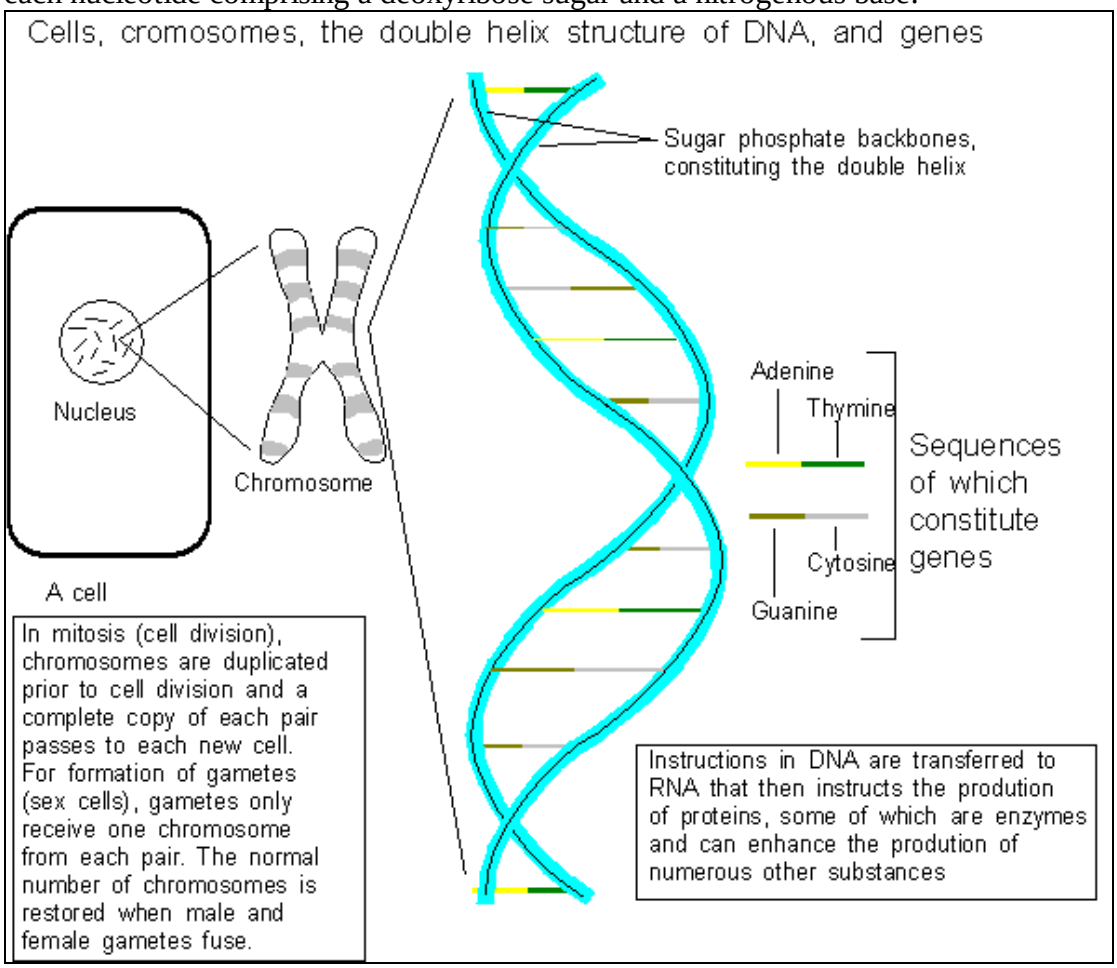
GENETICS, EMBRYOLOGY, AND PREGNANCY

GENETICS

Genetics is the study of hereditary and variation. The basic unit of inheritance for all leving creatures is deoxyribonucleic acid (DNA). DNA is a double helix consisting of two interwoven strands of nucleotides (= a purine or pyrimidine base linked to a sugar) each nucleotide comprising a deoxyribose sugar and a nitrogenous base.



In DNA there are four bases which always pair off adenine to thymine, and guanine to cytosine. If double stranded DNA is split into two single strands of DNA then this specific base pairing, given suitable circumstances, enables a complementary strand to be made.

RNA has only one ability: it makes proteins. Some proteins are used for bodily structural purposes but others are enzymes (an enzyme being a substance that assist chemical reactions without themselves being consumed), and enzymes can be used to synthesise non-protein substances including carbohydrates and fats.

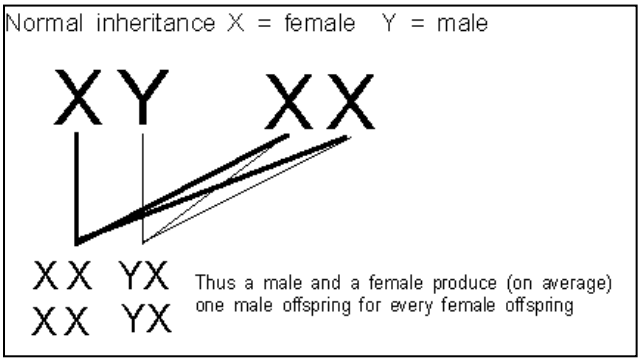
To make a protein a sequence of amino acids has to be assembled and DNA cannot do this on its own. A strand of DNA is used as a template and complementary information is transcribed onto messenger ribonucleic acid (m-RNA). Complementary information is ensured because adenine in DNA pairs specifically with uracil in m-RNA, cytosine in DNA specifically pairs with guanine in m-RNA and thymidine in

DNA specifically pairs off with adenine in m-RNA. Messenger-RNA thus contains DNA-directed sequences of bases which in turn attract complementary sequences of bases in transfer RNA (t-RNA). Each different t-RNA is linked with a specific amino acid. In effect there are three stacks of complementary plates coding DNA -> m-RNA -> t-RNA -> amino acid. The assembled sequence of amino acids is "zipped together" by enzymes to make a protein.

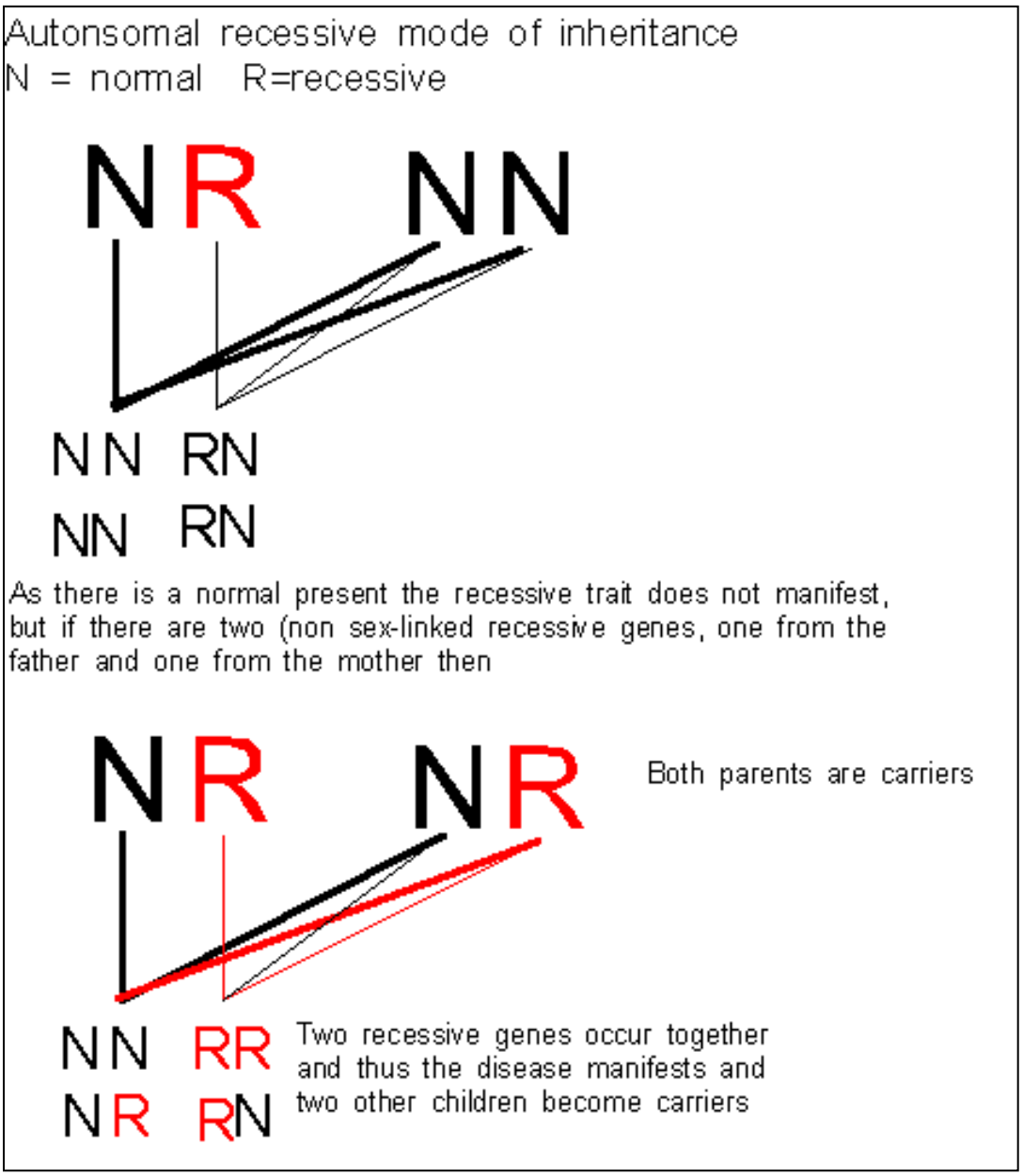
A chromosome consists of a continuous structure containing thousands of gene sequences (a gene typically consists of thousands of nucleotides). Some gene sequences appear to have no function but telomeres, structures at the end of chromosomes, decrease with each division and may be associated with ageing.

Chromosomes are used to manufacture *genetically similar* cells by mitosis (=growth or reproduction by non-sexual production of new somatic cells). In simple terms strands of DNA are separated and each of the two strands then makes a complementary copy of itself so that two genetically similar sets of chromosomes are formed from the original, each being in a separate cell. There are 46 chromosomes (22 pairs of somatic, non-sex, chromosomes and 1 pair of sex chromosomes, one male "Y" and one female "X").

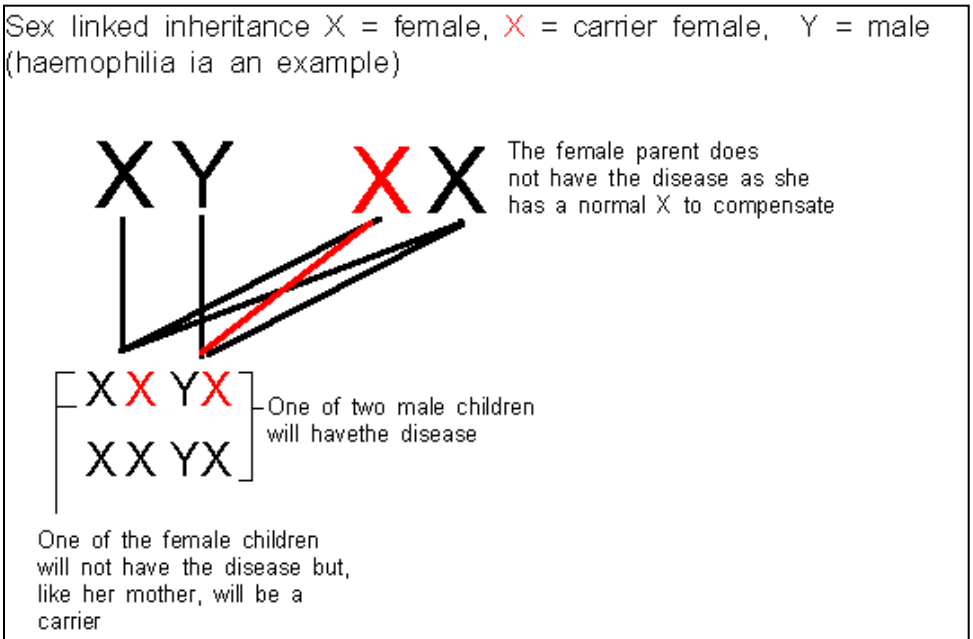
Chromosomes are used to manufacture *genetically dissimilar* germ cells by meiosis, each of which contains half the number of chromosomes (haploid). Fertilisation restores the chromosome complement to normal (diploid).



Sexual reproduction depends upon meiosis which in effect shuffles genes as if they were derived from a male and a female pack of cards. Sexual reproduction with meiosis provides *variations* by providing new combinations of genetic material. In contrast *mutations* occur when there is a change in information which is something new and not just shuffling: mutations can occur spontaneously but radiation and other factors may be causative. Most mutations result in non-viable cells but some survive and prove beneficial. In the nature of things large genetic mutations are likely to produce drastic changes in the resulting organism such that it will not develop and would be unlikely to survive to reproduce itself. Small mutations will produce small changes and the resulting organisms will survive and be available for natural selection to operate. Evolutionists argue about whether changes ever occurs by large mutations. It seems unlikely but probably does occur, albeit very rarely.



The paired genes for particular manifestations are at identical points (loci) on each member of a pair of chromosomes. The genes themselves may be identical (homozygous) or different (heterozygous). If a gene is *dominant* then it will manifest



independently of its pair (sometimes penetrance is incomplete). The effects of *recessive* genes are less vigourous aws bothmembers of a pair have to be present to cause full manifestations. If *one* parent is heterozygous for a particular recessive gene theb half the offspring will be heterozygous and asymptomatically carry the tendency for the gene to manifest but if both parents are heterozygous for a recessive gene then a quarter of their offspring will be homozygous and half will be carriers.

During meiois all 46 chromosomes pair up including the X and Y (sex) chromosomes (if two Xs, one from the mother and one from the father, are present then a female offspring results whereas if X and Y are present a male offspring results). In the female only one of the potential four haploid germ cells develop in meitotic telophase II , and this of course is an X, whereas in the male germ cells two of the germ cells are Y and two are X, and thus the male contribution determines the sex of the offspring. In population terms there should be in theory an equal number of male and female children.

Chromosome abnormalities occur if there is:

- An extra chromosome (trisomy)
- One chromosome missing (monosomy, usually the Y chromosome)
- Breakage or splitting of a chromosome
- Exchange of inappropriate information between two different chromosomes
- Reversal of a sequaence ocontained within a chromosome
- Joining of two chromosome ends to produce a ring form

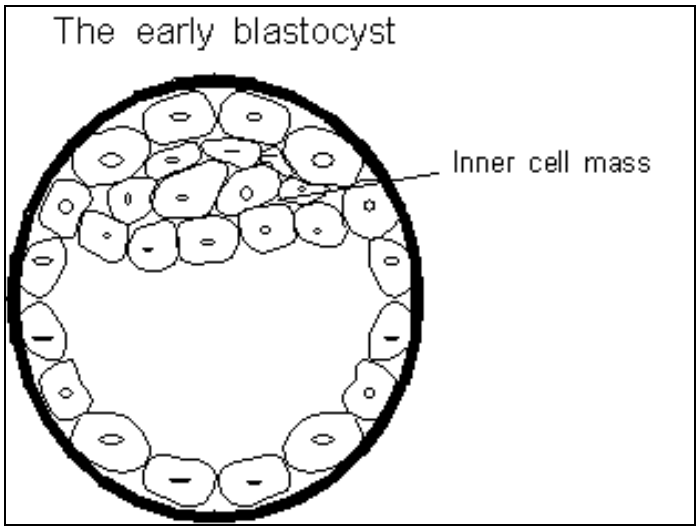
Because the Y chromosome is largely passive and does not oppose X genes, an unopposed X-linked gene (which probably produced no effects in the mother, because she had a counterbalancing X) will produce an effect in male offspring only (females although having only one affected X chromosome will be unaffected but will be carriers). In addition the condition will only affect alternating generations because affected males could not pass on any X-linked genes to their sons as they can only give him a Y, but they can give their X-linked gene to their daughters (who will become carriers because their other normal X gene will oppose the affected X gene) and only when she produces male offspring will the condition manifest. Hence generations are skipped.

Not all inheritance is derived from DNA in the nucleus. Mitochondiral DNA is inherited separately from the mother. This fits in with the theory that mitochondria were originally parasites that invaded human cells and eventually achieved a permanent and irreviersible symbiotic relationship.

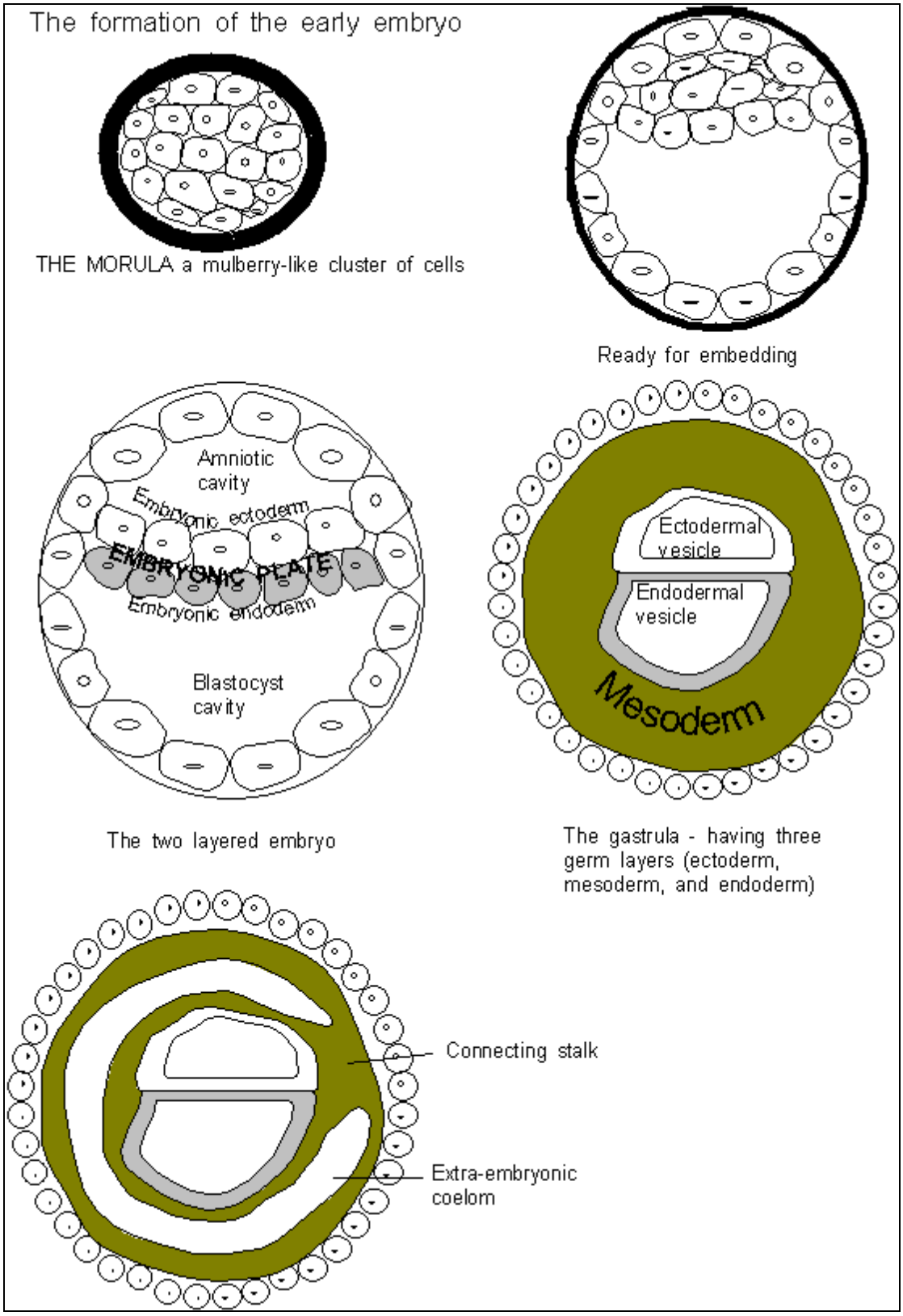
EMBRYOLOGY

Why is the human structure the way it is? To answer this question it is necessary to understand how humans evolved from their ancestors. These evolutionary changes (phylogeny) to a certain extent are repeated in the development of the human embryo (ontogeny). For a comprehensive understanding of our anatomy it is necessary to visualise how bodily structures develop from the single cell formed after fertilisation. The exact timing of various developments is omitted from the text..

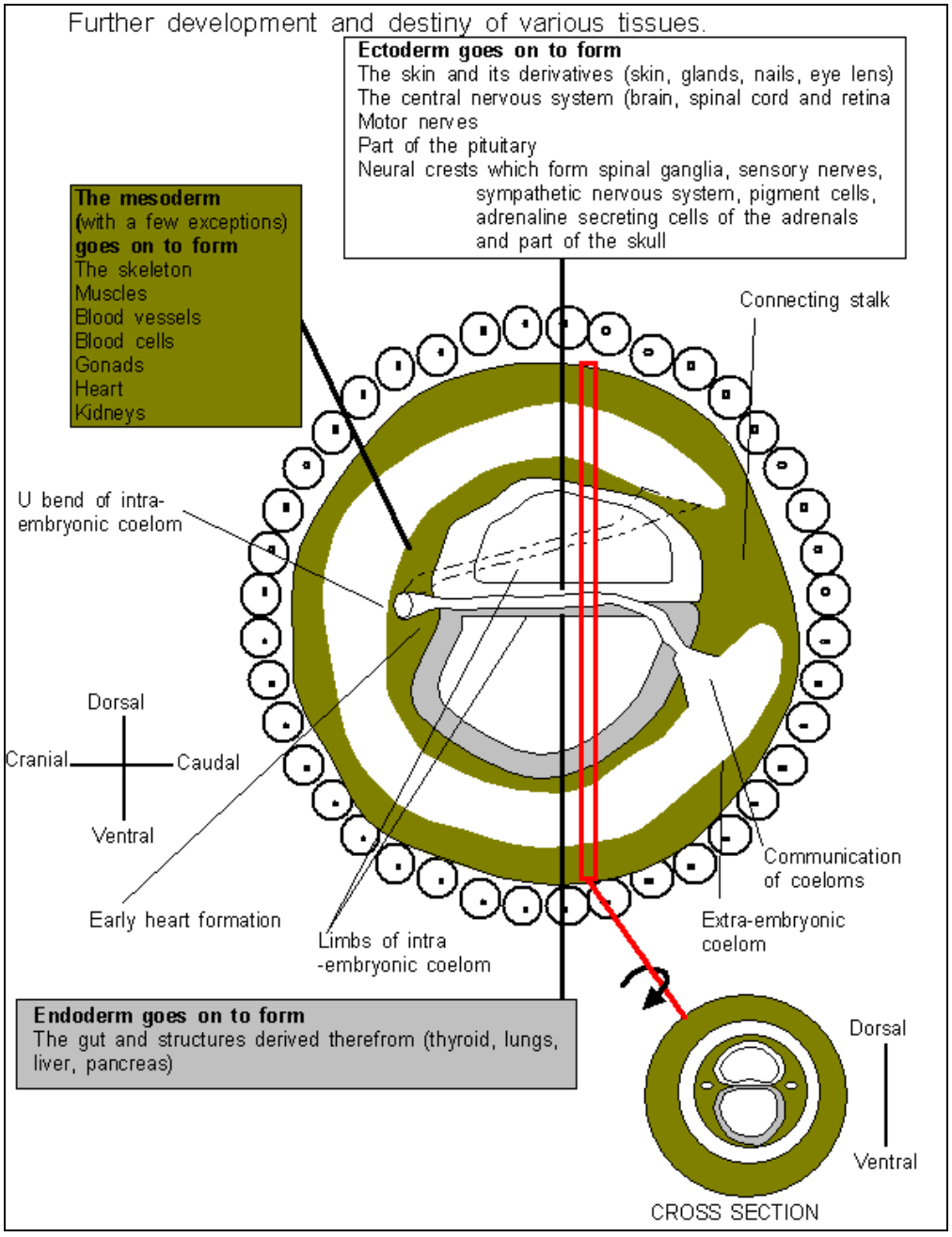
For the purposes of this account:
The *cranial* end is the end at which most symmetrical creatures with spinal columns have the major sense organs (eyes, ears, smell) and the brain
The other, rear, end is termed *caudal*
The *dorsa,* usually upper, surface is the surface interior to which is the spinal column
The *ventral,* usually lower, "belly" surface is the surface interior to which is the gut
The zygote is the cell formed by gametic union and the group of cells developing from this
The embryo is the further development of the original zygote *until the end of the second month*
The foetus is the further development of the embryo *after the end of the second month*



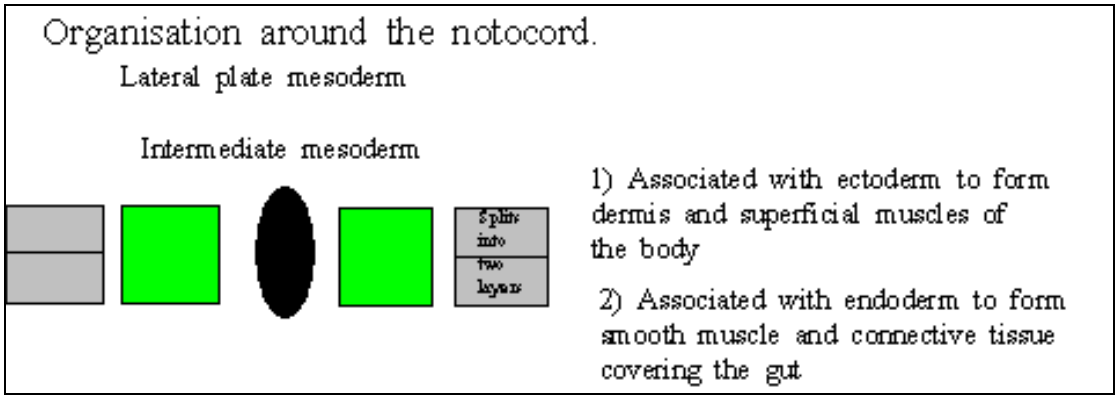
Fertilisation results in a single cell, the zygote (= yolked) with 46 chromosomes, which is less than one hundredth of a millimetre in diameter which then divides repeatedly by mitosis, toreach the uterus, where it embeds 3-4 days after fertilisation. Initially there is a ball of cells, the morula which then develops a cavity with a peripheral inner cell mass, to become the blastocyst (= germ + bladder). The ectoderm (=outside + skin) of the inner cell mass then develops a cavity (an ectodermal vesicle known as the amniotic cavity) whilst the endoderm (=within + skin) utilises the blastocyst cavity to form an endodermal vesicle.

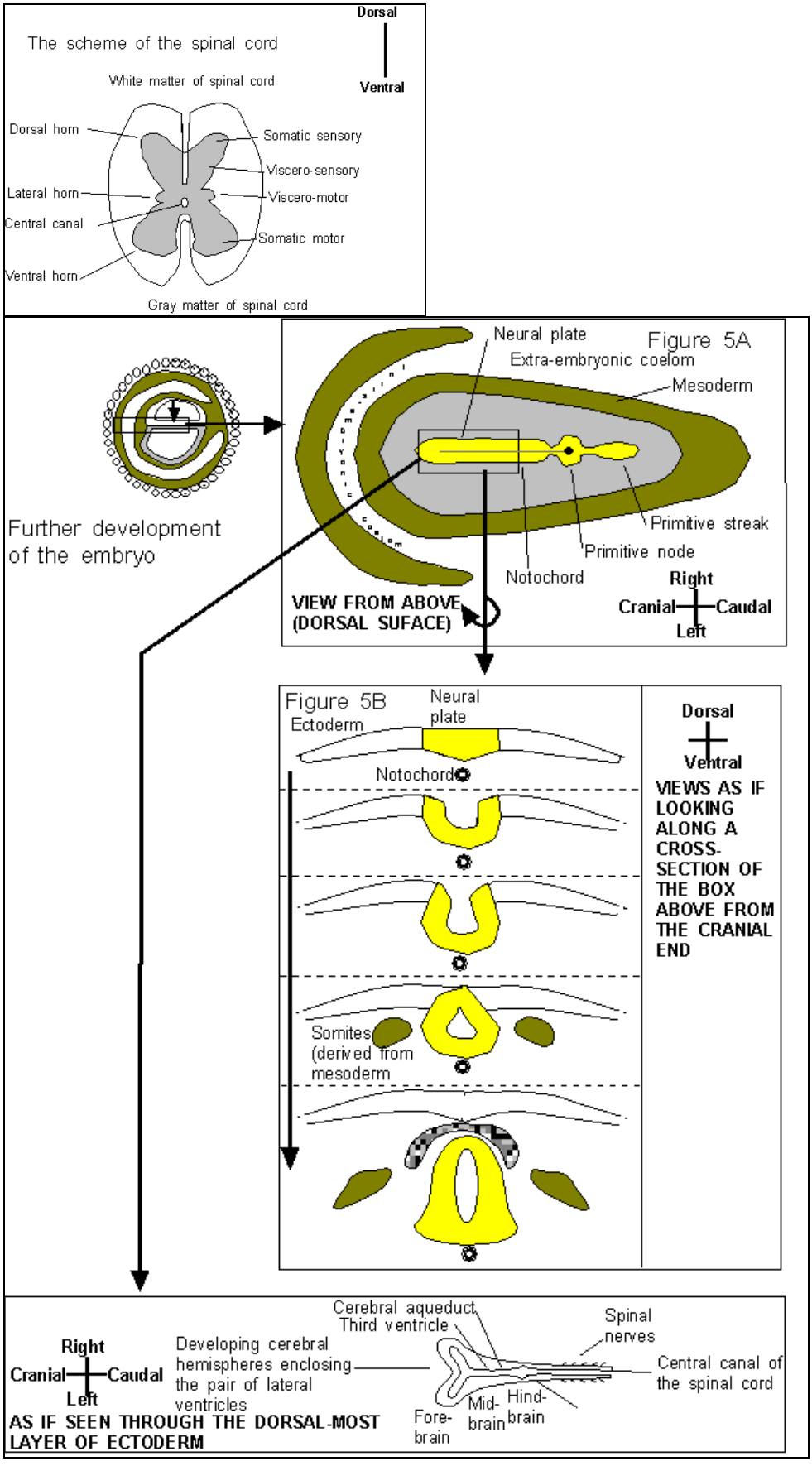


The next figure shows the further development and the destiny of various parts of the embryo.



A primitive streak with a primitive node forms in the ectoderm of the embryonic plate Tissue from the cranial end of the primitive node forms a hollow canal (the notochord, the forerunner of the vertebrae) which projects ventrally between the ectoderm and endoderm.




The scheme of the spinal cord
Dorsal
Ventral
White matter of spinal cord
Dorsal horn
Somatic sensory
Viscero-sensory
Lateral horn
Viscero-motor
Central canal
Somatic motor
Ventral horn
Gray matter of spinal cord
Further development of the embryo
Figure 5A
Neural plate
Extra-embryonic coelom
Mesoderm
Primitive streak
Primitive node
Notochord
VIEW FROM ABOVE (DORSAL SUFACE)
Right
Cranial
Caudal
Left
Figure 5B
Neural plate
Ectoderm
Notochord
Somites (derived from mesoderm
Dorsal
Ventral
VIEWS AS IF LOOKING ALONG A CROSS-SECTION OF THE BOX ABOVE FROM THE CRANIAL END
Right
Cranial
Caudal
Left
AS IF SEEN THROUGH THE DORSAL-MOST LAYER OF ECTODERM
Developing cerebral hemispheres enclosing the pair of lateral ventricles
Cerebral aqueduct
Third ventricle
Spinal nerves
Central canal of the spinal cord
Fore-brain
Mid-brain
Hind-brain

Mesoderm, which had developed around the primitive streak, starts to intrude between the ectoderm and endoderm. Mesoderm thickens in segmental fashion on either side of the spinal cord (and will eventually initiate formation of segmental body structures including the skeleton, and muscles).

The mesoderm closest to the central axis is associated with paired segmental elements, the somites, sclerotomes (which later form vertebrae), myotomes (which later form muscle groups), dermatomes, and the paired organs including the limbs, the gonads, kidney, lung and heart..

An ectodermal thickening, the neural plate, surrounds the primitive node at the cranial end and projects further cranially. The dorsal part of the ectoderm grows relatively quickly and curves over itself and fuses, thus forming a hollow neural tube which will form the central nervous system. The neural tube is wider cranially (where its walls will eventually form the brain) and is narrower caudally (where its walls will eventually form the spinal cord).

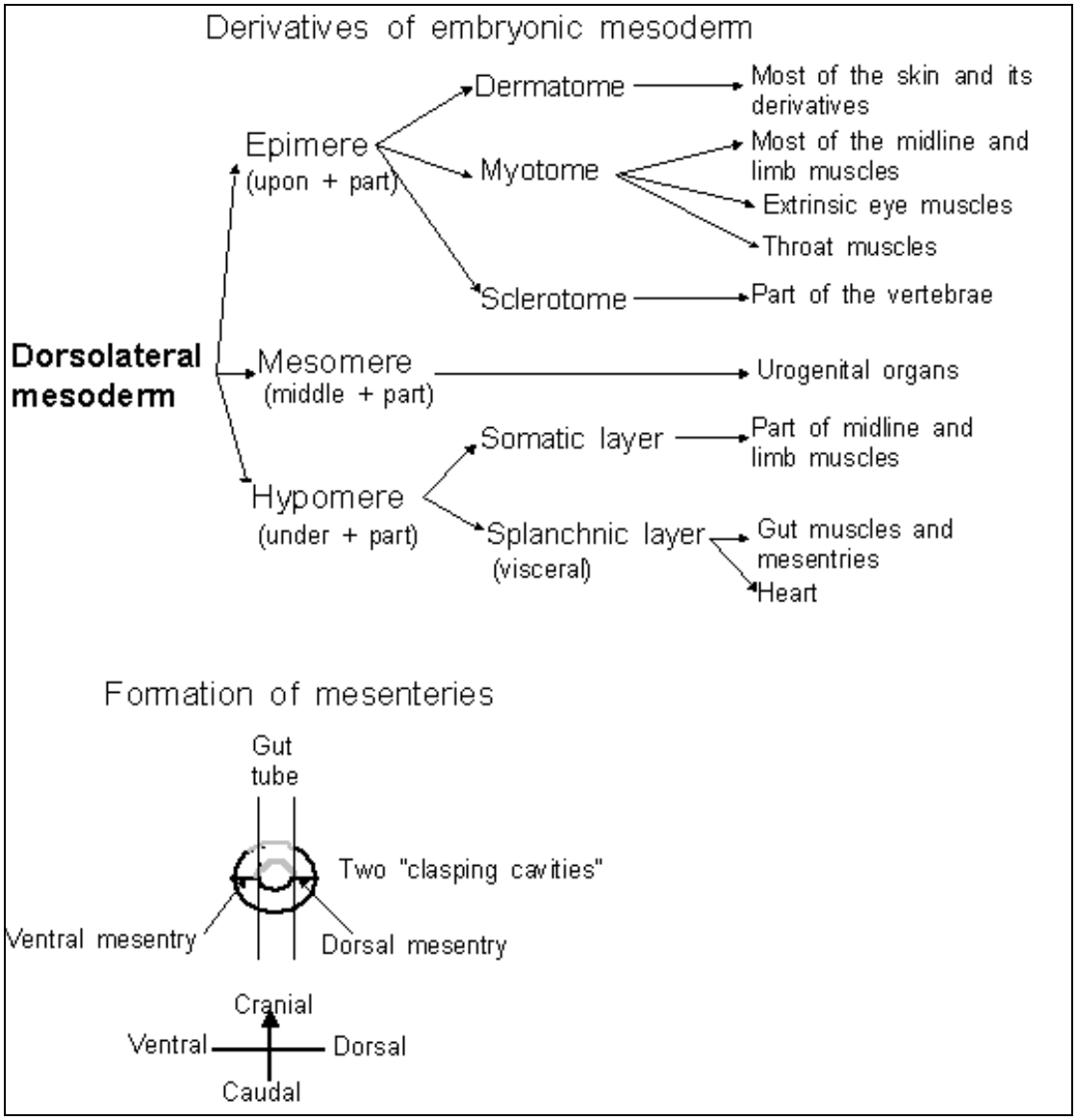
The lateral parts of the embryo fold inwards (ventrally) as do the cranial and cephalic ends to form the longitudinal cavity of the gut tube with a yolk sac connected by the yolk stalk. The future umbilical cord contains the yolk stalk, the blood vessels and the allantoic canal.

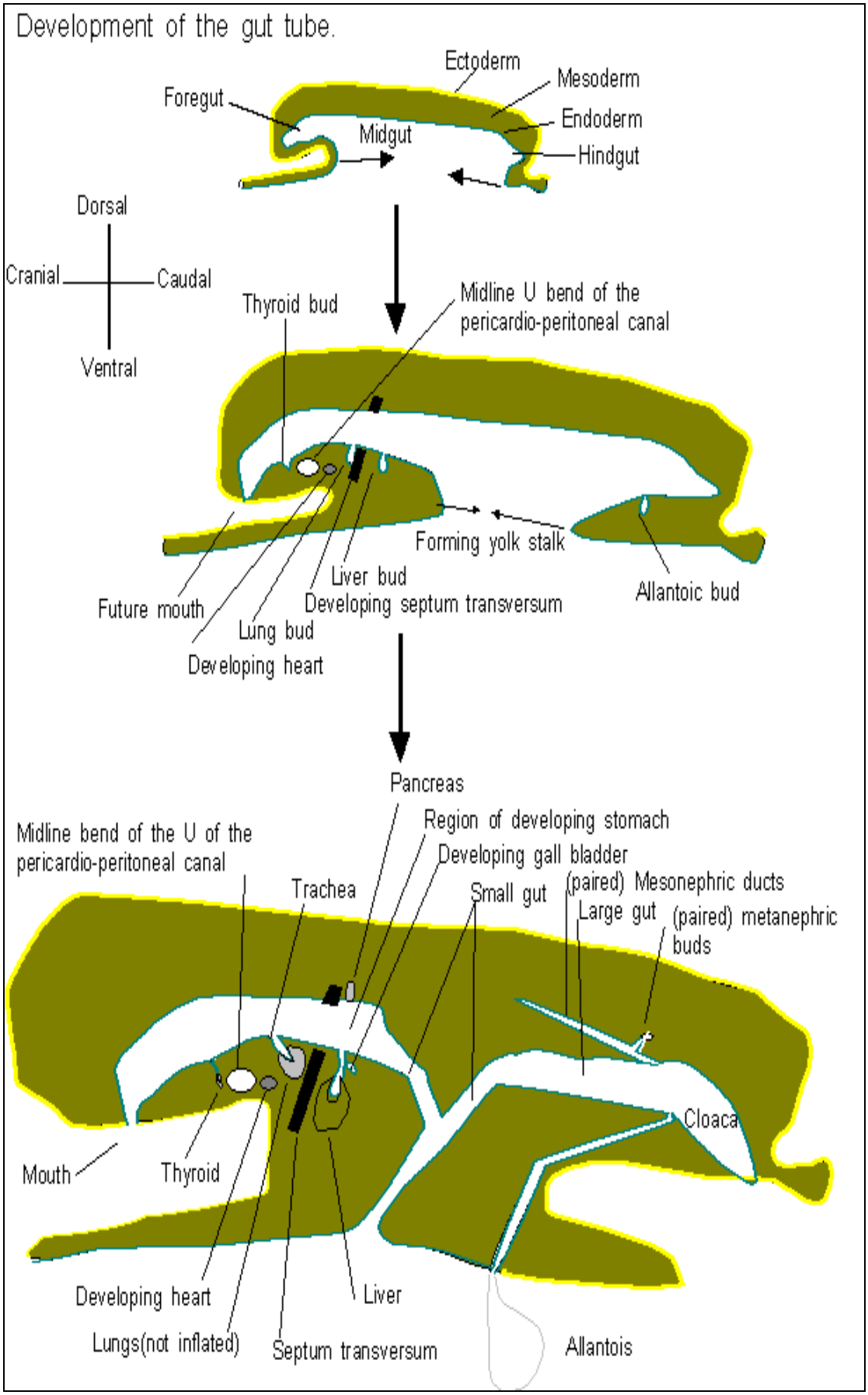
At the cephalic end the contiguous ectoderm and endoderm fuse to form what will become the mouth. At the caudal end the endoderm fuses with the ectoderm to form the cloacal membrane.

At the time of folding the yolk sac develops blood vessels and blood forming tissue. Because of the folding, the lateral, cephalic and caudal edges of the original disc arrive at the (ventral) midline and fuse with the corresponding layer of the opposite side.

In association with the folding and midline fusion of the ventral ectoderm a U shaped tubular cavity (the intra-embryonic coelom) appears in the mesoderm cranial and lateral to the primitive streak (the bend of the U later forms the pericardial cavity and limbs of the U the pleural cavities) and the ends of the arms of the U communicate with the extra-embryonic coelom (also known as the chorionic cavity).

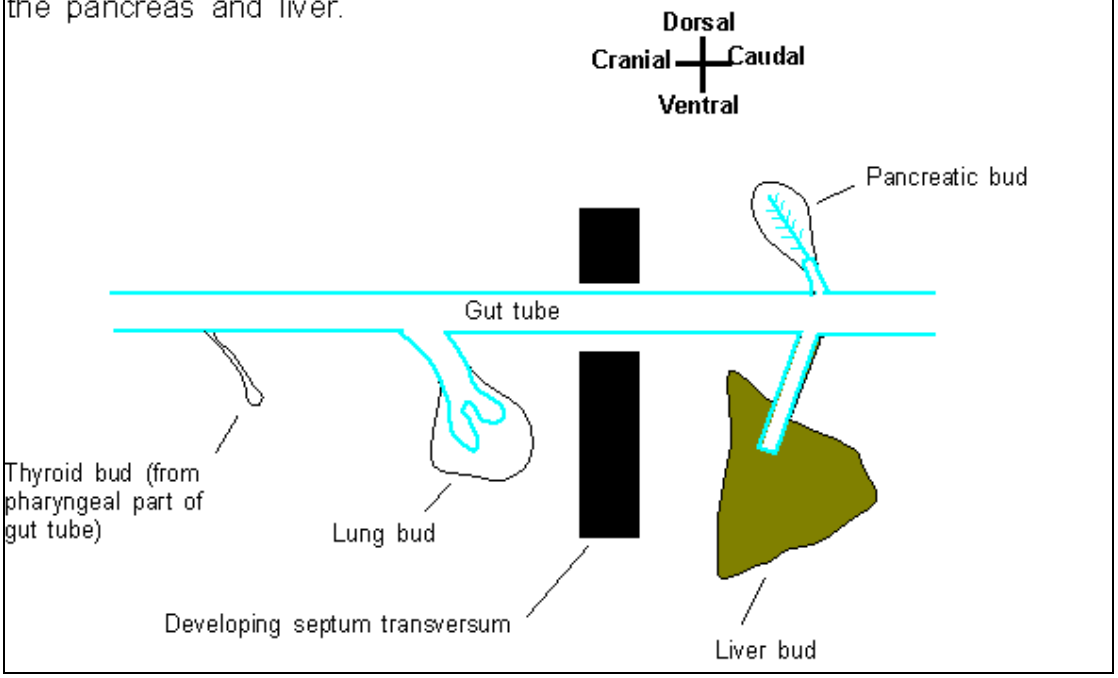
Eventually the embryo and its surrounding amnion expands to almost completely obliterate the extra-embryonic coelom. The ventral fusion of endoderm in effect creates the gut tube.


Derivatives of embryonic mesoderm
Dorsolateral mesoderm
Epimere
(upon + part)
Dermatome
Most of the skin and its derivatives
Myotome
Most of the midline and limb muscles
Extrinsic eye muscles
Throat muscles
Sclerotome
Part of the vertebrae
Mesomere
(middle + part)
Urogenital organs
Hypomere
(under + part)
Somatic layer
Part of midline and limb muscles
Splanchnic layer
(visceral)
Gut muscles and mesentries
Heart
Formation of mesenteries
Gut tube
Two "clasping cavities"
Ventral mesentry
Dorsal mesentry
Cranial
Ventral
Dorsal
Caudal



As the gut tube is forming the buds of the future thyroid, lung, liver and pancreatic buds are also forming.

Scheme of the devloping gut tube. The gut tube gives rise to several organs, venterally the thyroid, the lungs, and more caudally, the pancreas and liver.



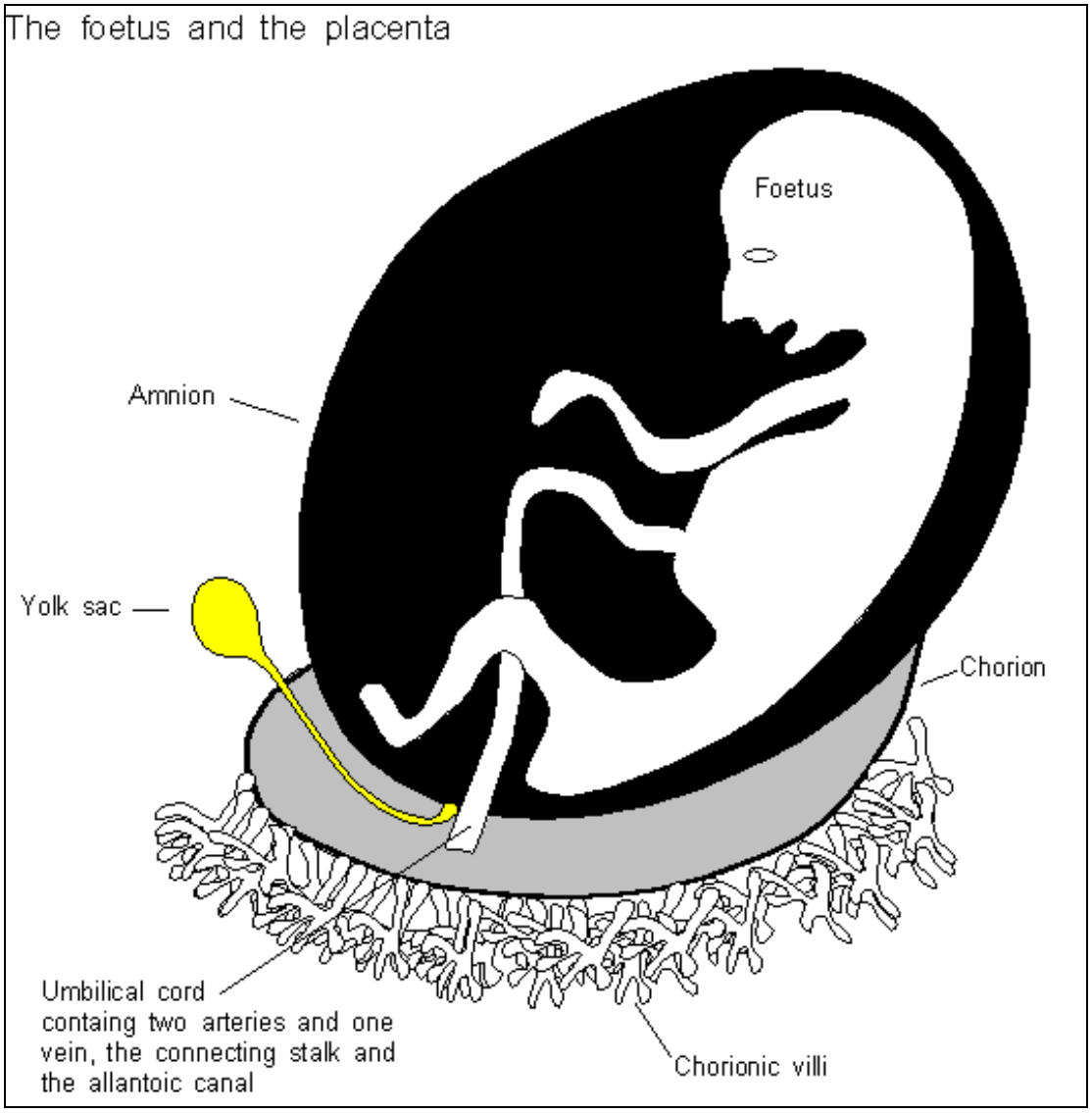
As the liver enlarges the yolk sac becomes smaller and the liver takes over the formation of blood cells (later still the bone marrow will take over this function). As a general rule all the ducts of internally secreting organs are lined with endoderm, indicating their derivation from the gut tube.

Just caudal to the U of the intra-embryonic coelom the mesoderm starts differentiating to form the heart and the septum transversum (which will later form the diaphragm) which separates the heart and lungs from the abdominal cavity.

Primitive blood vessels, some of which are potentially contractile, develop in the embryo. These vessels communicate with those of the yolk sac (humans do not require a significant yolk sac because the placenta supplies all necessary nutrients) and caudally with those of the placenta via the umbilical blood vessels. Blood is oxygenated at the placenta, reaches the embryonic heart by umbilical veins mixes with deoxygenated blood from the embryo and leaves the embryonic heart via the aortas (of which there are two, which later fuse).

The heart later develops, the lungs pouch off from the pharyngeal part of the gut tube) and push into the pleural part of the pericardiopleural part of the intra-embryonic coelom.

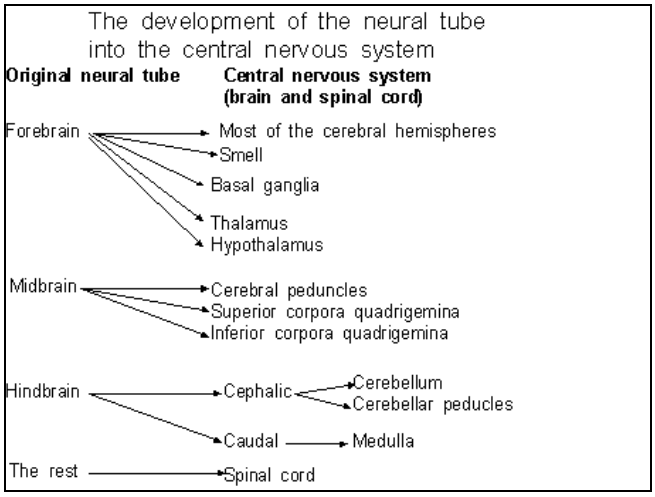
The thyroid gland and four parathyroid glands also develop from pharyngeal endoderm in the cephalic end of the gut tube. The paired thyroid areas fuse across the midline and the four parathyroids are situated just dorsal to (and may be embedded in) the thyroid.



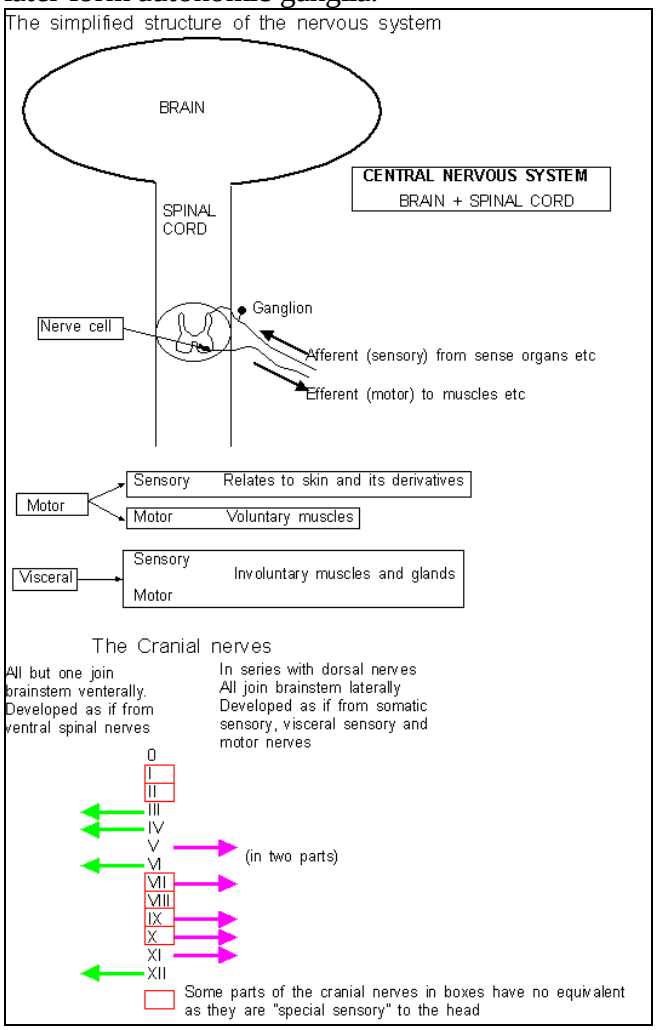
The placenta is the part of the foetus that embeds in the uterine wall. Villi (=minute projections) are developed through which are absorbed (from the mother) all nutrients and from which all necessary foetal excretory products pass (to the mother).

Certain substances do not pass through the placenta to the foetus. Antibodies, except IgG, do not pass and neither do maternal blood cells. At birth some of the foetal blood may enter the maternal circulation to cause the mother to make antibodies that may damage the blood cells of the next foetus if this next foetus has the same blood as its prior sibling (this is the basis of Rhesus incompatibility).

The umbilical cord joins the placenta to the foetus and it comprises a connecting stalk, two arteries, one vein, the allantoic canal and part of the extra-embryonic coelom which, in early pregnancy, had allowed part of the foetus' gut tube to protrude from its developing abdominal cavity constituting the normal foetal umbilical hernia of early pregnancy.



The spinal cord has two main areas. The dorsal parts are mostly sensory in function and the ventral parts are mostly motor in function. Axons grow out from the ventral parts to provide motor innervation for somites (experiments on animals have shown that somites induce nerve production (showing that body segmentation is imposed on the nervous system rather than the other way round). Some cells migrate from the neural tube to form two bands of neural tissue on each side, the neural crests which later form autonomic ganglia.



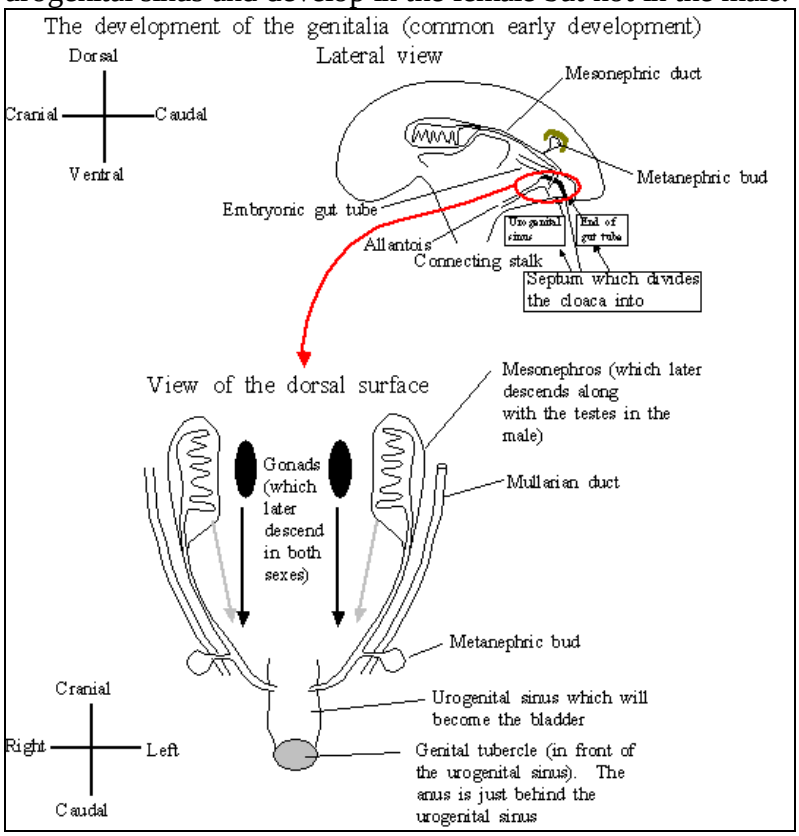
The paired segments formed by the transverse subdivisions of the mesoderm each side of the developing spine are called somites. The trunk muscles are formed from the dorsal part of the somites and the limbs are formed from limb buds.

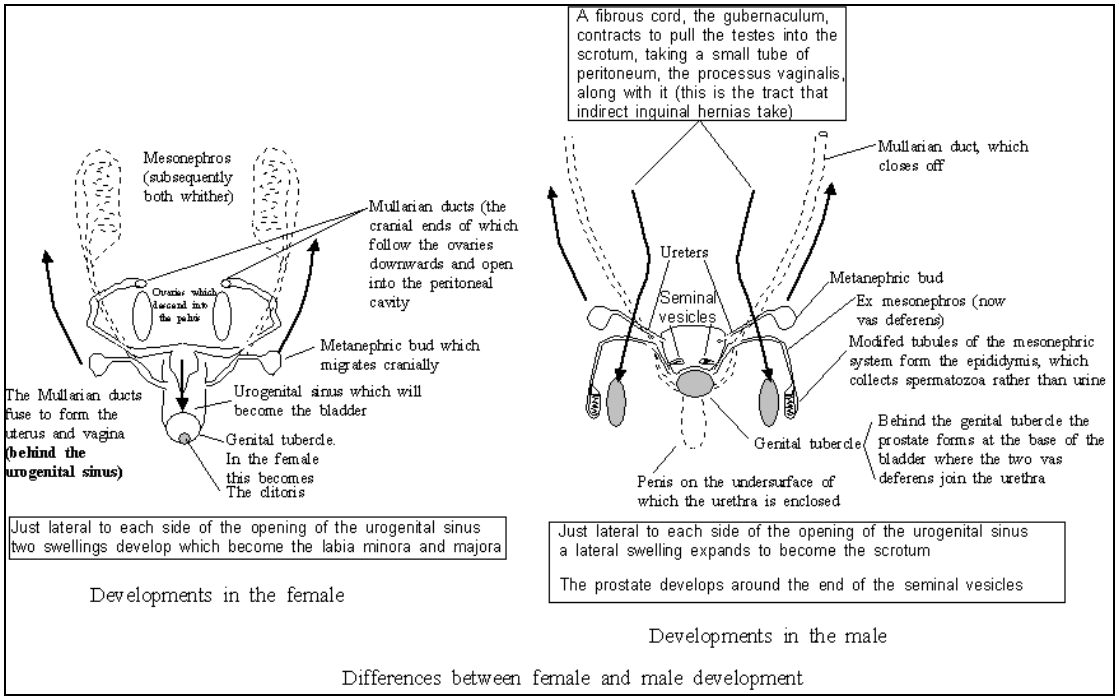
In foetal life the lungs are not expanded so little blood can flow through them, but the ductus arteriosus provides a bypass which is situated so that the oxygenated blood preferentially goes to the developing head and upper limbs.

Initially the pair of mesonephric ducts (off which come the metanephric buds) enter into the cloaca, the end of the hind gut. A septum grows into the cloaca from the sides to divide it into two, the ventral urogenital sinus and the caudal, dorsal, end of the gut (later to become the rectum). The cranial part of the urogenital sinus forms the bladder. The part of the urogenital sinus at the base of the bladder forms the whole of the female urethra but only part of the male urethra (in the male a grove forms in the underside of the penis which is later enveloped by penile tissue). The mesonephric duct, which leads from the developing gonads forms the vas deferens (=vessel + carrying) which enters the male urinary tract just below the bladder.

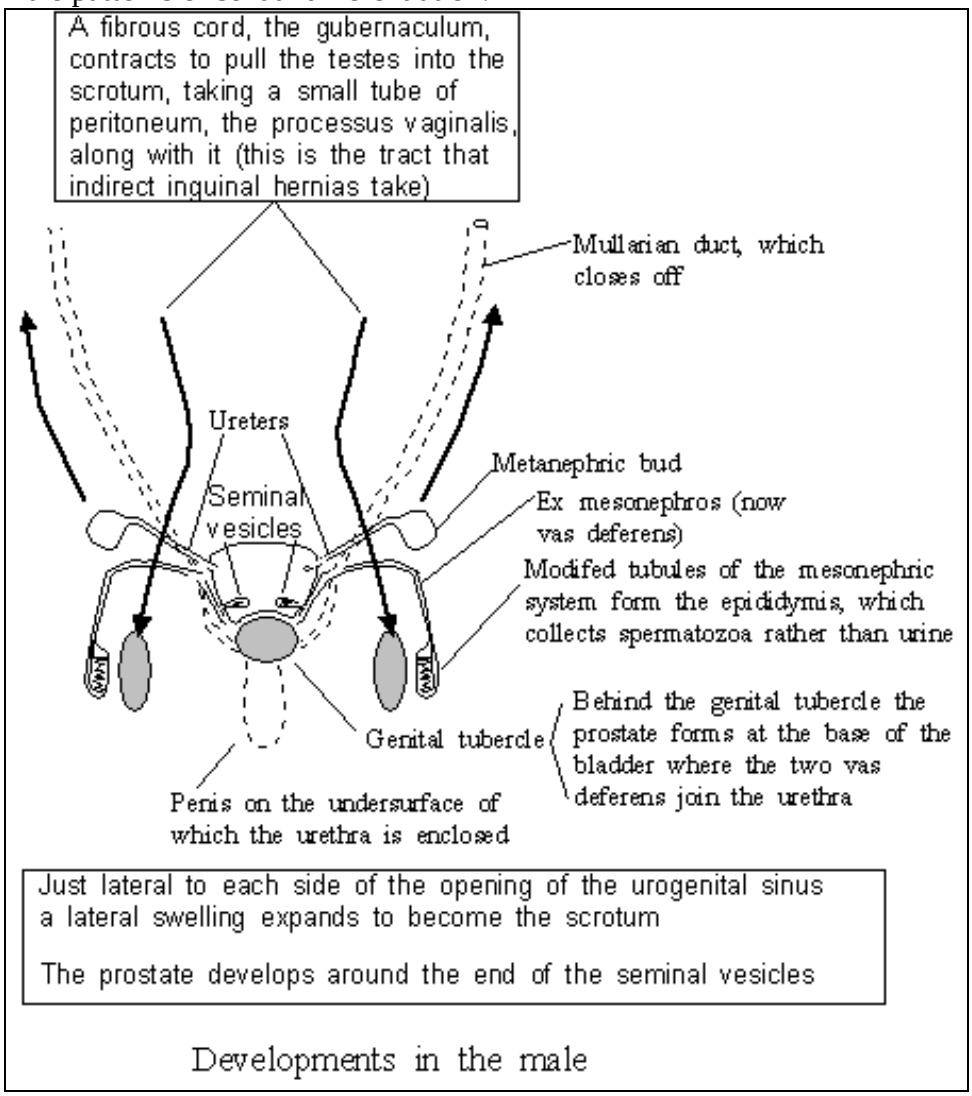
In both sexes a genital tubercle forms in the mesoderm between the connecting stalk and the urogenital sinus which later forms the clitoris in the female and the penis in the male.

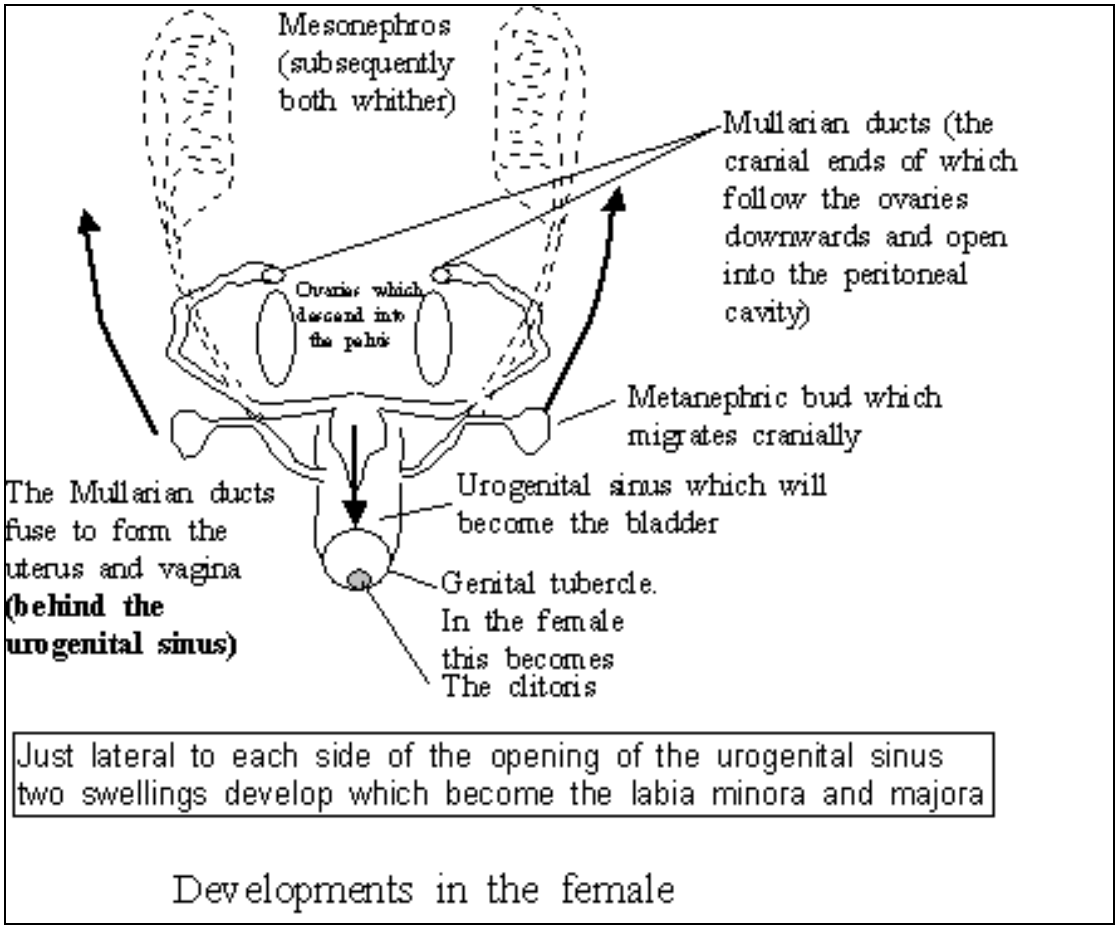
The gonads (testes in the male, ovaries in the female) are derived from germ cells on the yolk sac which migrate to develop each side of the midline, medial to the cranial end of the mesonephric duct. In both sexes (Mullarian) ducts form lateral to both the mesonephric duct and the developing gonads. The Mullarian ducts lead to the urogenital sinus and develop in the female but not in the male.





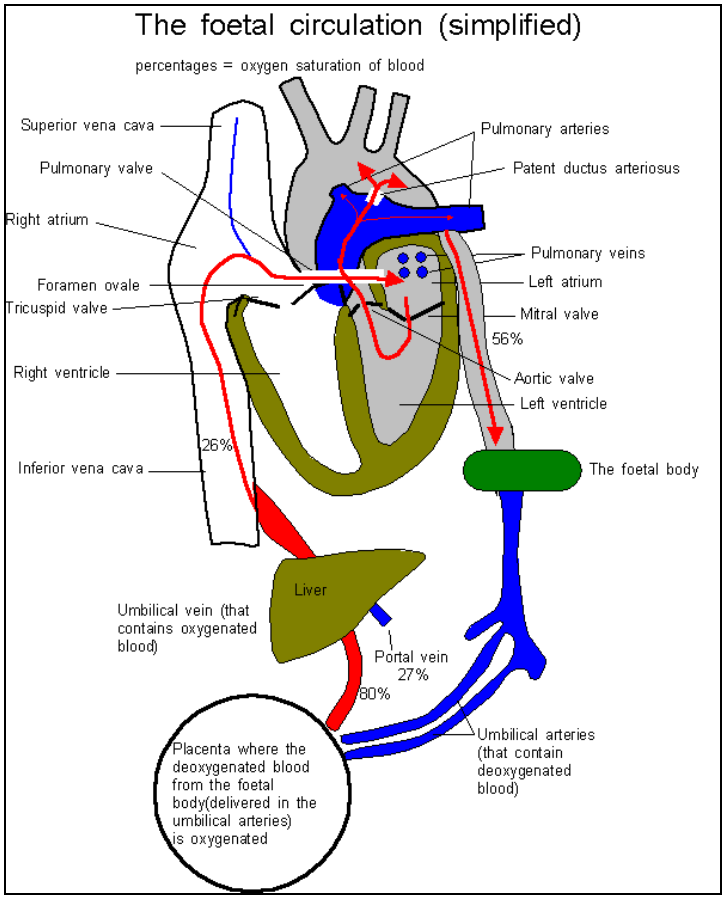
The following figures show the similarities and differences between the female and male patterns of sexual differentiation.





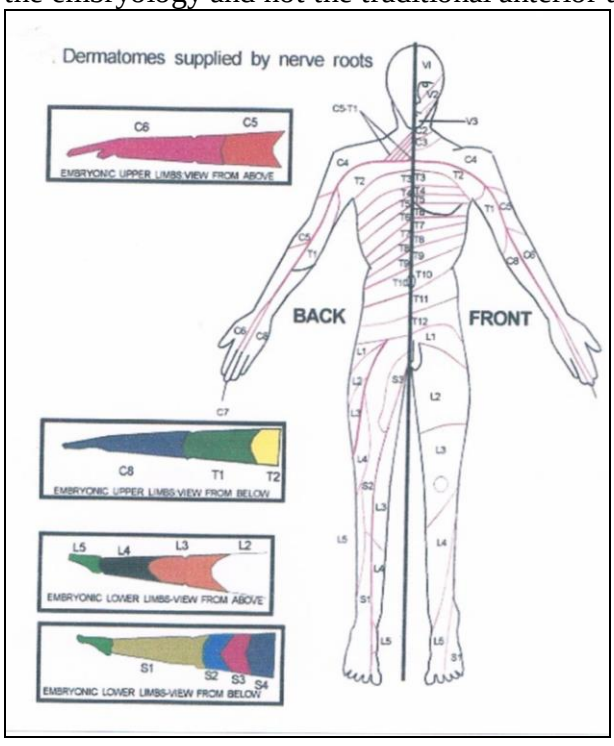
Blood flow and the foetal heart

Oxygenated blood returning from the placenta enters the intra-foetal circulation by the main abdominal vein, the inferior vena cava, either directly or via the liver. The stream of oxygenated blood from the placenta and the deoxygenated blood from the foetal tissues are both delivered into the right atrium. Surprisingly little mixing of blood occurs in the right atrium. The *oxygenated* blood from the placenta tends to enter the left atrium via the foramen ovale and thereafter enters the left ventricle from where it is ejected to supply the foetus (initially the head and upper limbs). The *deoxygenated* blood from the foetus mostly enters the right ventricle. Some of this blood goes to the foetal lungs but most enters the aorta via the ductus arteriosus (the pressure in the pulmonary arteries being slightly higher than in the aorta). Thus the brain gets "better" blood. At or around birth the ductus arteriosus closes, the lungs expand as blood flow through them, extra blood returns to the left atrium whose pressure therefore rises, and the foramen ovale closes (if it does not then an atrial septal defect exists).



The embryological derivation of cutaneous innervation

The cutaneous innervation of the limbs by nerve root values is simple if one considers the embryology and not the traditional anterior and posterior views.



REPRODUCTION

The male and female reproductive systems have striking similarities with the testes and ovaries, penis and clitoris being, embryologically speaking, similar in derivation. The genetic sex is determined by the presence (male) or lack of presence (female) of a Y chromosome,. The testes and ovaries each provide germ cells with 23 chromosomes (haploid) which when combined produce the normal full (diploid) complement of 46 chromosomes.

Ova only carry X chromosomes whereas half the spermatozoa are XY and other half are XX. It is thus the male who decides the sex of offspring (this is not completely true because there are other factors that can influence the differential survival of either of the Y or non-Y spermatozoa).

In single celled organisms each member of a mating pair of cells is mobile whereas in multicellular organisms such as man one (the male germ cell) is intrinsically mobile and the other (the female germ cell) is not.

The female reproductive apparatus

The female reproductive organs comprise the:

- Ovaries
- Fallopian tubes
- The uterus, which is situated in the pelvis with the bladder in front and the rectum behind. It is a hollow organ with a strong thick muscular wall
- The vagina which extends from the labia minora to the uterus
- The vulva. The clitoris is analogous to the penis and also possesses two corpora cavernosa and a single corpus spongiosum

For details of the hormonal aspects of the menstrual cycle read the section dealing with hormones. Usually the ovaries of fertile women produce a single ovum from alternate ovaries at about the midpoint of each menstrual cycle. The start of the menstrual cycle is usually defined as menstruation (day one) with ovulation (release of the ovum from the ovary) at about day 14. The whole cycle usually last 28 days.

The ovaries also produce oestrogen, the hormone responsible for female secondary sexual characteristics:

- Breasts
- Female hair distribution
- Female pattern of fat distribution
- In part, a contribution to female psychology and emotions

The ovum, the largest human cell, which is just visible to the naked eye, develops in an ovarian (Graafian) follicle during the first half of the menstrual cycle under the influence of follicle stimulating hormone from the anterior pituitary. The total number of eggs have been formed in the foetal ovaries by the fifth month of intra-uterine life. The potential embryo enters the Fallopian tube and travels to the uterus where it, under the influence of luteinizing hormone, becomes the corpus luteum. The corpus luteum, under the influence of luteotrophic hormone, then produces progesterone which

discourages further ovulation. Spermatozoa are drawn to the egg by chemical means (chemotaxis). If the ovum is not fertilised the corpus luteum breaks down and is shed into the uterine cavity along with the inner lining of the uterus (endometrium) and a small amount of blood which is passed out via the vagina as the menstrual flow. The cycle then repeats itself. Withdrawal of progesterone after the degeneration of the unfertilised corpus luteum precedes menstruation.

The breasts

Both males and females have breasts but male breast do not develop unless oestogens or oestrogen-like compounds are given or secreted by tumours. The female breasts enlarge during pregnancy to prepare to feed the neonate. Each breast has about 15 milk draining ducts, each of which enters the lactiferous sinus beneath the nipple. During pregnancy the area surrounding the nipple, the areola, darkens in colour.

Lactation

Lactation occurs in association with oxytocin produced by the posterior pituitary and usually takes a few days to become established but, if not stimulated by suckling, milk production soon ceases. The milk produced in the first few days after birth is the colostrums, a thin milk which in particular contains antibodies which confer passive immunity to the baby. During the first few weeks of life babies gain about 20-30 grams daily. Milk provides (in the short term) all dietary requirements. Initiation of lactation, which occurs after progesterone levels have fallen at the end of pregnancy, is mostly an anterior pituitary function mediated by prolactin.

Milk contains all the dietary requirements of the new-born. Human milk contains:

- Protein. Lactalbumin, amino acids and certain plasma proteins
- Carbohydrate (mostly lactose which is made from maternal glucose)
- Fats
- Some drugs that the mother might be taking

Cows milk requires certain additives to make it suitable for human babies.

The male reproductive apparatus

The male organs of reproduction comprise

- Testes, which contain interstitial (Leydig) cells which produce steroid hormones, principally testosterone and tubule (Sertoli) cells which produce spermatozoa
- Epididymis
- Seminal vesicles
- Prostate which contributes a substantial part to the seminal fluid
- Penis

The male testis produces testosterone under the influence of luteinizing hormone from the anterior pituitary. Production of testosterone, which is responsible for male secondary sexual characteristics, commences at puberty and is responsible for:

- Male pattern of hair distribution
- Male pattern of growth and physique
- A low pitched voice

Spermatozoa are produced in the testis and are stored in the epididymis. Initially spermatozoa are non-motile and cilia are used to sweep them towards the epididymis. The spermatozoa then pass along the vas deferens, and pass through the prostate. Both seminal vesicles and the prostate contribute to the seminal fluid. With each ejaculate about 200 million spermatozoa are liberated. The testes are kept outside the body in the scrotum because the lower temperature favours sperm production (their intra-abdominal origins explain why testicular pain has many characteristics usually associated with visceral pain).

In the germ cells of both testes and ovaries the number of chromosomes is 23. There are 22 paired chromosomes which provide 22 similar contributions to the germ cells, the X and Y being the other two chromosomes.

Physiology of sexual intercourse

Penile erection is achieved by sacral parasympathetic activity which causes arteriolar dilatation and contraction of the penile drainage veins so that there is a rigid distension of the tissues. The erect penis can then deposit semen high up in the vagina. From there the spermatozoa swim upwards and one will succeed in fertilising a recently ovulated ovum.

In the male friction between the glans penis and the vagina cause discharge of semen in several jerks (ejaculations) brought about by rhythmical contraction of bulbocarvernosus and ischiocavernosus muscles. Just before ejaculation the internal and external bladder sphincters close. In females similar neuromechanical changes occur. The vulva becomes engorged with blood, the clitoris becomes erect and the vagina moistens.

During intercourse both the sympathetic and parasympathetic nervous systems are activated. The heart rate increases, the stroke volume increases, cardiac output increases, the blood pressure increases, the respiratory rate increases and there may be vasodilatory flushes.

Intercourse is not just a mechanical exercise. Humans, both males and females, unlike many other species, experience a pleasurable sensation called orgasm. However orgasm in the female is not essential for conception to occur. Ejaculation in the male usually coincides with orgasm.

PREGNANCY

Probably most ova are fertilised in the Fallopian tubes and penetration of the ovum by the successful spermatozoa triggers the second meiotic division. If a fertilised ovum embeds in the uterine wall then the corpus luteum does not degenerate but persists and becomes the corpus luteum of pregnancy, progesterone production continues, and menstruation therefore ceases. The corpus luteum involutes just before birth and progesterone levels fall.

Usually only one ovum develops in one ovary at a time to be released into the Fallopian tube of that side for fertilisation. Twins occur in about one in a hundred live births.

Twin (or more) pregnancies occur if more than one ovum is liberated at ovulation (to produce *non-identical* twins which have separate placentas and may be of different sex, or to produce identical twins if a single fertilised ovum splits into two.

The embryo develops two membranes, an outer chorion and an inner amnion. Part of the chorion forms the placenta (= small flat cake) from which chorionic villi invade the wall of the uterus and serve to transmit nutrients and (IgG) antibodies to the foetus. The foetus is connected to the placenta by the umbilical cord.

The placenta forms oestrogen, progesterone and gonadotrophic hormones (detection of chorionic gonadotrophins excreted in the urine form the basis for pregnancy tests).

CHILDBIRTH

Labour commences when intermittent painful contractions of uterine muscle (labour pains) develop in increasing frequency and strength until they occur every two minutes or so. The baby is pushed out through the dilated cervix and down through the vagina. There are multifactorial factors which initiate labour which is substantially outwith conscious control. It is not known how contraction are initiated but they are associated with release of hormones from the foetal adrenals which are associated with bursts of oxytocin from the mother's posterior pituitary. Contractions initially occur about once every 30 minutes and last for about 30 seconds. The frequency and intensity (and associated pain) increases so by delivery contractions have been occurring every two to three minutes and lasting 45-60 seconds. Uterine muscle fibres do not return to their original length after contraction and the upper uterine muscles compact themselves during labour whilst the lower segment muscles become thinner and more stretched

Babies with anencephaly (lacking a brain) are born weeks late, suggesting that something in the normal foetal brain is essential for the timing of onset of labour. This something might be produced because the foetus is under stress as the placenta starts to fail to adequately supply the foetus with certain key nutrients. Other factors may include hormones produced by the placenta itself. Oxytocin production by the posterior pituitary is important.

The foetal circulation prior to birth is that oxygenated blood from the placenta returns to the heart in the umbilical veins and mixes with deoxygenated blood from the embryo in the right atrium, passes via the ostium primum (and later the ostium secundum) into the left atrium. Very little blood can get through the unexpanded foetal lungs (the blood of course would not be oxygenated there even if it could get through) and blood in the pulmonary arteries has to be diverted into the aorta via the ductus arteriosus, a vessel that connects the pulmonary artery to the aorta (see earlier diagram).

At birth major changes have to occur rapidly because oxygenated blood can no longer be provided to the foetus from the placenta via the umbilical veins, but has to be provided by the "instantly inflated lungs" after the first inspirations. All the previous

developments of the heart have been gradual but at birth (the most dangerous journey in the world that any of us makes in terms of risk per distance travelled) two major rapid changes occur. 1) Inflation of the lungs is associated with extra blood flow through the lungs and extra return of blood to the left atrium. The pressure of blood rises in the left atrium (compared with the right atrium) and the foramen ovale is closed as septum I is pressed against septum II. 2) Muscle in the wall of the ductus arteriosus contracts and to close the ductus.

These two changes separate the blood flows of the two sides of the heart, which thereafter function as two separate but closely associated pumps, the *right heart* pumping deoxygenated blood from all veins through the lungs (except the pulmonary veins, which carry oxygenated blood to the *left heart*) for oxygenation whilst the left heart pumps oxygenated blood to the body (including the heart muscle).

Normally periods do not return for three to four months after childbirth, during which time a woman is relatively, but not absolutely, infertile.

Normal labour

Labour is the process by which babies are born and involves the uterus pushing the greatest dimensions of the baby (the head and shoulders) through the female pelvis which, to allow this, is of sightly different shape from the male pelvis.

Regular waves of contraction pass from two areas either side of the body of the uterus. The uterine muscle consists of an outer longitudinal layer and an inner circular layer but most muscle is spiral in orientation. Coordinated contraction narrows and shortens the uterine lumen. The cervix dilates, not because the baby's head dilates it, but rather because the ring of cervical muscle is pulled upwards as part of the uterine shortening..

Labour is divided into three stages.
First stage (onset to full dilatation of the cervix)
As the baby descends through the birth canal the head rotates so that the maximum diameter of the head passes through the widest diameter of the pelvis at each stage of its journey. Usually the skull bones move over one anther slightly at the suture lines to assist passage downwards. The cervix dilates but once it reaches 2 cms in diameter progress becomes more rapid.

Second stage (from full dilatation of the cervix to delivery of the baby)
Normally the baby's occiput is anterior and, as it is pushed downwards the head, which had previously been flexed, is extended as the head is delivered. The baby's shoulders pass through the transverse diameter of the pelvic outlet and, the head rotates through 90 degrees to allow the shoulders to be delivered in the antreoposterior axis of the mother' pelvis. The placenta usually separates from the uterus at the end of the second stage.

Third stage (from delivery of the baby to the delivery of the placenta and the foetal membranes). The uterus is now empty and the uterine muscle contracts to prevent bleeding, especially after the placenta has separated, to expel the placenta.