BIOLOGY

HUMAN REPRODUCTON

(28 pages)

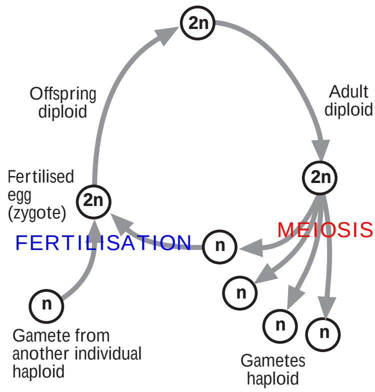
Contents

SEXUAL REPRODUCTION

The fusion of gametes results in a diploid zygote

Sexual reproduction involves the fusion of the nuclei of the sex cells, or **gametes**, from the male and female sex organs, to form a **zygote** in a process of **fertilisation**.

During gamete production (**gametogenesis**) in animals the number of chromosomes in the nucleus is halved in a process known as **meiosis**, so that normal gametes have half the normal number of chromosomes, that is they are **haploid**. A **diploid** zygote, which has twice the haploid number of chromosomes, is formed by fertilisation. Certain genetic 'mixing' events, which occur during meiosis, and the random fusion of the gametes result in genetic variation in the offspring which may be of adaptive advantage.



Meiosis

Meiosis is a special type of cell division called a **reduction division** in which the number of chromosomes is halved from the diploid to the haploid number.

Meiosis involves two divisions referred to as the first and second divisions (Meiosis I and Meiosis II). Remember that the nucleus of each cell contains two sets of chromosomes; one maternal, from the female gamete and one paternal, from the male gamete. As a result, each chromosome has a partner in the other set which carries genes for the same characteristics. Two such chromosomes are said to form a **homologous pair**. Meiosis is a continuous process but can be considered as occurring in a series of stages:

Interphase, before nuclear division by meiosis starts, the DNA replicates so that during

Prophase I the chromosomes are formed as double structures of a pair of **sister chromatids**. The doubled chromosomes then pair up with their homologous partners to form structures called **bivalents**. They twist around each other, and breaks occur in the chromatids. A break in one chromatid is matched by another in the corresponding non-sister chromatid. The broken ends rejoin with the ends of the non-sister chromatid resulting in a **crossing over** between non-sister chromatids. The homologous chromosomes begin to repel each other, and the points where crossing over has occurred serve to slow the repulsion and appear as a cross shape (**chiasma pleural chiasmata**). These crossing over points occur in a random fashion serving to reshuffle the genetic pack, mixing the DNA of the maternal and paternal chromosomes. Crossing over during meiosis is an important source of genetic variation in organisms which reproduce sexually. Prophase I may take several days to complete. In

Metaphase I the chromosomes are pulled to the equator of the cell, held only by the junction points of the chiasmata. They line up on the equator at random, with maternal and paternal chromosomes on either side. During

Anaphase I the homologous chromosomes pull apart from each other, separating towards the opposite poles of the cell, the completion of which is known as

Telophase 1.

Crossing over, and the random alignment and separation of maternal and paternal chromosomes ensure that each gamete is unique and therefore introduces genetic variation into the gametes.

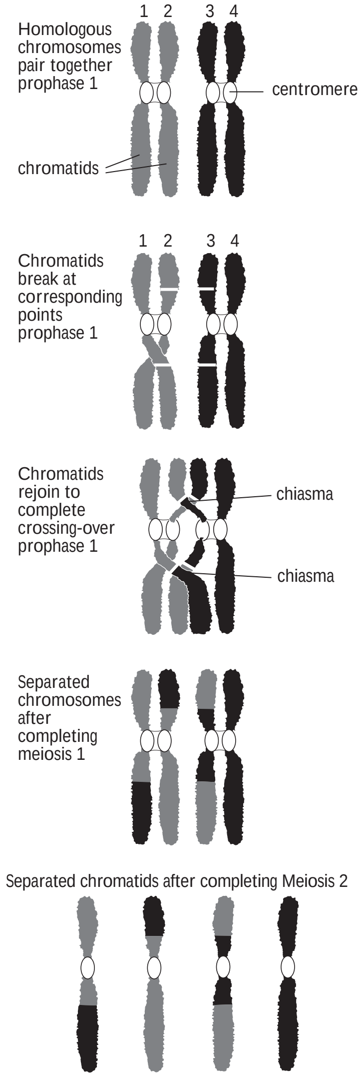
Two new spindles form at right angles to the first, one at each pole, and the chromosomes (each composed of two sister chromatids) move to the equator for

Metaphase II - from here on, the events are similar to mitosis, as the sister chromatids now move to opposite poles in

Anaphase II, and

Telophase II.

Cytokinesis follows with the formation of four new haploid daughter cells. Note that the result of meiosis is four cells (gametes) each containing half the original number of chromosomes with mixed sections of maternal and paternal DNA sequences, as well as mixed sets of maternal and paternal chromosomes.



Usually 2 or 3 cross-overs affect each chromosome pair. Note cross-overs can occur between 1&3; 1&4; 2&3; 2&4, but not 1&2 or 3&4

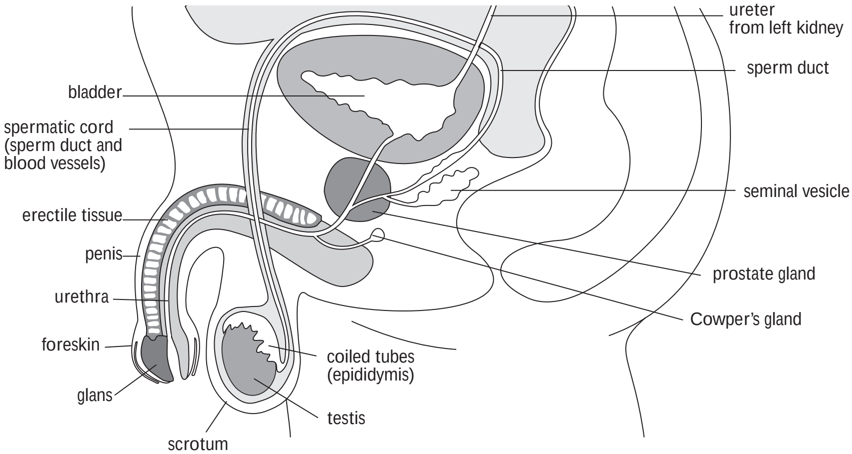
◆ CHECKPOINT SUMMARY

- Offspring result from the fusion of gametes, forming a zygote.
- This fusion of gametes involves various genetic mixing events and therefore leads to genetic variation in offspring.
- These genetic mixing events include events in the nuclear division (meiosis) involved in the production of gametes, and in the random fusion of gametic nuclei from different sexes.
- Meiosis is a reduction division in which the diploid number of chromosomes (two sets) is reduced to the haploid (one set).
- In the first phase of meiosis (Meiosis I) the two sets of chromosomes pair up, so that chromosomes occur in homologous pairs. Each chromosome is duplicated into two chromatids, so one pair of chromosomes is made up of four chromatids.
- The homologous chromosomes of a pair entwine, one chromatid of each pair breaks and rejoins with the broken chromatid of the other pair, in a process known as genetic recombination or crossing over.
- The chiasmata align on the equator of the nuclear spindle apparatus (NSA), before the homologous chromosomes repel each other to opposite poles.
- Cross overs are visible under the light microscope and are known as chiasmata (Greek for crosses), they result in the exchange of genes (alleles) between homologous chromosomes.
- Either chromosome of each pair can go to a particular pole, resulting in mixing of the original sets (independent assortment).
- Two daughter nuclei are thus formed, each with one (haploid) set of chromosomes, with each chromosome composed of two chromatids.
- The second phase of meiosis (Meiosis II) involves the centromeres of the chromosomes aligning on the equator of a each of two new NSA formed at right angles to the first.
- The chromatids then repel each other to form four new haploid nuclei.

REPRODUCTION IN HUMANS

Structure and function of the male reproductive system

The male reproductive system



The male gamete producing organs (**testes**) have two functions. Firstly, the production of haploid male gametes (sperm) capable of fertilising an ovum and so passing on the male's genes into a new generation. -

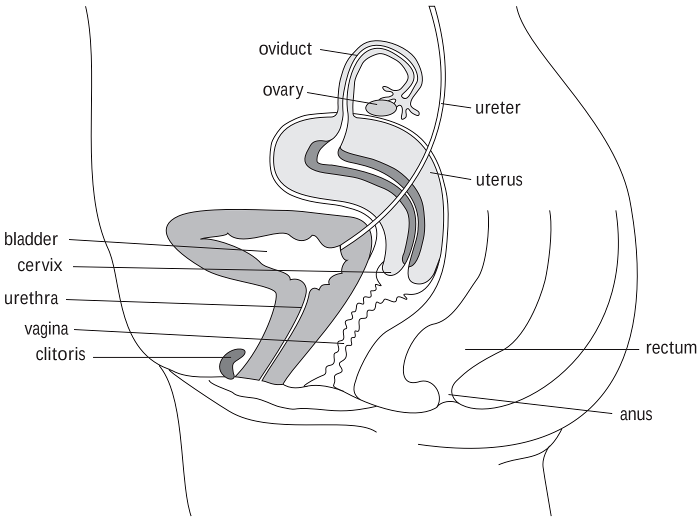
Secondly, the production of male hormones, particularly testosterone. This allows the development of the secondary sexual characteristics of the male and is also needed for sperm production and sexual activity. Both functions are performed in the **semeniferous tubules** which are packed into lobules inside each testis. **Spermatogenesis** (the production of sperm discussed later) occurs in the walls of the tubules whilst testosterone is secreted by cells in between the tubules (interstitial cells). The testes lie outside the body in the **scrotum**. The function of this is to keep the testes slightly cooler than body temperature (about 35ºC) for optimal sperm production.

The remaining components of the reproductive system are all concerned with moving sperm from the testes to the **urethra** and into the female reproductive tract during sexual intercourse. The sperm are moved from the seminiferous tubules and transported to the **epididymis**, a long coiled tube where fluid is reabsorbed from the sperm and chemicals secreted which allow sperm to complete their maturation and develop the ability to swim. From here sperm are moved to the sperm ducts (vas deferens), which lead into the urethra just below the exit from the bladder.

In order to perform their functions, sperm are mixed with a variety of secretions to form **semen** before they leave the body during ejaculation (see below). The paired **seminal vesicles** secrete a watery alkaline fluid containing sugars (e.g. fructose) for nourishing the sperm. Mucus is also secreted. The **prostate gland** and **Cowper's glands** also secrete alkaline fluid and mucus. The alkaline fluid helps to neutralise any traces of urine present in the urethra and to neutralise the acid environment of the vagina, so providing more suitable conditions for the sperm to function.

The **penis** is used to convey sperm into the reproductive tract of the female during sexual intercourse. It contains **erectile tissue** and a central tube, the urethra through which semen from the sperm ducts pass. At other times this tube carries urine from the bladder. A system of **sphincter muscles** closes the exit from the **bladder** during sexual activity.

The female reproductive system



The female gamete producing organs (ovaries) lie inside the abdomen. These have two functions: the production of haploid female gametes (ova) containing genetic information from the female; and the production of female hormones, particularly oestrogen and progesterone.

These hormones control the development of secondary sexual characteristics and, along with hormones from the pituitary gland, control the events of the menstrual cycle.

Close to the border of each ovary is the **oviduct**. The oviducts are narrow tubes whose function is to transport ova released from the ovary to the uterus. The oviducts aid the movement of ova to uterus in two main ways. Firstly they have a fringed funnel which help to 'catch' the ova and guide them into the oviduct. Secondly they are lined with ciliated epithelial cells which beat and so move the ovum along towards the uterus. Fertilisation usually takes place in the oviduct.

The **uterus** is a muscular organ about 7 x 5 cm in size in a non-pregnant woman whose function is to house a developing embryo. Its wall consists of three layers: an outer covering; a thick middle layer of smooth muscle (the **myometrium**); and the inner **endometrium** containing a dense network of blood vessels and glands. The characteristics of the endometrium vary during the menstrual cycle as discussed below. During pregnancy the uterus can expand to up to 10 times its normal size.

The **cervix** or neck of the uterus is a ring of smooth muscle containing mucus secreting cells which help to provide optimum conditions for sperm survival at around the time of ovulation. The cervix is normally tightly closed but during birth will dilate to allow the baby's to emerge head first in normal births.

The **vagina** is a short muscular tube which receives the penis during sexual intercourse. It is lined with epithelial cells secreting vaginal fluids. Like the cervix it must stretch to several times its normal size during birth.

The external female genitalia or **vulva** consists of the **labia majora** and **labia minora** which surround the vaginal opening, opening of the **urethra** and the **clitoris**, a small erectile structure. The clitoris is similar in structure to the penis. Stimulation of the clitoris may result in orgasm.

Glands within the vulva secrete mucus to lubricate the penis during sexual intercourse.

Spermatogenesis and oogenesis

Spermatogenesis is the term used to describe the production of male gametes (sperm).

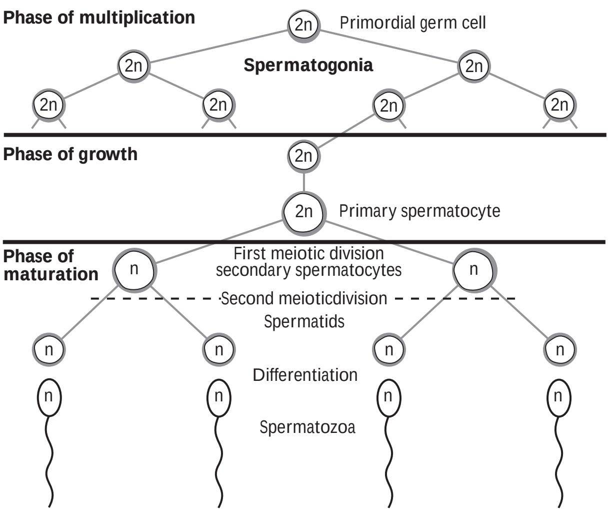
Oogenesis is the production of female gametes (ova). These two processes share many essential similarities, such as the central role of meiosis in creating haploid gametes. There are however several differences in the timing and organisation of the processes. These can help to explain why adult males produce several million small sperm per day whilst women produce just one large, mature 'egg cell' per month.

Spermatogenesis

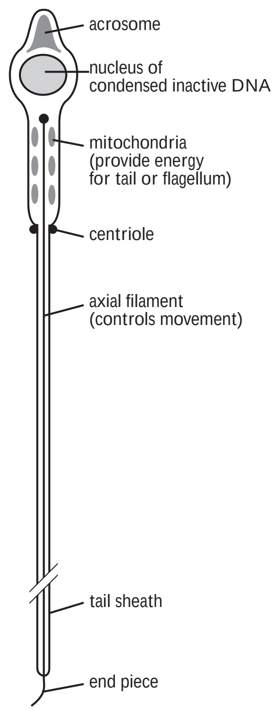
Sperm are produced in the seminiferous tubules within the testes of the adult male. The process of spermatogenesis is initiated by the hormone testosterone at the time of puberty. Epithelial germ cells in the outer layer of the seminiferous tubule divide by mitosis to form a population of diploid **spermatogonia**. These divide by mitosis and grow into **primary spermatocytes**. Each primary spermatocyte undergoes meiosis, forming two haploid **secondary spermatocytes** in Meiosis I and four **spermatids** in Meiosis II. In the final stage each spermatid develops from a round cell into a fully functional sperm cell (**spermatozoa**). This complete process of spermatogenesis takes about 70 days.

As spermatogenesis progresses, the developing sperm cells move towards the lumen of the seminiferous tubule into which they will eventually be released. The cells are attached to large **Sertoli cells** (nurse cells) until maturity. These cells provide oxygen and nutrients and remove waste products. They also play an essential role in remodelling the spermatid to form a sperm cell.

A mature sperm is approximately 20 μm in length and 2.5 μm in diameter, the smallest cell in the human body. It consists of a **head**, containing a haploid nucleus and a membrane bound sac of enzymes at the tip, (the **acrosome**), a **middle piece** containing many mitochondria to provide energy for swimming, and a **tail** containing microtubules.



Spermatozoon



Oogenesis

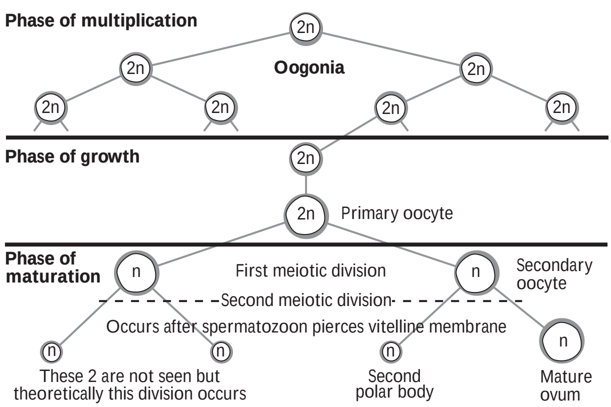
Unlike spermatogenesis, oogenesis does not begin at puberty, but in the unborn foetus. Oogenesis begins in the germinal epithelium of the ovary where germ cells divide by mitosis to form **oogonia**. Further mitosis and growth of these cells produces **primary oocytes**. These cells begin Meiosis I but are halted during prophase. A layer of granular cells develops around each primary oocyte forming a **primary follicle**. Several million of these follicles are present at birth of which only a fraction will complete their development into gametes during the reproductive life span of the woman. From puberty onwards one follicle per month will complete its development into an **ovarian follicle** (Graafian follicle) containing a female gamete (secondary oocyte). The stages in the development of one follicle and the primary oocyte within it can be summarised as follows:

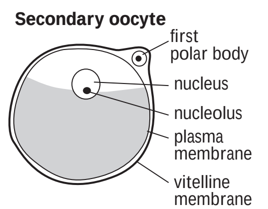
The primary oocyte inside the follicle enlarges whilst its surrounding granular cells increase in number, and are surrounded by an outer layer of cells (the **theca**) derived from the tissue of the ovary. Under the influence of **follicle stimulating hormone** (FSH) and **luteinising hormone** (LH) the follicle continues to grow into a secondary follicle, developing a central space filled with fluid secreted by the granular cells. Further enlargement, under the influence of oestrogen secreted by the granular cells, produces a mature Graafian follicle up to 1cm in diameter.

Meanwhile, inside the follicle the primary oocyte completes its first meiotic division, forming a haploid **secondary oocyte** and a small functionless **polar body** (containing the other half of the chromosomes). The second meiotic division begins but is halted in metaphase. At this point, mid way through the menstrual cycle, the Graafian follicle bursts to release the secondary oocyte. Meiosis II is not completed until the moment of fertilisation when a second polar body is formed. Strictly speaking the term ovum should not be used until that point.

The secondary oocyte which is released at ovulation is a large cell, about 140 μm in diameter. It contains a haploid nucleus and a large quantity of grainy cytoplasm. It is surrounded by a jelly like layer, the **zona pellucida**. The ovarian (Graafian) follicle after releasing the secondary oocyte becomes the **corpus luteum** which has an important role in the secretion of progesterone and oestrogen.

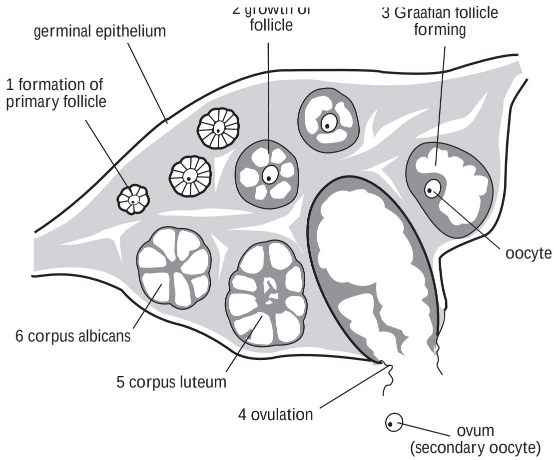
All of the changes described above occur during a single menstrual cycle. Further details of the menstrual cycle are given below.





Polar bodies take no part in reproduction and disappear, therefore only one functional cell is produced from the primary oocyte.

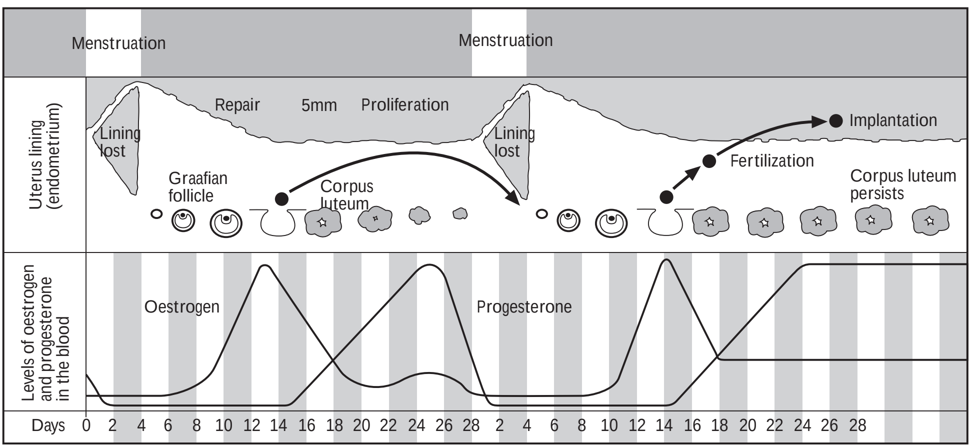
Mammalian ovary section



The menstrual cycle

Between puberty (average age 12) and the menopause (average age 45) human females experience regular sexual cycles, known as menstrual cycles. Each cycle is approximately 28 days long and involves a series of changes within the ovary and uterus. These can be considered as two separate but closely linked cycles: the **ovarian cycle** which is concerned with the development and release of an 'egg cell' around the mid point of the cycle, offering the chance of fertilisation if mating occurs; and the **uterine cycle** which is concerned with the development of the endometrium (uterus lining) to ensure the highest chance of implantation of a fertilised ovum or zygote.

Unless pregnancy occurs, one menstrual cycle will follow directly on from the next. (Therefore when interpreting graphs of the cycle note that day 28 is followed by day 1.)



The events of the menstrual cycle

The menstrual cycle relies on interactions between four main hormones: the ovarian hormones oestrogen and progesterone and the pituitary hormones Follicle Stimulating Hormone (FSH), and Luteinising hormone (LH). A further hormone, from the hypothalamus, Gonadotrophin Releasing Hormone (GnRH) is also involved. The events of the menstrual cycle are summarised below:

- Release of GnRH from the hypothalamus causes FSH to be released from the anterior pituitary. FSH travels in the bloodstream to the ovaries where it stimulates the development of several follicles (primary oocytes). One or more of these will eventually mature into an ovarian (Graafian) follicle containing the secondary oocyte.
- FSH stimulates the production of oestrogen from the follicles within the ovaries. This oestrogen in turn stimulates the growth of the endometrium, replacing cells lost during the previous menstrual period. At this point oestrogen has a negative feedback effect on FSH, reducing its production.
- Oestrogen levels increase until the mid point of the cycle when they bring about a peak of LH production from the anterior pituitary causing ovulation (the release of the secondary oocyte from the Graafian Follicle). A small peak of FSH production also occurs at the time of ovulation.
- LH causes the Graafian Follicle to develop into a corpus luteum which begins to secrete progesterone and oestrogen.
- Progesterone stimulates further development of the endometrium, in particular an increase in the density of spiral arteries and an increase in the secretion of mucus and fluid from glands in the endometrium. This is sometimes known as the secretory phase and its function is to prepare the uterus in case the newly released secondary oocyte ('egg' cell) is fertilised.
- The other function of progesterone is to inhibit the production of both FSH and LH and hence the development of further follicles. This is an example of negative feedback.
- If fertilisation does not occur, the corpus luteum degenerates and secretion of progesterone and oestrogen falls. This fall causes the uterine blood vessels to rupture and the uterus lining to degenerate and pass out of the body via the vagina. This is known as menstruation or the menstrual period and lasts for 4-5 days. Decline in progesterone levels causes the inhibition of FSH and LH to be removed and a new cycle can begin. Note that a new cycle begins whilst menstruation is still occurring.
- If fertilisation does occur then the corpus luteum does not degenerate but continues to secrete progesterone and oestrogen, maintaining the uterus lining and preventing further follicles from developing. After about 12 weeks of pregnancy in humans and corresponding times in other mammals the developing placenta takes over this hormonal (endocrine) role.

CHECKPOINT SUMMARY

- The male reproductive system consists of the testes which produce spermatozoa by meiosis.
- A system of tubes and erectile tissue transfer them to the female reproductive tract.
- Accessory glands are important in secreting substances essential for successful fertilisation of the female.
- The female system consists of ovaries which release egg cells (ova) into the abdominal cavity, from where they are swept down the oviducts by ciliated epithelium, into the uterus where they may or not be implanted.
- The uterus connects to the exterior by the vagina.
- The ova are produced (oogenesis) by meiosis in the germinal epithelium of the ovaries. Of the products of meiotic nuclear division, one accumulates all the cytoplasm to form the relatively large ovum, and the others are reduced to polar bodies.
- Spermatozoa are produced (spermatogenesis) by meiosis in the germinal epithelium of the testes. The four products of meiosis all develop into spermatozoa.
- The menstrual cycle is a monthly version of the ovarian cycle found in all mammals.
- A sequence of hormonal secretions from the brain, pituitary gland, and the ovaries themselves, coordinated by negative feedback loops control the events of the cycle.
- Luteinising hormone stimulates the release of the an ovum from an ovarian follicle, and the development of the corpus luteum. In the male it stimulates the secretion of testosterone by the testes.
- Follicle stimulating hormone initiates the development and growth of the ovarian follicles, and stimulates the ovary to secrete oestrogen. In males it stimulates spermatogenesis by the testes.
- Oestrogen stimulates the development of the primary and secondary sexual characteristics, the development of the uterus lining in the first half of the menstrual cycle.
- Progesterone stimulates the secretory phase of the uterus in the second half of the cycle, and maintains pregnancy whilst suppressing further ovulation

The transfer of male gametes and fertilisation

If fertilisation is to occur then male gametes must come into contact with the female gametes. Under natural circumstances male gametes are transferred into the reproductive tract of the female via the penis during sexual intercourse.

For sexual intercourse to occur, the male's penis must first become erect. This occurs following sexual stimulation and involves an increase of blood flow into the spongy erectile tissue of the penis. Movement of the erect penis inside the vagina during intercourse stimulates the sensory cells at the tip of the penis. A series of stages, co-ordinated by the sympathetic nervous system then follow, eventually leading to ejaculation: the release of semen containing sperm into the vagina. These stages include:

- contraction of the involuntary muscle lining the sperm duct and epididymis so forcing the sperm towards the urethra;
- contraction of the seminal vesicles, Cowper's and prostate glands which add their secretions to the sperm;
- closure of the bladder sphincter muscle; and reflex contractions of the muscles surrounding the urethra, forcing the semen out of the penis and high into the vagina of the female. Ejaculation is accompanied by the intense sensation of orgasm.

A single ejaculation can contain several hundred million sperm. Once in the vagina these sperm acquire the ability to swim and begin their journey through the cervix (first aligning themselves with long chains of mucus), across the uterus and up into the oviducts. The speed with which they may reach the oviducts suggests that muscular movements of the uterus and oviduct may in fact be more important than swimming at this stage. It has been suggested that chemicals called prostaglandins contained in seminal fluid could bring about this effect. If ovulation has occurred within 24 hours prior to this, a secondary oocyte should be present in one of the oviducts and it is here that fertilisation may take place.

Fertilisation

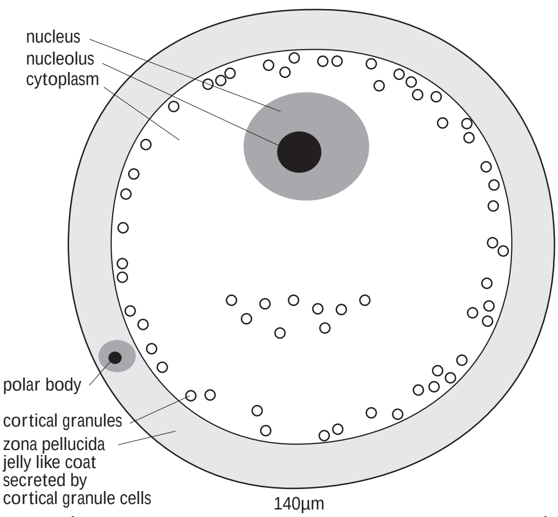
Fertilisation is the process by which the haploid nucleus of a single sperm cell fuses with the haploid nucleus of a single ovum creating a diploid zygote.

Before a sperm can fertilise the secondary oocyte it must undergo a process known as **capacitation** where it is 'primed' for the process by the acid environment of the uterus. The main feature of this involves changes in the cell membrane of the sperm in the region around the acrosome vesicle. Firstly the membrane is weakened and becomes more permeable, and the acrosome membrane fuses with the cell membrane.

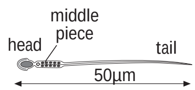
When a sperm comes into contact with the zona pellucida of a secondary oocyte the acrosome reaction occurs. This involves the acrosome splitting open and releasing the lytic enzymes contained within it. These begin to digest the zona pellucida, allowing the sperm to move through it to reach the cell membrane of the secondary oocyte. When it reaches the membrane it fuses with it and its head enters the cytoplasm. The tail is left behind. Entry of the sperm stimulates the nucleus of the secondary oocyte to complete its second meiotic division so that it can fuse with the nucleus of the sperm.

One of the surprising things about fertilisation is the mechanism which allows just one single sperm to penetrate the secondary oocyte when several hundred or thousand sperms are surrounding this cell. As the sperm enters the secondary oocyte a number of changes occur which result in the layer surrounding the egg cell (zona pelucida) becoming impermeable to other sperm.

Human female gamete (secondary oocyte) just before fertilisation



Human male gamete just before fertilisation



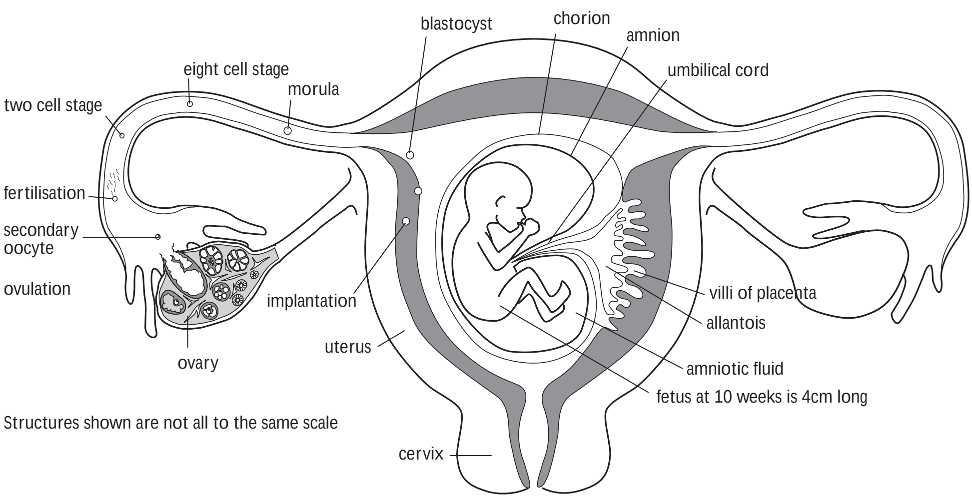
140μm is smaller than the smallest dot you can make with a fine ball point pen

Implantation

Following fertilisation the zygote undergoes cell division by mitosis forming a small ball of identical cells within a few days. Gradually the cells start to differentiate (become specialised for different tasks) and the ball of cells becomes a hollow sphere filled with fluid (blastocyst). The outer wall of the blastocyst is made of cells called **trophoblasts** which will form the villi which grow into the wall of the uterus at implantation. A small mass of cells inside this layer will form the embryo. As these changes occur, the zygote moves slowly down the oviduct and towards the uterus where it must implant in the uterine wall if further development is to take place. The cells secrete a hormone called **human chorionic gonadotrophin (hCG)** which maintains the corpus luteum, ensuring that it continues to secrete oestrogen and progesterone. (The presence of hCG in the urine is detected in a 'pregnancy test'.)

When the blastocyst arrives in the uterus it is still contained within the zona pellucida. As this breaks down the trophoblastic cells of the blastocyst come into contact with the endometrium of the uterus. They begin to invade the endometrium, secreting digestive enzymes and growing into the maternal tissues. This process, which results in the blastocyst becoming embedded in the endometrium, is known as implantation. It occurs as early as seven days after fertilisation.

Implantation is the first stage in the crucial association between maternal and fetal tissues and circulation which form the basis of mammalian development. As the trophoblastic cells become embedded in the endometrium of the uterus they differentiate to form finger like projections which penetrate deep into the endometrium. These are the **chorionic villi**. Enzymes secreted by the cells of the villi digest the walls of the spiral arteries and veins within the endometrium and create blood filled spaces around each villus. From here the maternal blood nutrients and oxygen diffuse into the villi and are delivered to the cells of the blastocyst. Carbon dioxide and other waste materials diffuse out of the blastocyst and into the maternal blood down their concentration gradients. The efficiency of these exchanges is improved by the large surface area of chorionic villi.



Over the following weeks rapid growth and development of both the chorionic region and the embryo occur. Within three to four weeks of fertilisation blood is circulating through embryo and villi. This improves the efficiency of exchange.

The structure and function of the placenta

The placenta is fully formed 12 weeks after fertilisation. On the maternal side it consists of projections of the endometrium between which lie a series of blood filled spaces. Blood from the maternal arteries enters the spaces where exchange is performed and then returns to the circulation in the maternal veins. On the fetal side, chorionic villi project into the blood filled spaces. Each villus contains branches of the umbilical artery and vein which form a dense network of capillaries. These join up to form the **umbilical artery** and **veins** which run through the umbilical cord to the embryo (at this stage called the fetus). It should be noted that the blood of mother and fetus are kept entirely separate. This helps to regulate exchanges between mother and fetus, protects the fetus from the effects of high maternal blood pressure which would damage its small blood vessels, prevents possible immune reactions which might occur if the fetus was of different blood group to the mother, and prevents the entry of mature female hormones which would be dangerous even for a female fetus.

The placenta has two main roles in relation to the development of the human embryo and fetus. Firstly it is the organ of exchange between mother and fetus, supplying the fetus with nutrients and oxygen and removing carbon dioxide and urea. Antibodies are also supplied to the fetus which protect it from infections in the first months of life. Secondly it is an endocrine organ producing several hormones throughout the gestation period (development time before birth).

In order to perform its exchange roles efficiently the placenta must provides a large surface area for exchange of nutrients and gases; a thin yet selectively permeable barrier between maternal and fetal blood; and a steep concentration gradient for each substance in the appropriate direction.

A large surface area is provided by the numerous villi and the highly branched capillaries within the villi between the fetal blood contained in vessels and the maternal blood in the large blood filled spaces of the placenta. Maternal and fetal blood are separated by just a few layers of cells creating a short diffusion distance. Small molecules (eg. oxygen, carbon dioxide, urea, water) move across by simple diffusion whilst amino acids and glucose cross by facilitated diffusion. Some vitamins and minerals move by active transport.

Oxygen, glucose, amino acids and other substances required by the fetus need to be at a much higher concentration in the maternal blood than they are in the fetal blood for efficient diffusion to occur. Similarly, carbon dioxide and urea must be at a low concentration in the maternal blood if they are to diffuse out of the fetal blood and be removed. Favourable gradients are maintained by the fact that the fetus has a small volume of blood but a high rate of blood flow whilst the mother has a slower rate of blood flow but a larger volume of blood in the spaces of the placenta, and by an overall counter-current system of blood flow in which the maternal and fetal blood flow in opposite directions maintaining steeper diffusion gradients. Just before birth about 10% of the mothers blood flows through the placenta on each circuit of the body, aiding rapid exchanges.

Hormones secreted by the placenta

The placenta secretes three main hormones:

- Human chorionic gonadotrophin (hCG)
- Progesterone
- Oestrogen.

Each has specific roles relating to fetal development and/or maternal changes associated with pregnancy, birth and lactation (milk production).

hCG is secreted in only small amounts by the placenta but is thought to have roles in suppressing FSH and LH from the pituitary and in stimulating development of some fetal systems.

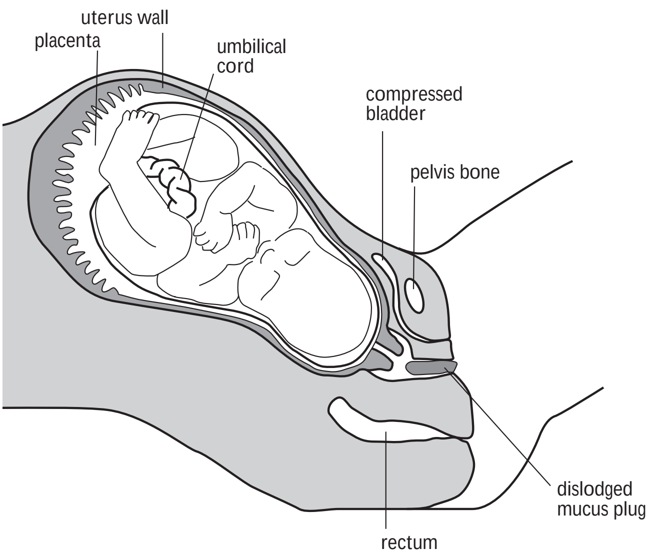
Progesterone is secreted in relatively large quantities (250-350mg/day). High levels prevent shedding of the endometrium, inhibit ovulation and may aid breast development.

Oestrogen is necessary for the maintenance of pregnancy (perhaps through inhibiting FSH) and is thought to be involved in preparing the body for birth and in breast development.

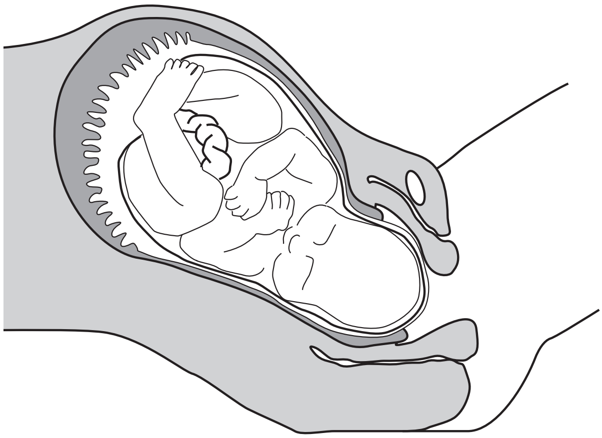
Birth

Approximately 38 weeks after fertilisation the fetus is ready to be born. At around this time the level of the hormone progesterone decreases rapidly and the level of oestrogen increases. The effect of this is to make the uterus wall more susceptible to the effects of **oxytocin**, a hormone produced by the posterior pituitary gland, which causes contraction of the muscle layer of the uterus (the myometrium). The exact signals which trigger these changes in hormone levels and hence initiate the birth process are not clear but are thought to involve a mixture of physical and hormonal signals from both mother and fetus.

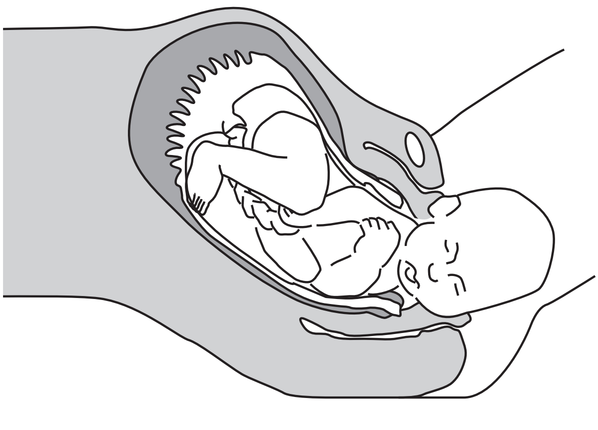
The birth process can be divided into several stages.

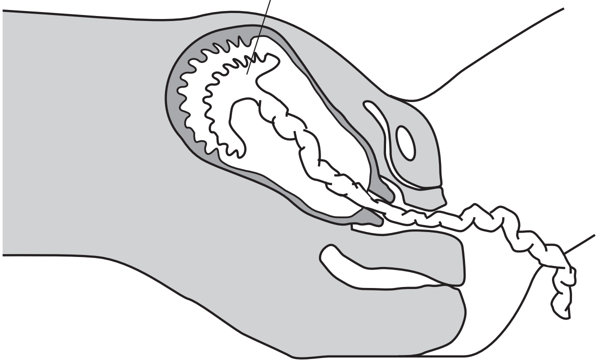


In the **first stage**, which may last 12 hours or more, the uterus begins to contract and the cervix begins to dilate. During, or sometimes before the main contractions begin the amniotic sac bursts and the fluid is released via the vagina. A plug of mucus which blocks the cervix during pregnancy also detaches and passes out of the vagina. Over time the force and frequency of the contractions increases under the control of oxytocin and they spread out through the muscle fibres of the uterus from top to bottom, gradually pushing the fetus downwards toward the cervix. By the end of this stage the cervix has dilated to about 10cm in diameter, wide enough to allow the fetal head to 'engage' and then pass through.



The **second stage** involves the actual birth of the baby which is pushed out of the uterus, through the cervix and down the vagina. The majority of babies are born head first, having moved into this position in the uterus in the weeks leading up to birth. The head and shoulders of the baby are the widest part so once these have passed through the cervix the rest of the body, still attached to the placenta via the umbilical cord, follows more easily. Once it emerges the baby begins to breathe. Since it no longer requires an oxygen supply via the placenta the umbilical cord is cut and tied/clipped.





The third stage involves the loss of the placenta from the body. Final contractions allow this structure to detach itself from the uterus wall and pass out of the vagina. Although a large loss of blood may be expected, muscle fibres around the blood vessels contract to limit this.

Lactation

In its first nine months of life before birth the fetus obtains all its nutritional requirements via the placenta. After birth it must ingest milk produced by the mammary glands of the mother and delivered via the nipple. Suckling begins soon after birth and a new born baby may spend several hours per day engaged in feeding. For the first four months of life babies are rarely given any other food or drink, and in many cultures breast feeding may continue to supplement other foods for several years. The production of milk is known as lactation.

Milk, is a watery fluid containing the sugar lactose along with fat, and proteins, some vitamins and minerals. It is produced in the milk glands of the breast and its secretion is stimulated by suckling. The substances contained in milk are easily digested in and absorbed from the baby's gut.

Milk production is controlled by the interaction of several hormones. During pregnancy, the hormones oestrogen and progesterone stimulate the development of breast tissue containing milk glands and milk ducts. However, milk is not produced and released at this stage as progesterone and oestrogen inhibit another hormone, **prolactin** which is also required. The fall in levels of progesterone and oestrogen after birth removes this inhibition and allows prolactin from the anterior pituitary gland to act on the breast tissue. It stimulates the milk glands of the breast which are lined with milk producing epithelial cells to secrete milk.

Milk is not released until the milk ejection reflex is initiated by the sucking action of a baby. The following steps are involved:

- nerve impulses from sensory receptors in the nipple are sent to the hypothalamus; this stimulates the posterior pituitary gland to produce **oxytocin**;

Biotechnology - the manipulation of reproduction in humans and domestic animals

Contents

REPRODUCTION and its HORMONAL CONTROL

MANIPULATION and CONTROL of REPRODUCTION

Introduction

In both male and female mammals all aspects of sexual reproduction, including gamete production and mating behaviour, is under hormonal control. In both sexes interactions occur between reproductive hormones produced by the pituitary gland under the brain, and those produced within gonads (ovary and testes) which function to ensure optimum fertility. Understanding these interactions, particularly within the female, has provided many opportunities for human intervention in the process of reproduction.

Sexual cycles in the female mammal

In the sexually mature female mammal regular sexual cycles occur, during which one or more female gametes (ova, singular ovum) develop inside follicles and are released from the ovary, offering the chance of fertilisation if mating occurs. The general term for such cycles is the oestrus cycle. Oestrus cycles really consist of two closely linked cycles which are synchronised by hormonal interactions. These are:

- the **ovarian** or follicular cycle in the ovary which is concerned with the development and release of ova.
- the **uterine** cycle which is concerned with the development of the endometrium (uterus lining) to ensure the highest chance of implantation of a fertilised ovum.

In the human female each cycle is approximately 28 days long. Ovulation which usually involves the release of a single ovum, occurs around the 14the day. The endometrium reaches a peak of thickness on day 21 and begins to break down on around day 28. This tissue, consisting of blood and cell debris is lost via the vagina during a menstrual period (menstruation). One cycle follows directly on from another throughout the year assuming that fertilisation does not take place.

Hormonal control of the oestrus cycle

The sexual cycle relies on interactions between four main hormones: the ovarian hormones **oestrogen** and **progesterone** and the anterior pituitary hormones **Follicle Stimulating Hormone** (FSH), and **Luteinising Hormone** (LH). Although timings of the cycle vary between species the same basic pattern holds true. This can be summarised as follows.

a) FSH is released from the anterior pituitary and travels in the bloodstream to the ovaries where it stimulates the development of several follicles (primary oocytes). One or more of these will eventually mature into an ovarian (Graafian follicle) containing the ovum (secondary oocyte)

b) FSH stimulates the production of oestrogen from the follicles within the ovaries. This oestrogen in turn stimulates the proliferation of the uterus lining (endometrium), replacing cells lost during the previous menstrual period in humans (or, in the case of animals, those cells which were broken down and absorbed). At this point oestrogen inhibits the secretion of FSH (negative feedback control).

c) Oestrogen levels increase until the mid point of the cycle when they bring about a peak of LH production from the anterior pituitary causing ovulation (the release of the ovum (pleural ova) secondary oocytesfrom Graafian follicles). A small peak of FSH production also occurs at the time of ovulation.

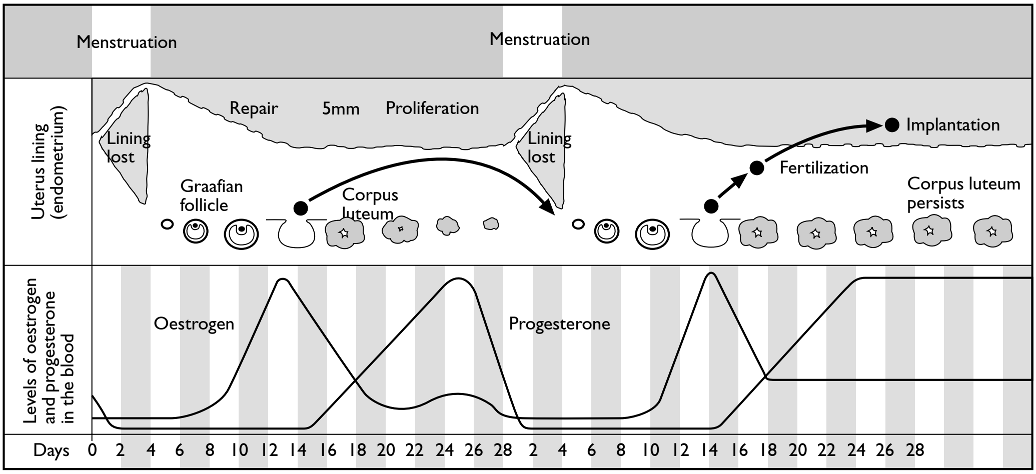
d) LH causes the empty Graafian follicle to develop into a corpus luteum which begins to secrete progesterone and oestrogen.

e) Progesterone stimulates further development of the endometrium, in particular an increase in the density of blood vessels and the secretion of mucus and fluid from glands in the lining. This is sometimes known as the secretory phase and its function is to prepare the uterus in case the newly released ovum is fertilised.

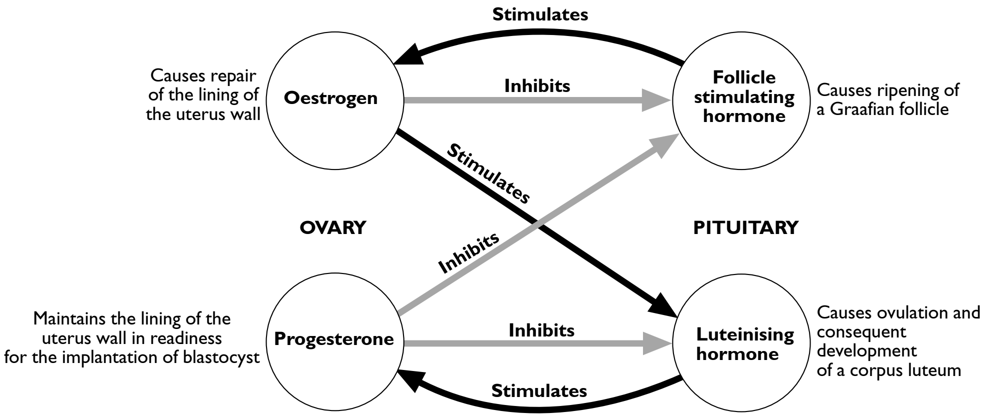
f) The other function of progesterone is to inhibit the production of both FSH and LH and hence the development of further follicles.

g) If fertilisation does not occur the corpus luteum degenerates and secretion of progesterone and oestrogen falls. This fall causes the uterus lining and some of its blood vessels to break down. In humans this is lost during menstruation, whilst in other mammals it is reabsorbed. Decline in progesterone levels causes the inhibition of FSH and LH to be removed and a new cycle can begin.

h) If fertilisation does occur then the corpus luteum does not degenerate but continues to secrete progesterone and oestrogen, maintaining the uterus lining and preventing further follicles from developing. After about 12 weeks of pregnancy in humans and corresponding times in other mammals the developing placenta takes over the secretion of progesterone and oestrogen.



Oestrus cycle



Timing of sexual cycles

The length and details of the oestrus cycle varies amongst other mammals. Cycles may be as short as 4-5 days in the rat, extending to 21 days in the cow. In many wild animals, such as deer, only one cycle occurs per year which is associated with a particular breeding season probably triggered by environmental factors including changes in day length (photoperiod). Other animals with distinct breeding seasons such as the sheep may have several cycles within a given season whilst some such as cows and pigs resemble humans in having continuous cycles. This is known as being polyoestrus. Many large mammals (cow, horse) resemble humans in the release of a single ovum per cycle, whilst others such as the cat and rat may release as many as ten.

Oestrus and its significance

Oestrus is a change in the behaviour or appearance of a female mammal which occurs around the time of ovulation, indicating sexual receptiveness to males. It may involve the secretion of chemicals known as pheromones, swelling or change in colouration of the genital region or distinctive behavioural patterns, as discussed below. The human sexual cycle shows several unusual features which distinguishes it from the cycles of other mammals. Chief amongst these is the absence of oestrus, humans have the unusual feature of being sexually receptive at all times, regardless of the phase of the cycle.

In farm animals, such as cows, pigs and sheep, the presence of particular signs of oestrus which are detectable by humans, allows intervention in the process of reproduction. This is of great significance in modern farming where efficient breeding programmes are needed to allow the farm to exist as a profit-making business.

For a variety of reasons, including economic and safety reasons, many farms do not own male animals such as bulls, rams, stallions, or boars. Instead they may pay for the services of a male belonging to another individual, or, increasingly commonly, they may buy in semen with which to artificially inseminate the female animals. The use of semen (which is collected and stored in carefully controlled conditions to ensure high sperm quality and absence of sexually transmitted diseases) has many advantages over the use of natural breeding with a male animal. One of the most significant advantage is the ability to select and obtain semen from a male animal whose offspring are known to have specific desirable qualities such as high milk yield and quality, high meat quality, attractive appearance, and docility.

If artificial insemination (A.I.) or indeed mating, is to be used effectively then a farmer must be sure that the female animal is in oestrus before it is attempted. Insemination at other times will not result in pregnancy.

Signs characterising oestrus in the cow, pig and sheep are listed below. Careful observation by farmers, often several times per day, is necessary to spot these signs. Individual animals differ in the extent to which signs of oestrus are shown: some will show no signs, whilst others will show some or all of the signs.

The Cow

- Cows attempting to mount other females and then standing still and allowing themselves to be mounted by other females is the best sign of oestrus. On farms this may be detected in the following way: a type of paint is applied to the top part of the tail which will be rubbed off if the cow is mounted by another cow.
- Increased excitability. The cow shows a restless pattern of behaviour with increased time spent walking around and grooming other cows and decreased time resting.
- The cow may make a bellowing noise.
- A swollen vulva

NB. A bull may detect oestrus by sniffing the genital region of the cow (he detects chemical signals). In response to this he will show a lip curling response known as the 'flehmen response'.

The pig (sow)

- The most reliable sign of oestrus is the demonstration of the 'standing reflex' when pressure is applied to the lower back of the sow by the farmer. This is a rigid posture with the back legs extended that a female would adopt during mating. It occurs most frequently when pressure is applied to the back in the presence of a boar or when the female can detect the sound or scent of a boar. Synthetic 'boar odour' aerosols and tapes of boar sounds can be used instead of a real boar.
- A red swollen vulva and production of clear mucus from the vagina
- Sniffing of the genitals of other pigs and making a roaring or grunting noise may also occur.

The Sheep (Ewe)

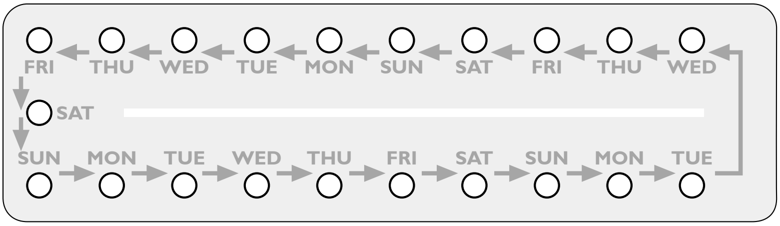
Detection of oestrus in the ewe is difficult since the sheep will only show signs if a ram is present. A farmer must therefore place a ram in with the sheep and watch the behaviour of both ram and ewes carefully. This ram may be a castrated animal and not therefore the male to be used for mating purposes. Under these circumstances oestrus is signalled by:

- Ewe standing firm and looking backwards, sometimes 'fanning' her tail (moving tail rapidly from side to side).
- Ram sniffing the genital region of the ewe, (suggesting the presence of chemical signals), curling his lip (flehmen response), pawing the ground and emitting a low pitched gurgling sound.

The control of reproduction: fertility and infertility.

The past century has seen a dramatic decline in the fertility of populations in most parts of the developed world and more recently within many developing countries. Fertility, in population terms, refers to the number of live births per 100 000 people and reflects the fertility of individual couples within that population. In Britain today each couple has, on average, 2 children compared to 6 or 7 a century ago. The main reasons for this is are an increase in the availability of contraception, associated with improvements in health (high chance of children surviving), education, and income.

Contraception can be defined as the prevention of conception (fusion of male and female gametes). Of the contraceptive techniques available to limit fertility, the most effective apart from abstinence or sterilisation, and most widely used, is the contraceptive pill (often called simply 'the pill'). First produced in 1951, and used but modified since that date, it works by interfering with the natural menstrual cycle of the human female and preventing ovulation. If used correctly it is over 99% effective in preventing pregnancy.



The most frequently used type of pill is known as the **combined contraceptive pill** which contains low doses of both of the steroid hormones oestrogen and progesterone in synthetic form. The effect of the pill is to prevent release of both LH and FSH via the negative feedback inhibition by oestrogen and progesterone. Without these hormones follicles do not develop in the ovary each month and are thus an ovum is not released.To achieve this effect the pill must be taken daily for 21 days in each 28 day cycle. In the 7 pill-free days which follow, the uterus lining breaks down in response to the withdrawal of progesterone, giving a type of light menstrual period. (In biological terms this is not strictly necessary but is built into the design of the contraceptive pill so that a semblance of normal cycles is achieved).

The contraceptive pill also exerts effects on other parts of the reproductive tract. Firstly it causes the mucus in the cervix region to thicken, making it more difficult for sperm to enter, and secondly it limits the thickness of the endometrium, making it more difficult for implantation of a fertilised ovum. If a progesterone only pill, the 'mini pill' is taken the effects are limited to these changes, inhibition of ovulation does not necessarily occur.

The development of other types of contraception based on hormones is continuing. One method which is already in use involves implanting tubes containing progesterone crystals under the skin which will release a constant low level of the hormone sufficient to reduce fertility. These may last for up to 5 years and have the advantage over the pill in that they do not need to be taken daily.

Treating infertility

Infertility, the inability to achieve pregnancy, easily or at all, is a growing problem in the developed world. Up to 1 in 8 couples in the UK may be affected. The causes are varied and can be associated with either the male partner, the female partner, or both. Causes include the long term consequences of some sexually transmitted diseases, genetic factors, physiological factors (including hormonal imbalance), psychological factors, environmental factors (exposure to some pollutants or to radiation), and increasing age of women trying to conceive. Whatever its cause infertility is a serious and distressing problem for many couples and it should be noted that whilst medical technology is improving the options for such couples, many of the treatments are lengthy, expensive and have low success rates. There are also a range of ethical and moral issues associated with some forms of infertility treatment which are discussed later.

In about 20 % of women who fail to conceive the underlying causes are hormonal. Hormonal imbalances can prevent the development of follicles or prevent the release of ova. In both cases treatment using synthetic or naturally occurring female hormones is highly successful in restoring fertility. A range of treatments is available most being based around stimulating the release of either FSH, LH or both. The first approach is to use a cheap synthetic anti-oestrogen drug called Clomiphene to stimulate the production of FSH and LH. If this is unsuccessful, FSH and LH themselves, may also be taken to stimulate the cycle at appropriate points. This treatment is more expensive since these hormones must be purified from the urine of post-menopausal women or produced by recombinant micro-organisms.

Where other infertility problems exist (including blocked oviducts in a woman and low sperm count of the male partner) treatment relies on various types of in vitro fertilisation (IVF). IVF involves the extracting of both ova and sperm from the body, encouraging fertilisation outside the body, and then transferring any resultant zygotes back into the uterus of a woman (who may or may not be the donor of the ova). In order to extract large numbers of ova to allow for several attempts at IVF, both FSH and LH are commonly used to encourage multiple ovulation.

A further use of female hormones is in hormone replacement therapy (HRT) used to treat some of the unpleasant symptoms of the menopause in older women. In such women, synthetic oestrogens are given to make up for the decline in natural production which occurs as the menstrual cycle stops. This has many benefits: it reduces some of the physiological and psychological changes that often occur at the menopause.

◆ CHECK LIST SUMMARY

- ◆ Contraception can be defined as the prevention of conception (fusion of male and female gametes). The most widely used is the contraceptive pill
- ◆ The 'pill' works by interfering with the natural menstrual cycle of the human female and preventing ovulation
- ◆ The commonest used type of pill is the combined contraceptive pill which contains low doses of hormones oestrogen and progesterone in synthetic form
- ◆ The effect of the pill is to prevent release of both LH and FSH via the negative feedback inhibition by oestrogen and progesterone
- ◆ To achieve this effect the pill must be taken daily for 21 days in each 28 day cycle. In the 7 pill-free days which follow the uterus lining breaks down in response to the withdrawal of progesterone, giving a type of light menstrual period
- ◆ The contraceptive pill also exerts effects on other parts of the reproductive tract. Firstly it causes the mucus in the cervix region to thicken, making it more difficult for sperm to enter, and secondly it limits the thickness of the endometrium, making it more difficult for implantation of a fertilised ovum
- ◆ If a progesterone only pill, the 'mini pill' is taken the effects are limited to these changes: inhibition of ovulation does not necessarily occur
- ◆ The development of other types of contraception based on use of hormones are being investigated. One method which is already in use involves implanting tubes containing progesterone crystals under the skin which will release a constant low level of the hormone sufficient to reduce fertility
- ◆ In about 20 % of women who fail to conceive the underlying causes are hormonal. Treatment using synthetic or naturally occurring female hormones is highly successful in restoring fertility
- ◆ A range of treatments for infertility in the female are available based around stimulating the release of either FSH, LH or both
- ◆ Both FSH and LH are commonly used to encourage multiple ovulation for in vitro ('test tube') fertilisation.

HORMONES in DOMESTIC ANIMALS

Superovulation and embryo transfer

As discussed above, artificial insemination gives farmers the ability to select semen from male animals showing particular desirable characteristics, so improving the quality of his stock. Recently technology has become available to allow selection of breeding females in a similar, although slightly more limited way. This procedure involves manipulating the reproductive biology of females (usually cows) by superovulation and embryo transfer and involves the following stages:

- Cattle, or other farm animals are treated with hormone injections to stimulate the development and release of much larger numbers of ova than would naturally occur. As in humans, the main strategy involves using FSH and LH at appropriate times. Theoretically up to 50 ova may be released per cycle, but generally it is between 3 and 8.
- When ovulation occurs (detected by the signs of oestrus mentioned above, or by calculation of time since LH injection) the cow is artificially inseminated.
- The fertilised ova are allowed to develop for up to 7 days and are then washed out of the uterus before implantation occurs.
- The embryos are frozen and stored until required.
- Embryos are then introduced into the uterus of cows other than those from which they were obtained; they implant and develop until full term. This process is known as **embryo transfer**. It should be noted that whilst embryos may be implanted in females from the same farm they may also be sold for implantation in cows in different regions or countries.

By this process a single high quality cow may produce a very large number of offspring allowing the quality of a herd to improve very quickly. Estimates from the 1980s show that superovulation of a cow is possible every 2-3 months. Each time 6-7 normal embryos will result from artificial insemination, of which 3-4 will successfully develop into calves. This gives a total of 15-18 calves per donor female per year. As these calves grow up their qualities in terms of meat and milk production can be assessed allowing farmers to rapidly ascertain the best cattle to breed from.

There are variants on the type of embryo transfer described above and the reasons for performing it. One main aim is to use embryo transfer to establish twin pregnancies in cattle where twinning is uncommon. This can potentially double productivity. Twin pregnancies are most often obtained by transferring two embryos into a cow who has not been inseminated, although they may be added to an existing zygote in the uterus of a cow who has already been inseminated. In some cases the sex of embryos may be determined before transfer. This is valuable to farmers as it ensures that they can achieve desired ratios of male to female cattle (more males than females required for beef farming and vice versa for dairy). The embryos may also be split to produce clones (genetically identical individuals) before transfer.

◆ CHECK LIST SUMMARY

- In the sexually mature female mammal regular sexual cycles occur, during which one or more female gametes (ova, singular ovum) develop inside follicles and are released from the ovary, offering the chance of fertilisation if mating occurs
- These cycles really consist of two closely linked cycles which are synchronised by hormonal interactions.
- The follicular or ovarian cycle which is concerned with the development and release of ova.
- The uterine cycle which is concerned with the development of the endometrium (uterus lining) to ensure the highest chance of implantation of a fertilised ovum or zygote.
- The sexual cycle relies on interactions between four main hormones: the ovarian hormones oestrogen and progesterone, and the pituitary hormones Follicle Stimulating Hormone (FSH), and Luteinising hormone (LH). Although timings of cycle vary between species the same basic pattern holds true.
- FSH is released from the anterior pituitary and stimulates the development of several follicles (primary oocytes) in the ovary. One or more of these will eventually mature into a Graafian follicle containing the ovum
- FSH stimulates the production of oestrogen from the follicles within the ovaries. This Oestrogen in turn stimulates the proliferation of the endometrium. At this point oestrogen inhibits FSH (negative feedback control).
- Oestrogen levels increase until the mid point of the cycle when they bring about a peak of LH production from the anterior pituitary causing ovulation (the release of the ova from Graafian Follicles).
- LH causes the Graafian Follicle to develop into a corpus luteum which begins to secrete the progesterone and oestrogen.
- Progesterone stimulates further development of the endometrium to prepare the uterus in case the newly released ovum is fertilised.
- The other function of progesterone is to inhibit the production of both FSH and LH and hence the development of further follicles.
- If fertilisation does not occur the corpus luteum degenerates and secretion of progesterone and oestrogen falls. This fall causes the uterine blood vessels to rupture and the uterus lining to degenerate. Decline in progesterone levels causes the inhibition of FSH and LH to be removed and a new cycle can begin.
- If fertilisation does occur then the corpus luteum does not degenerate but continues to secrete oestrogen and progesterone, maintaining the uterus lining and preventing further follicles from developing. Eventually the developing placenta takes over this endocrine role.
- Oestrus is a change in the behaviour or appearance of a female mammal which occurs around the time of ovulation, indicating sexual receptiveness to males.
- Cows attempting to mount other females and then standing still and allowing themselves to be mounted by other females is the best sign of oestrus.
- Detection of oestrus by humans, allows intervention in the process of reproduction, e.g. by artificial insemination (AI).

Synchronisation of oestrus

The synchronisation of oestrus cycles in flocks of sheep (ewes) or herds of cows is a very desirable way of manipulating animal reproduction. The aim of this process is to ensure that all animals in the herd come into oestrus on approximately the same day and can be mated or artificially inseminated at the same time. This allows substantial savings for the farmer in terms of both time and money, as well as improving conception rates and ensuring that the entire flock will be producing offspring at the same time the following season. Synchronised oestrus is particularly desirable in ewes, as opposed to cows or sows for two reasons: firstly these animals have distinct breeding seasons and cannot become pregnant outside of this season and secondly, many flocks of sheep live in isolated hill regions. It is much more efficient to herd the sheep together to start treatment and then again for mating or A.I.

The process of synchronisation is based on the administration and then withdrawal of the female hormone progesterone. Progesterone inhibits FSH and LH secretion and hence prevents the development of follicles and the release of ova. The process is as follows:

- All ewes in a flock are treated with progesterone for 5-9 days. The hormone is administered in one of three ways: orally, via an implant under the skin, or via a sponge in the vagina.
- The progesterone is stopped in all ewes on the same day. This removes the inhibition of FSH and LH and allows follicles to start development in the ovaries of the ewes.
- Several days later the ewes come into oestrus.
- A ram is obtained and used to fertilise all the sheep at the same time. Alternatively A.I. may be used. This may ensure higher fertilisation rates, be quicker, prevent the spread of disease and allow semen to be chosen from a wide range of rams.
- All ewes who were fertilised produce lambs at approximately the same time.

In addition to its use in synchronising oestrus during the breeding season, the use of hormonal treatments has also allowed flocks of ewes to come into oestrus (synchronised) at other times of the year. In these cases progesterone is given as described above but an extra hormone, gonadotrophin, is required to stimulate FSH and LH secretion. Light stimulation is sometimes used as well since the breeding season is triggered by changes in light intensity. Such manipulation may be used to shift the timing of oestrus and hence of lambing to more suitable times of the year based on known or predicted environmental or economic conditions. In some cases, where environmental conditions permit, farmers may divide their flocks into two, having half mating in October and lambing in March and the rest mating in July and lambing in December.

Milk production in cows

Over the thousands of years of animal husbandry, cows have been selectively bred to give high milk yields. Traditional breeding techniques combined with the modern use of A.I. and embryo transfer and improved understanding of bovine (cow) nutrition and management has led to enormous increases in yield in domestic breeds compared to wild cattle. Even though a high yielding cow may produce over 40 litres of milk per day (up to 12,000 litres/year) there is still an interest in further boosting production. One reason for this is that in many countries (including Britain), prices paid to farmers for milk are very low, forcing farmers to maximise productivity if they are to make a profit. One solution to this is to boost production using hormones.

The hormone BST, (bovine somatotrophin), is a pituitary growth hormone which occurs naturally in young cattle. Its function is to increase cell division, protein synthesis and growth. Trials with BST, which is now produced by genetically engineered bacteria, showed that injecting dairy cows with the hormone led to a 10-15% increase in milk yield, presumably through an increase in growth and activity of milk producing tissue in the udder. Some of the advantage was offset by the fact that cows injected with BST require more food, but a net profit still resulted. These early trials showed no apparent change in behaviour, health or reproductive capacity of the cows.

Although BST is approved for use in cows in the USA, the hormone is banned in the European Union. This decision followed public protest as well as further scientific investigations of cows treated with BST which did suggest some health problems, including reduced resistance to disease.

Moral and Ethical Issues associated with interventions in reproduction

Any intervention in the process of reproduction is likely to be considered unethical by some groups in society. One widely held view is that increased availability of contraceptives, and particularly of the contraceptive pill, encourages sexual promiscuity. In addition, some religions, including Roman Catholicism and Islam condemn the use of contraceptives of any kind, arguing that limiting procreation is against God's will. Such religions do indeed value large families, and in many parts of the world the large family does provide an effective support system for elderly people. In opposition, however, many other groups would point to the benefits to both individuals and societies that contraceptive technology has brought. In dramatically decreasing birth rates it has improved the physical and emotional well-being of women across the world. In limiting family size it has also helped to contribute towards improvements in child health and economic status in many regions.

Intervention in human reproduction to treat infertility (mainly that involving IVF) is also the subject of much debate. Although the number of people undergoing such treatments is very small compared to the numbers using contraception, the issues raised concern society as a whole. Increasingly issues concerning the rights of individuals to have children are becoming high profile legal cases, emphasising the fact that medical and scientific advances in this field must be matched by progress in the fields of ethics and law.

A major argument exists over the fate of spare embryos (or pre-embryos) that have been conceived by IVF. There is a case for using them in medical research; particularly research associated with improving understanding of infertility and the development of new techniques to treat it. Others, however, believe that embryos are new individuals and that this would be immoral or unethical. As with discussions surrounding abortion one of the issues here concerns the right to life and the ownership of the embryos.

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- By this process a single high quality cow may produce a very large number of offspring allowing the quality of a herd to improve very quickly.
- The synchronisation of oestrus cycles in flocks of sheep (ewes) or herds of cows ensures that all animals in the herd come into oestrus on approximately the same day and can be mated or artificially inseminated at the same time.
- Synchronised oestrus is particularly desirable in ewes, as opposed to cows or sows for two reasons: firstly these animals have distinct breeding seasons and cannot become pregnant outside of this season and secondly, many flocks of sheep live in isolated hill regions. It is much more efficient to herd the sheep together to start treatment and then again for mating or A.I.
- All ewes in a flock are treated with progesterone for 5-9 days. The hormone is administered in one of three ways: orally, via an implant under the skin, or via a sponge in the vagina.
- The progesterone is stopped in all ewes on the same day. This removes the inhibition of FSH and LH and allows follicles to start development in the ovaries of the ewes.
- Several days later the ewes come into oestrus.
- A ram is obtained and used to fertilise all the sheep at the same time. Alternatively A.I. may be used. This may ensure higher fertilisation rates, be quicker, prevent the spread of disease and allow semen to be chosen from a wide range of rams.
- All ewes who were fertilised produce lambs at approximately the same time.
- Even though a high yielding cow may produce over 40 litres of milk per day (up to 12 000 litres/year) there is still an interest in further boosting production.