific approach

It is used to check for a known gene of chromosomal defect

Ethics of PGS and PGD

People who support these practices –

Believe they offer reassurance to couples at high risk of producing children with serious genetic disorders

It may also be claimed that the reduced frequency of genetic diseases is of benefit to society

Others believe it is morally wrong to make conception 'selective'

They say that these procedures could be the start of Eugenics – human race could be subject to 'selective breeding' and this could lead to 'designer babies'

Health issues

About 6% of patients undergoing treatments, involving drugs to stimulate the ovaries, suffer hyperstimulation of their ovaries

Medical experts are concerned about an increased risk of uterine cancer in later life

Most children conceived through IVF have a mass at birth which is significantly lower than normal

Children born with low birth weight are more likely to suffer long term health problems in later life –

These include obesity, diabetes, and hypertension and heart conditions (same may be true for IVF children)

The prevention of conception (or pregnancy) by natural or artificial means

Physical methods (3)

Barrier Method

The barrier method physically blocks the ability of the sperm to reach the ovum

Devises include

- Condom (fits over penis)
- Diaphragm (dome shaped rubber cap inserted into the vagina blocking the cervix)
- Cervical cap (rubber structure which fits tightly around the cervix and can be left in place for a few days)

Avoidance of 'Fertile Period' is also a method of contraception

Intra Uterine Device

An IUD is a plastic T-shaped structure with copper wound around its outside

It is fitted into the uterus for months (or even years)

It has threads attached for easy removal

It prevents the implantation of an embryo

It should really be termed a contragestic device as it prevents gestation

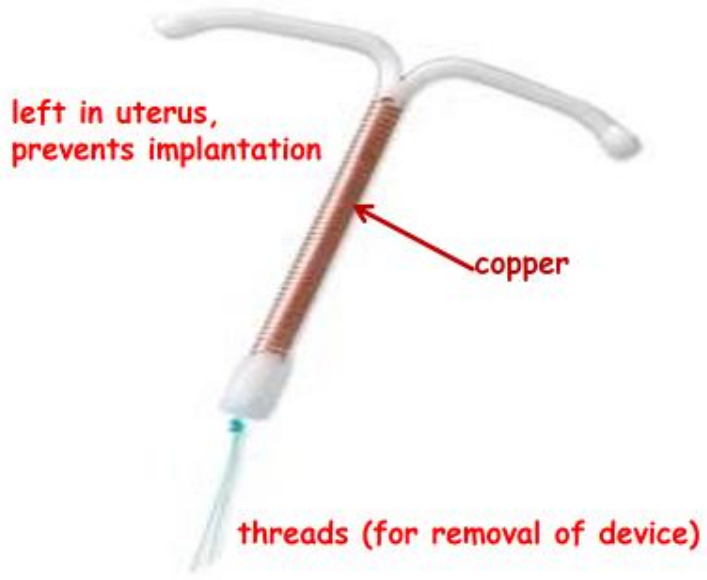
The presence of an IUD stimulates the presence of white blood cells which are hostile to sperm (and embryo)

It impairs the mobility of the sperm

It irritates the lining of the uterus, making it unreceptive to the embryo

IUD can cause complications – inflammation of the uterus and Ectopic Pregnancy

Many people are uneasy about the Ethics involved



Sterilisation Procedures

3(a). Vasectomy

This involves cutting and tying the two sperm ducts

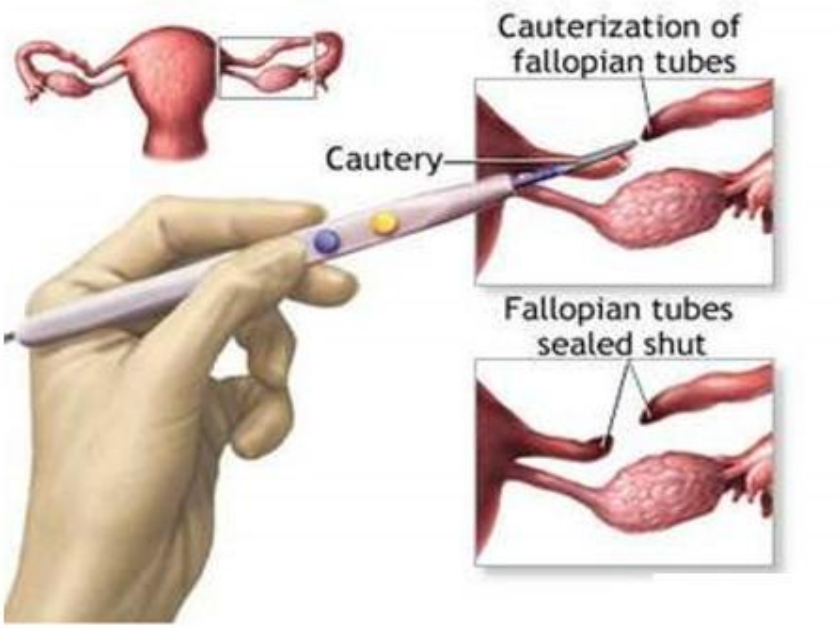
This prevents sperm being released

The sperm produced undergo Phagocytosis

3(b). Tubal Ligation

This involves cutting and tying the two oviducts

This prevents eggs meeting sperm



Chemical methods of Contraception

<u>Pills containing a combination of hormones</u>

Oral contraceptive pills usually contain synthetic oestrogen combined with synthetic progesterone

The pill is taken every day for 3 weeks from the final day of the previous menstrual period

This increases the concentration of oestrogen and progesterone in the bloodstream and exerts negative feedback control

Secretion of FSH and LH by the pituitary is inhibited

Follicle maturation remains inhibited

Ovulation does not occur

Placebo pills are taken during week 4 to allow oestrogen and progesterone levels to degrease

As a result, menstruation takes place

'Morning-after Pill'

Contain higher doses of hormones than the standard oral contraceptive pill

They are taken after unprotected sex to prevent implantation (if fertilisation has occurred)

'Mini Pills'

These are known as progesterone-only pills

They do not contain synthetic oestrogen

Mini pills thicken the cervical mucus, reducing the viability of sperm

This form of contraception can also be given as an implant, under the skin

It can give protection for up to 3 years

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Mini pills thicken the cervical mucus, reducing the viability of sperm

This form of contraception can also be given as an implant, under the skin

It can give protection for up to 3 years

Advantages include -

Can be used during breast feeding

Can reduce cramps and heavy bleeding

Can be taken by women who cannot take oestrogen

Can be taken by women who have high blood pressure

Disadvantages include -

Must be taken at the same time every day

Can cause breast tenderness

Can cause mood swings

Can lead to weight gain

Can lead to irregular menstruation

Ante- and postnatal screening (chapter 10)

Antenatal care includes . . . .

1. Ultrasound imaging

2. Biochemical tests

3. Diagnostic testing

4. Rhesus antibody testing

1. An ultrasound scanner picks up high frequency sounds that have bounced off the foetus

A 'dating scan' is performed at 8-14 weeks to determine the stage of pregnancy and to calculate the due date

Dating scans are used in conjunction with biochemical tests for marker chemicals which vary normally during pregnancy

It is worthwhile noting that measuring a substance at the wrong time could lead to a false positive result

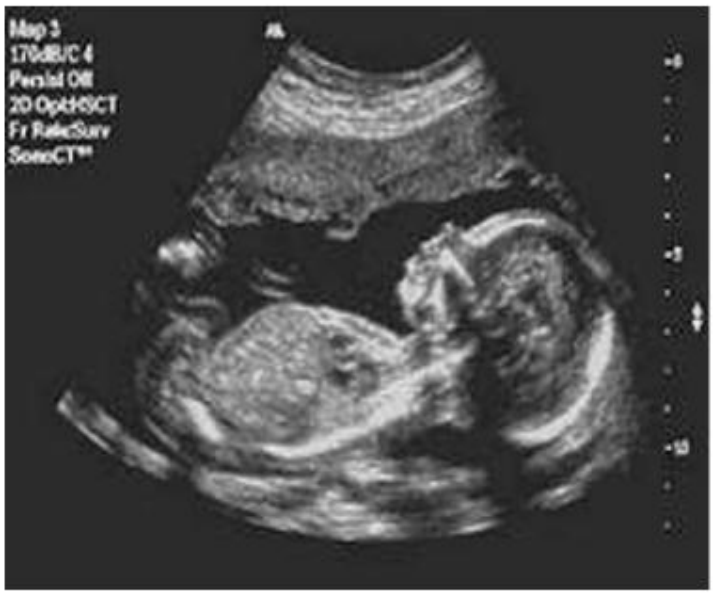
For example, at one stage in pregnancy the presence of a high level of a certain chemical marker may indicate that the foetus has a genetic disorder

At another stage in pregnancy the same high level would have no significance

Another scan is carried out at 18-20 weeks and this produces an 'anomaly scan'

At this scan, checks for physical abnormalities can be made

20 weeks



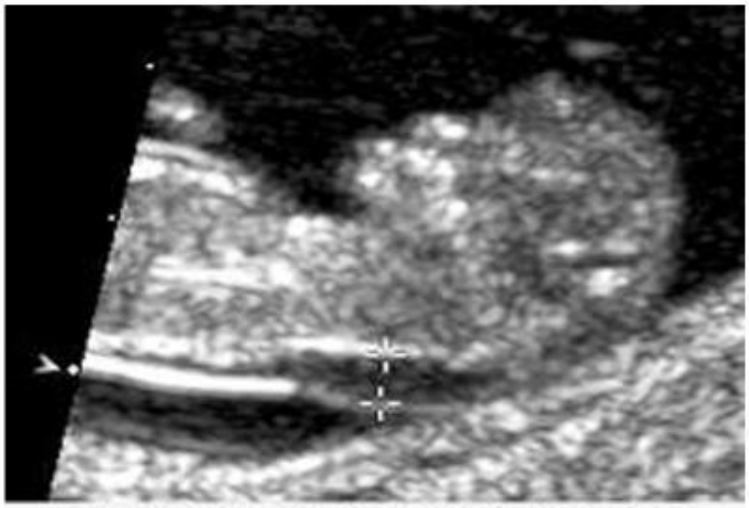
A NT scan helps experts to estimate, more accurately, the risk of a Down's syndrome baby

The test is carried out at 11-14 weeks (most reliable results at this time)

It allows an assessment to be made of the thickness of fluid at the nape of the neck of the foetus

If the Nuchal Translucency exceeds a normal value then there is a risk of chromosomal abnormality (this is not a diagnostic, definite, test)

fluid exceeds 'normal' value



Abnormal Nuchal Lucency Thickening

2. Biochemical tests

The detection of the marker Human Chorionic Gonadotrophin (HCG) in the blood and urine is the basis of early pregnancy tests

Health of mother and foetus is monitored by biochemical tests that detect normal physiological changes during pregnancy

Routine tests are carried out to check altered liver, renal and thyroid functions

Pre-eclampsia

This is the most common cause of dangerous complications during pregnancy

The sufferer displays some or all of the symptoms –

High blood pressure

Excess protein in the plasma

Changes to blood biochemistry caused by altered liver and renal function

For women with pre-eclampsia the concentration of urea in the plasma is significantly higher than normal

The concentration of calcium in the urine is significantly lower

These differences are thought to be due to a decrease in renal blood flow and glomerular filtrate rate

As there is no cure, the baby may be induced early or delivered by Caesarean section

'Marker', False Positives and False Negatives

At 16-18 weeks the mother is offered a series of biochemical tests that check for 'markers'

Example. HCG increases during weeks 6-10 then decreases to a steady low level

It remains high if the foetus has Down's syndrome

Results at 10 weeks would be meaningless (could give a false positive) since normal pregnancy and a Down's pregnancy would show elevated results at week 10

Times chosen for biomedical tests are synchronised with information from ultrasound scans to minimise the chance of obtaining false positive or false negative results

AFP is produced by the foetus and the concentration in the mother's blood increases

The normal range of values during pregnancy is 0.5-2.49 units AFP

Levels lower than 0.4 units are found in Down's syndrome (trisomy 21) pregnancy and Edward's syndrome (trisomy 18)

This test marker is part of a biochemical screening test – it does not mean that an abnormality has been diagnosed

A Nuchal Translucency scan is a more accurate way to estimate the risk of Down's syndrome

Again, this is not a diagnostic test

Risks associated with Down's syndrome testing –

1. Age, older woman's eggs are more prone to a type of mutation that leads to eggs being formed that have an extra copy of chromosome 21

2. Woman are often advised to have invasive diagnostic tests, Amniocentesis or Chorionic Villus Sampling – both carry a risk of miscarriage

Screening Test

A screening test detects signs and symptoms associated with a disorder

A degree of risk can be assessed

Diagnostic test

A diagnostic test is a definite test which establishes, without doubt, whether a person is suffering from a specific disorder

3. Diagnostic Testing

Diagnostic tests may be offered if:

Any problems emerged from routine screening tests

There is a history of genetic disorder(s) in the family

The woman is already in a 'high risk' category, over 35 years of age

Risks

Amniocentesis carries a slightly increased risk of miscarriage

CVS has a much higher risk of miscarriage

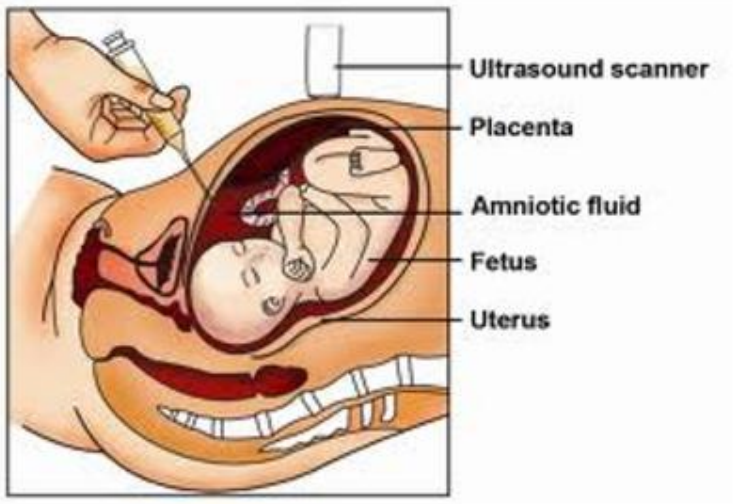
Amniocentesis is carried out at about 14-16 weeks of pregnancy

A small amount of amniotic fluid is withdrawn and this contains foetal cells

The cells are cultured to produce a karyotype, this usually takes about 2 weeks

A karyotype is a visual display of a person's complete chromosome complement, arranged in pairs

foetal cells removed from amniotic fluid, increased risk of miscarriage



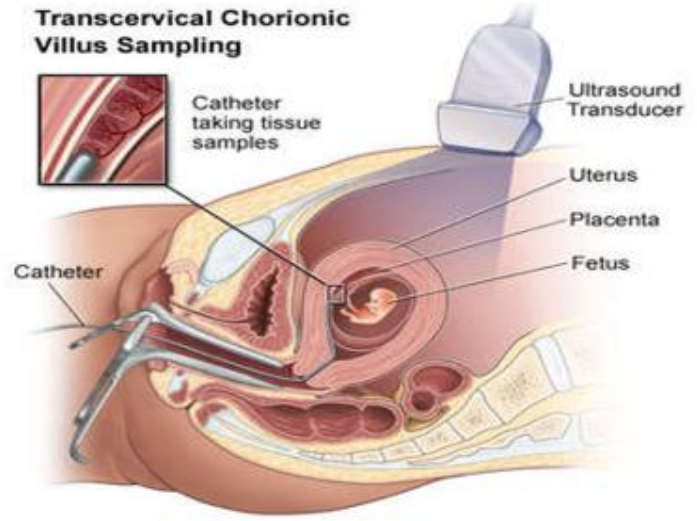
Chorionic Villus Sampling (CVS)

This involves taking a sample of placental cells

The cells are cultured and used for karyotyping

One benefit of CVS is that it can be carried out as early as 8 weeks into pregnancy

Can be carried out at 8 weeks, invasive and carries higher risk of miscarriage



4. Rhesus antibody testing

A problem arises when a Rhesus-negative mother is pregnant with a Rhesus-positive baby

Rhesus antigens on the surface of the baby's red blood cells are regarded as 'foreign' by the mother's immune system if she comes into contact with them at a 'sensitising event' such as birth

After the birth . . . .

The mother is given anti-Rhesus antibodies to destroy any of the Rhesus antigens left behind before the mother's immune system has time to respond to them (and become 'sensitised')

If she became sensitised she would see any future Rhesus-positive foetus as 'foreign'

Postnatal Screening – diagnostic testing for

metabolic disorders

PKU is an inborn error of metabolism

Newborn babies are routinely screened for PKU

Their blood is tested for the presence of excess phenylalanine

Sufferers are placed on a restricted diet containing the minimum amount of phenylalanine needed for normal growth

If PKU is not detected soon after birth the baby's mental development will be adversely affected

Lactose, the sugar in milk, is broken down by enzyme to glucose and galactose

The galactose is converted to glucose under the action of 3 enzymes

Galactosaemia is an inherited disorder caused by a mutation

It occurs when one or more of enzymes is non-functional

e. g. When enzyme 2 is non-functional there is a toxic accumulation of the intermediate 1 compound

Normal pathway

Galactose-enzyme1→ intermediate 1 –enzyme2→ int.2

Intermediate 2 –enzyme3→ glucose

Enzyme 2 non-functional

Galactose-enzyme1→ intermediate 1 = toxic build- up of intermediate 1

The blood of infants is screened for the 3 enzymes, needed to convert galactose to glucose

Affected babies that go untreated may die within a few days of birth

The condition is treated by eliminating lactose and galactose from the diet

Some sufferers may still go on to have learning difficulties despite their restricted diet

The hormone Thyroxin is essential for the development of the nervous system, regulation of the body's metabolism and normal growth and development

The pituitary produces thyroid stimulating hormone which stimulates the thyroid gland to release thyroxin

Congenital hypothyroidism results in severe deficiency in the functioning of the thyroid gland

2-3 days after birth, babies are screened to measure their thyroxin levels

Affected individuals are given a daily dose of thyroxin

Amino acid disorders are a group of rare, inherited conditions that affect infants from birth.

They are caused by enzymes that do not work properly.

Protein is made up of smaller building-blocks, called amino acids.

A number of different enzymes are needed to process these amino acids (build protein) for use by the body.

People with amino acid disorders cannot process certain amino acids.

These amino acids, along with other toxic substances, then build up in the body and cause problems.

Newborns may develop symptoms such as poor appetite, sleepiness, vomiting, or irritability.

If the condition is not treated promptly, babies can develop more serious problems including breathing problems, seizures, swelling of the brain, or even coma or death.

There is no cure for amino acid disorders.

However, the outcome is best in infants who are treated early and continue with lifelong treatment.

Treatment usually consists of a special diet and sometimes medications or supplements.

<u>Genetic screening and counselling</u>

<u>Autosomal Recessive Inheritance</u>

X and Y chromosomes are Sex Chromosomes

All others are known as Autosomes

Cystic Fibrosis is an example of autosomal recessive inheritance

Sufferers are homozygous recessive, cc

Non sufferers are homozygous dominant or heterozygous (CC or Cc)

Cystic fibrosis results from a 3 base pair deletion on chromosome 7 – this produces a non- functional protein

Mucus is found at various sites in the body

These sites include the lungs, the pancreas and the alimentary canal

The mucus produced by sufferers of cystic fibrosis becomes thicker and stickier than normal

The organs become congested and blocked

The frequency, in GB, of being a carrier is 1 in 25

Sandra's parents are 'carriers' of Cystic Fibrosis

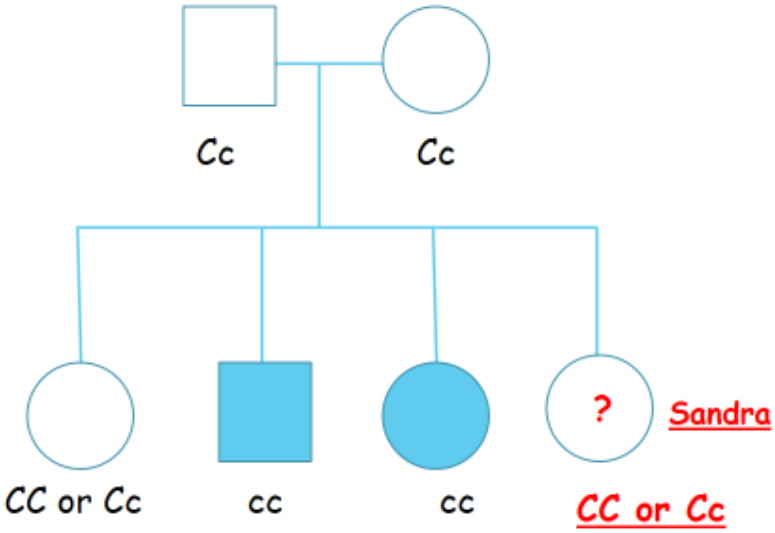
Sandra does not suffer from Cystic Fibrosis, but she may be a carrier

Sandra has a brother unaffected by the condition – he could be CC or Cc

She also has a brother and sister who suffer from Cystic Fibrosis, cc

What is the chance of her being a carrier?

Sandra's parents are heterozygous



Cystic Fibrosis, both parents 'carriers'

gametes	egg C	egg c
sperm C	CC	Cc
sperm c	Cc	cc

Of the offspring that do not have Cystic Fibrosis, 2 out of3 will be carriers, Sandra could well be a carrier

Cystic Fibrosis is **not** known to exist in her partner's family

Sandra and Ian want to know the risk of them having a children with cystic fibrosis

The chance of Ian being a 'carrier' is 1 in 25

Sandra has a 2 in 3 chance of being a 'carrier'

The counsellor concludes that the risk of Sandra and Ian having a child with Cystic Fibrosis is fairly low

Autosomal Dominant Inheritance

Huntington's chorea is an example of autosomal dominant inheritance

The trait appears in every generation

Each sufferer of the trait has an affected parent

When a branch of the family does not express the trait, the trait fails to reappear in future generations of that branch

Males and females are affected in approximately equal numbers

All non- sufferers are homozygous recessive, hh

All sufferers are HH or Hh

From previous study, in unit 1, we know that Huntington's disease is caused by an affected gene on chromosome 4

The type of mutation involved results in the codon CAG being repeated more than 35 times

Lack of correct protein leads to:

Premature death

Decreased production of neurotransmitters

Progressive degeneration of the central nervous system

John and Ann want to know the chances of them having a child with Huntington' Chorea

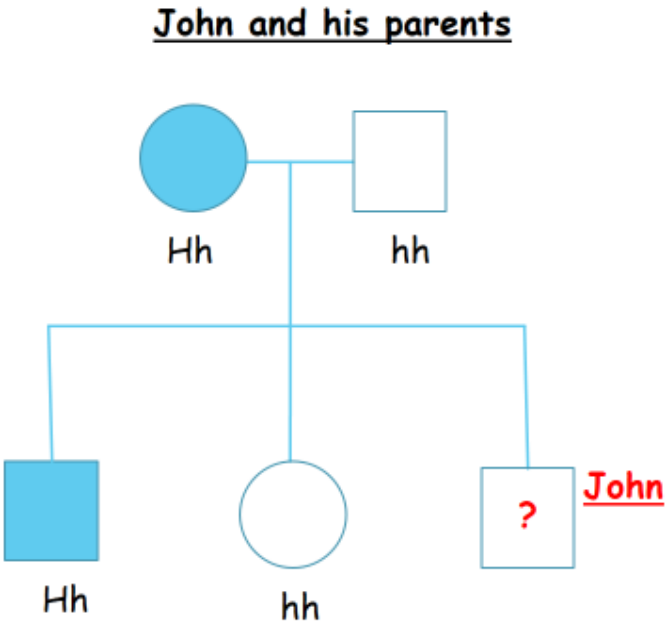
John's mother has Huntington's

Ann's mother also has Huntington's

Both fathers are non- sufferers

The disease usually develops later in life

John and Ann are too young to know whether or not they have received the harmful allele

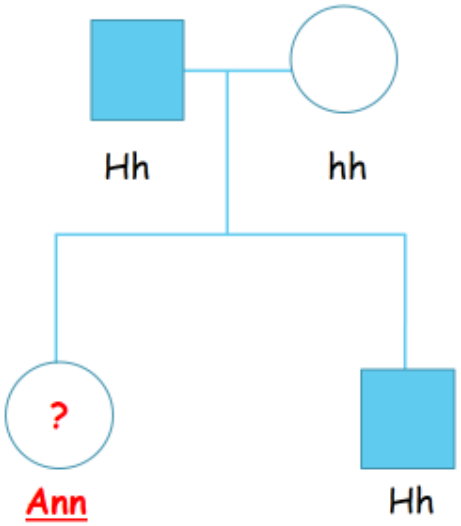


Huntington's Chorea, John

gametes	egg H	egg h
sperm h	Hh	hh
sperm h	Hh	hh

John has a 1 in 2 chance of being Hh, having Huntington's

Ann and her parents



Huntington's Chorea, Ann

gametes	egg h	egg h
sperm H	Hh	Hh
sperm h	hh	hh

Ann also has a 1 in 2 chance of being Hh, having Huntington's

From the information available, the counsellor would conclude that there is a high risk that each of their children would suffer this debilitating disease

If John and Ann turn out to be Hh then 3 in 4 of their would suffer Huntington's chorea

Offspring of John and Ann

gametes	egg H	egg h
sperm H	HH	Hh
sperm h	Hh	hh

3 in 4 of their children would have Huntington's Chorea

Postnatal screening – incomplete dominance

Sickle-cell disease and sickle-cell trait illustrate a typical autosomal incompletely dominant pattern of inheritance because:

The fully expressed form occurs relatively rarely

The partially expressed form is much more frequent

Each sufferer of the fully expressed form has two parents who suffer the partly expressed form

Males and females are affected in equal numbers

Non sufferers are homozygous for one incompletely dominant allele, represented by HH

All sufferers are homozygous for the other incompletely dominant allele, SS

Sufferers of the partly expressed disorder are heterozygous, HS

From previous study of sickle-cell disease we know that people who are homozygous with the mutant allele suffer drastic consequences

Their haemoglobin fails to perform the normal function properly

The sickle-shaped cells tend to stick together, interfering with the blood circulation

This results in a severe shortage of oxygen, damage to vital organs and death

Heterozygous individuals have the milder condition, sickle-cell trait

Their red blood cells do not show 'sickling'

They do suffer from anaemia

40% of the population of some parts of Africa have sickle-cell trait

They are resistant to Malaria

The parasite cannot use red blood cells containing haemoglobin S

Two sickle-cell trait parents

gametes	egg H	egg S
sperm H	HH	HS
sperm S	HS	SS

There would be a 1 in 4 chance having the fully expressed condition, SS and 1 in 4 chance of being unaffected

Sex-linked recessive gene

The X chromosome is larger than the Y

The X carries many more genes not present on the Y

These genes are said to be sex linked

When an X meets a Y, each sex linked gene is expressed in the phenotype

Red green colour blindness is an example of a sex linked gene

C represents normal colour vision and is dominant to c which represents red green colour blindness

Colour blindness is caused by a recessive gene

Many more males are affected than females

None of the sons of an affected male show the trait

Some grandsons of an affected male do show the trait

All sufferers are homozygous recessive

Non-sufferers are homozygous dominant or heterozygous 'carrier' females

Red Green Colour Blindness

Genotype	Phenotype
$X^C X^C$	Normal female
$X^C X^c$	'Carrier' female
$X^c X^c$	Colour blind female
$X^C Y$	Normal male
$X^c Y$	Colour blind male

'Carrier' female, Normal male

gametes	egg X^C	egg X^c
sperm X^C	$X^C X^C$	$X^C X^c$
sperm Y	$X^C Y$	$X^c Y$

1 'normal' female, 1 carrier female, 1 'normal' male and 1 colour blind male

A protein called Factor VIII is required for the blood clotting

Haemophilia (blood does not clot or takes a very long time to clot) is caused by a recessive gene which is carried on the X chromosome

H represents normal blood clotting and h represents haemophilia

Colour blindness and haemophilia are rare in females since two recessive alleles must be inherited

Haemophilia

Genotype	Phenotype
$X^H X^H$	Normal female
$X^H X^h$	'Carrier' female
$X^h X^h$	Haemophiliac female
$X^H Y$	Normal male
$X^h Y$	Haemophiliac male

Normal female, Haemophiliac Male

gametes	**egg** X^H	**egg** X^H
sperm X^h	$X^H X^h$	$X^H X^h$
sperm Y	$X^H Y$	$X^H Y$

2 'carrier' females and 2 normal sons

'Carrier' female, Haemophiliac Male

gametes	egg X^H	egg X^h
sperm X^h	X^HX^h	X^hX^h
sperm Y	X^HY	X^hY

1 carrier female,1 haemophiliac female,1 normal male and 1 haemophiliac male

A haemophiliac male who has a 'normal' partner does not pass the trait on to his sons

Remember, he only passes a Y to his sons

He does however pass the haemophilia allele to any daughters, making them 'carriers'

If a carrier female has sons, they would have a 1 in 2 chance of have haemophilia

Pre-implantation genetic diagnosis

During IVF fertilised eggs form embryos each composed of 8 or more cells

Two or three of these embryos are inserted into the mother's uterus

Before this stage is carried out, one or two cells may be removed and tested for genetic abnormalities

The tests may take one of two forms:

Pre-implantation genetic screening

Pre-implantation genetic diagnosis

Pre-implantation genetic screening (PGS)

This is a non-specific approach that checks the embryo for single gene disorders and chromosomal abnormalities in general

Pre-implantation genetic diagnosis

This is a specific approach

It is used to check for a known chromosomal or gene abnormality

The tests allow the experts to select which embryos should and which should not be implanted

N.B. this is the last 'Pupil Note' for Unit 2, section 1