

Embryology is the study of embryo development. This includes the developmental process of a single-cell embryo to a baby. Embryology usually refers to the prenatal development of a foetus.



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Embryogenesis is the process by which an embryo develops into a foetus. It begins when an ovum and sperm meet and fertilization occurs. The fertilization results in the formation of a zygote. The zygote divides mitotically multiple times without any significant growth and cellular differentiation, leading to the development of an embryo.

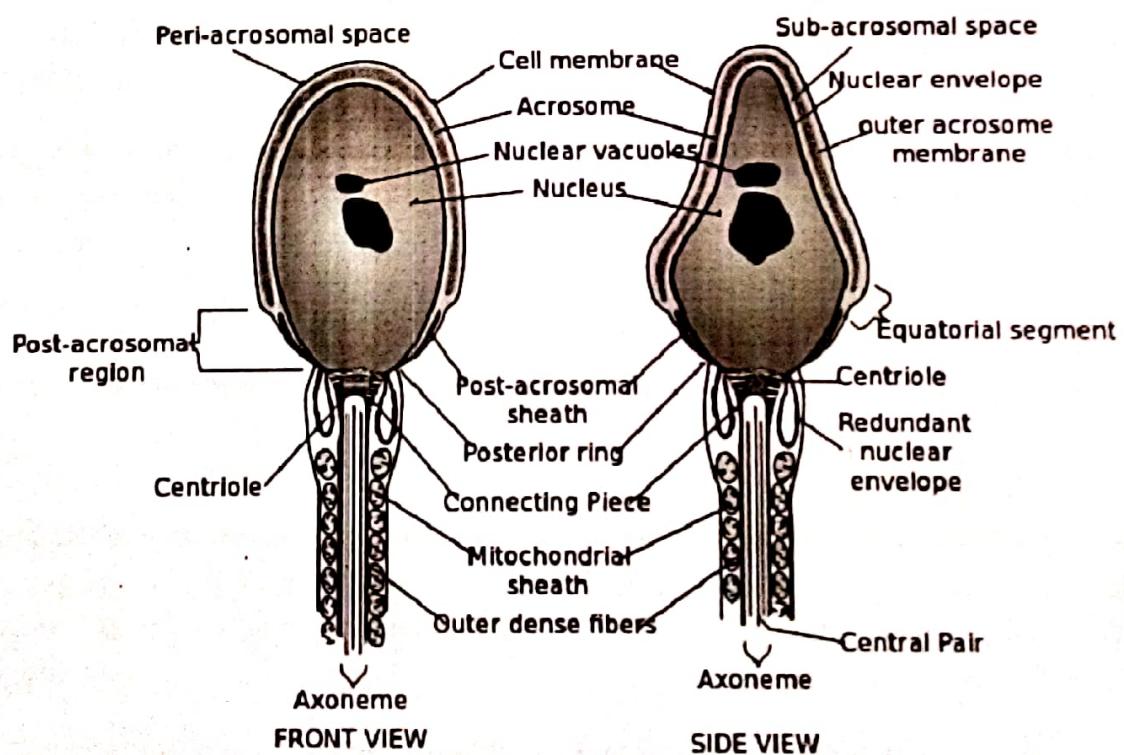
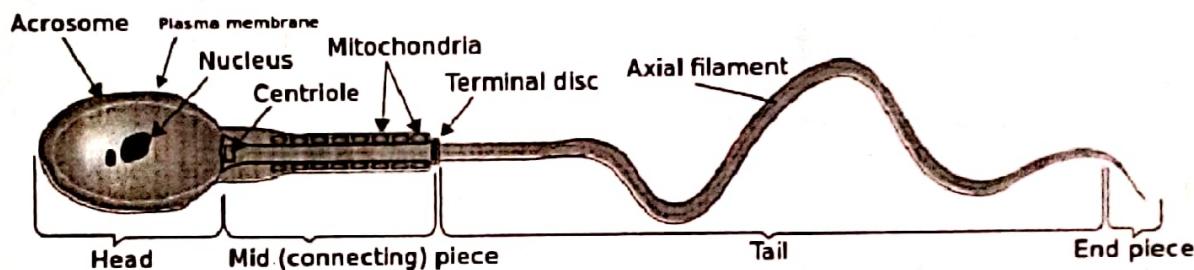
A germ cell is any cell that gives rise to the gametes (Gametes are an organism's reproductive cells, also referred to as sex cells) of an organism that reproduces sexually. Germ cell gives rise to the gametes (Gametes are an organism's reproductive cells, also referred to as sex cells) of an organism that reproduces sexually. The formation of egg cells, or ova, is technically called oogenesis, and the formation of sperm cells, or spermatozoa, is called spermatogenesis.

In many animals, the germ cells originate in the primitive streak and migrate via the gut of an embryo to the developing gonads. There, they undergo meiosis, followed by cellular differentiation into mature gametes, either eggs or sperm.

REPRODUCTIVE CELLS

The Sperm cells

Sperm is the male reproductive cell, or gamete. Animals produce motile sperm with a tail known as a flagellum, which are known as spermatozoa, while some red algae and fungi produce non-motile sperm cells, known as spermatia. Sperm cells form during the process known as spermatogenesis, which in amniotes (reptiles and mammals) takes place in the seminiferous tubules of the testes. This process involves the production of several successive sperm cell precursors, starting with spermatogonia, which differentiate into spermatocytes. The spermatocytes then undergo meiosis, reducing their chromosome number by half, which produces spermatids. The spermatids then mature and, in animals, construct a tail, or flagellum, which gives rise to the mature, motile sperm cell. This whole process occurs constantly and takes around 3 months from start to finish.



Sperm cells cannot divide and have a limited lifespan, but after fusion with egg cells during fertilisation, a new organism begins developing, starting as a totipotent zygote. The human sperm cell is haploid, so

that its 23 chromosomes can join the 23 chromosomes of the female egg to form a diploid cell with 46 paired chromosomes. In mammals, sperm is stored in the epididymis and is released from the penis during ejaculation in a fluid known as semen.

SPERMATOGENESIS

In the beginning:

Males start producing sperm when they reach puberty, which is usually from 10-16 years old. Biological males continually produce sperm in large quantities (~200 million a day). This maximises the likelihood of sperm reaching the egg following ejaculation. Sperm production occurs in the testes of the male, specifically in the seminiferous tubules. In the testicles, a blood-testis barrier forms to keep the tubules separate from the systemic circulation.

Protecting the sperm

Sertoli cells form the blood-testis barrier. This is important in preventing substances found in blood from affecting the developing sperm. These products might include hormones or waste products. It is also important as it prevents the immune system of the male from recognising the sperm as foreign – the sperm are genetically different from the male and will express different surface antigens.

Forming functional sperm

Spermatogonia are the initial pool of diploid cells that divide by mitosis to give two identical cells. One of these cells will be used to replenish the pool of spermatogonia – these cells are A1 spermatogonia. This replenishment of spermatogonia means that males are fertile throughout their adult life. The other cell – type B spermatogonium – will eventually form mature sperm.

Type B spermatogonia replicate by mitosis several times to form identical diploid cells linked by cytoplasm bridges, these cells are now known as primary spermatocytes. Primary spermatocytes then undergo meiosis.

Meiosis I produces two haploid cells, known as secondary spermatocytes.

Meiosis II produces four haploid cells, known as spermatids.

Maturation

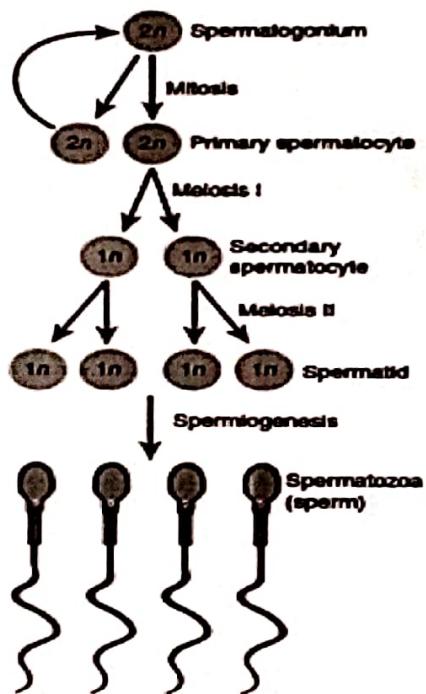
The cytoplasmic bridges break down and the spermatids are released into the lumen of the seminiferous tubule – a process called spermiation. The spermatids undergo spermiogenesis (remodelling and differentiation into mature spermatozoa) as they travel along the seminiferous tubules until they reach the epididymis.

From the seminiferous tubule, cells will travel to the rete testis. This acts to “concentrate” the sperm by removing excess fluid. Then, cells move to the epididymis where the sperm is stored and undergoes the final stages of maturation. Spermatogenesis takes approximately 70 days, therefore in order for sperm

production to be continuous and not intermittent, multiple spermatogenic processes are occurring simultaneously within the same seminiferous tubule, with new groups of spermatogonia arising every 16 days (spermatogenic cycle). Each of these populations of spermatogenic cells will be at different stages of spermatogenesis.

Following ejaculation

Note that once sperm leave the male body and enter the female reproductive tract, the conditions cause the sperm to undergo capacitation. This is the removal of cholesterol and glycoproteins from the head of the sperm cell to allow it to bind to the zona pellucida of the egg cell.



OOGENESIS

The Egg cell

Also called ovum (plural ova), is the female reproductive cell, or gamete. When egg and sperm fuse during fertilisation, a diploid cell (the zygote) is formed, which rapidly grows into a new organism.

Oogenesis differs from spermatogenesis in that it begins in the foetus prior to birth. Primordial germ cells (which originate in the yolk sac of the embryo) move to colonise the cortex of the primordial gonad. Replication by mitosis peaks at approximately 7 million by mid-gestation (~20 weeks).

Cell death occurs after this peak to leave 2 million cells. Meiosis I begins before birth and forms primary oocytes. There is therefore a finite supply of ova.

Primary oocytes are arranged in the gonads as clusters. They have flattened epithelial cells surrounding them, and this is called the primary follicle.

During childhood, further atresia (cell death) occurs, leaving ~40,000 eggs at puberty.

Once puberty begins, a number of primary oocytes (15-20) begin to mature each month, although only one of these reaches full maturation to become an oocyte.

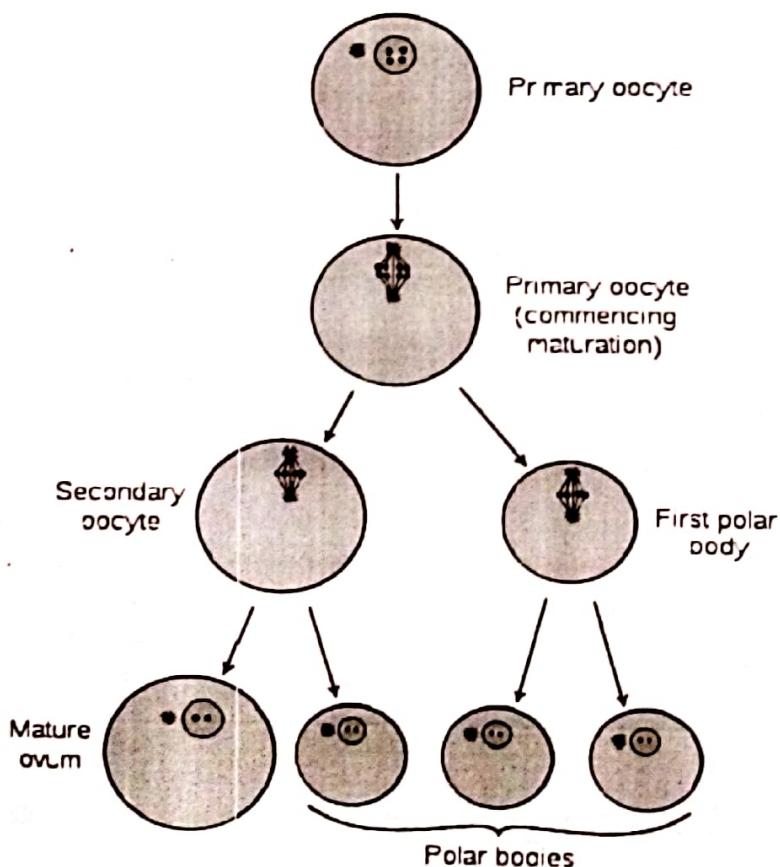
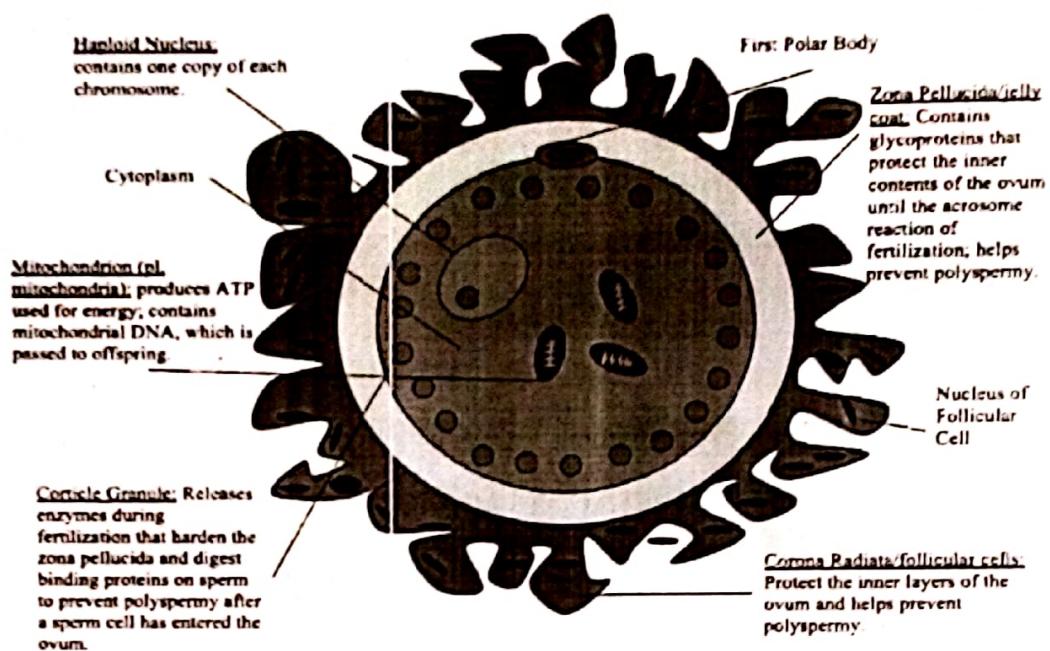


Diagram demonstrating the overall process of oogenesis

The primary oocytes undergo 3 stages:

- Pre-antral
- Antral
- Preovulatory

Pre-Antral Stage

The primary oocyte is still in meiosis I, but will grow dramatically in this stage. The follicular cells grow and proliferate to form a stratified cuboidal epithelium. Now, we call these granulosa cells and they secrete glycoproteins. These chemicals form the zona pellucida around the primary oocyte.

Surrounding connective tissue cells also differentiates to become the theca folliculi, a specialised layer of surrounding cells that is responsive to LH and can secrete androgens under its influence.

Antral Stage

Fluid filled spaces form between granulosa cells, these eventually combine together to form a central fluid filled space called the antrum.

We now call the follicles secondary follicles. In each monthly cycle one of these secondary follicles becomes dominant and develops further under the influence of FSH, LH and oestrogen. (See article on the menstrual cycle).

Pre-Ovulatory Stage

The LH surge induces this stage and meiosis I is now complete. Inside the follicle, 2 unequally sized haploid cells form. One of the daughter cells receives far less cytoplasm than the other and forms the first polar body, which will not go on to form an ovum.

Another haploid cell is also formed, known as the secondary oocyte. Both daughter cells then undergo meiosis II. An initial polar body will replicate to give two polar bodies but the secondary oocyte arrests in metaphase of meiosis II. This happens 3 hours prior to ovulation.

CYCLIC CHANGES IN THE FEMALE GENITAL TRACT

OVULATION

Now, the follicle has grown in size and is mature – it is called a Graafian follicle. An LH surge occurs and increases collagenase activity. This is an enzyme that disrupts collagen. Therefore, there is weakening of the follicular wall. This, combined with muscular contractions of the ovarian wall, results in the ovum being released from the ovary. The ovum is then taken up into the fallopian tube via the fimbriae (finger-like projections of the fallopian tube).

Fertilization – the final stage of female gametogenesis

The secondary oocyte will only complete meiosis II following fertilization. Here, it gives off a third polar body. Following meiosis II, a fertilised egg results. If fertilization doesn't occur, the oocyte degenerates 24 hours after ovulation, remaining arrested in meiosis II. If fertilization does occur, peristaltic

movements of the fallopian tube move the egg to the uterus where it can implant into the posterior uterine wall.

The ovarian cycle refers to the growth and maturation of an oocyte in preparation for fertilization and reproduction. The ovarian cycle repeats every 28 days from puberty until menopause, as long as the female is not pregnant. The ovarian cycle consists of the follicular phase, ovulation, and luteal phase.

The ovarian cycle lasts approximately 28 days and consists of three phases, which include the following:

Follicular phase — days 1 to 14; includes the recruiting and prepping of oocyte follicles for ovulation

Ovulation — on day 14; the release of a mature egg

Luteal phase — days 15 to 28; includes the development of a group of cells called a corpus luteum that produces estrogen and progesterone

MENSTRUAL CYCLE

A menstrual cycle begins when you get your period or menstruate. This is when you shed the lining of your uterus. This cycle is part of your reproductive system and prepares your body for a possible pregnancy. A typical cycle lasts between 24 and 38 days.

Menstruation is the monthly shedding of the lining of your uterus. This is also known by the terms menses, menstrual period, menstrual cycle or period. Menstrual blood — which is partly blood and partly tissue from the inside of your uterus — flows from your uterus through your cervix and out of your body through your vagina. Menstruation is driven by hormones. Hormones are chemical messengers in your body. Your pituitary gland (in your brain) and your ovaries (part of your reproductive system) make and release certain hormones at certain times during your menstrual cycle.

These hormones cause the lining of your uterus to thicken. This happens so that if a pregnancy would occur, an egg can implant into your uterine lining. Hormones also cause your ovaries to release an egg (ovulation). The egg moves down your fallopian tubes, where it waits for sperm. If a sperm doesn't fertilize that egg, pregnancy doesn't occur. The lining of your uterus breaks down and sheds. This is your period. The menstrual cycle is a term to describe the sequence of events that occur in your body as it prepares for the possibility of pregnancy each month. Your menstrual cycle is the time from the first day of your menstrual period until the first day of your next menstrual period. Every person's cycle is slightly different, but the process is the same.

The average length of a menstrual cycle is 28 days. However, a cycle can range in length from 21 days to about 35 days and still be normal. The days between periods is your menstrual cycle length. The average menstrual cycle lasts 28 days. However, cycles lasting as little as 21 days or as long as 35 days can be normal. Most people have their period (bleed) for between three and seven days. The rise and fall of your hormones trigger the steps in your menstrual cycle. Your hormones cause the organs of your reproductive tract to respond in certain ways. The specific events that occur during your menstrual cycle are:

The menses phase: This phase, which typically lasts from day one to day five, is the time when the lining of your uterus sheds through your vagina if pregnancy hasn't occurred. Most people bleed for three to five days, but a period lasting only three days to as many as seven days is usually not a cause for worry.

The follicular phase: This phase typically takes place from days six to 14. During this time, the level of the hormone estrogen rises, which causes the lining of your uterus (the endometrium) to grow and thicken. In addition, another hormone — follicle-stimulating hormone (FSH) — causes follicles in your ovaries to grow. During days 10 to 14, one of the developing follicles will form a fully mature egg (ovum).

The luteal phase: This phase lasts from about day 15 to day 28. Your egg leaves your ovary and begins to travel through your fallopian tubes to your uterus. The level of the hormone progesterone rises to help prepare your uterine lining for pregnancy. If the egg becomes fertilized by sperm and attaches itself to your uterine wall (implantation), you become pregnant. If pregnancy doesn't occur, estrogen and progesterone levels drop and the thick lining of your uterus sheds during your period.

People start menstruating at the average age of 12. However, you can begin menstruating as early as 8 years old or as late as 16 years old. Generally, most people menstruate within a few years of growing breasts and pubic hair. People stop menstruating at menopause, which occurs at about the age of 51. At menopause, you stop producing eggs (stop ovulating). You've reached menopause when you haven't gotten a period in one year.

Some people experience symptoms of menstruation and others don't. The intensity of these symptoms can also vary. The most common symptom is cramps. The cramping you feel in your pelvic area is your uterus contracting to release its lining.

Other signs you're getting your period are:

- Mood changes
- Trouble sleeping
- Headache
- Food cravings
- Bloating
- Breast tenderness
- Acne

Your menstrual cycle can change from your teen years to your 40s or 50s. When you first get your period, it's normal to have longer cycles or a heavier period flow. It can take up to three years for young people to have regular cycles after they begin menstruating. A normal menstrual cycle is a cycle that:

- Occurs roughly every 21 to 35 days
- Causes bleeding for between three and seven days

Once you reach your 20s, your cycles become more consistent and regular. Once your body begins transitioning to menopause, your periods will change again and become more irregular. It's also normal for your period to change during other life events that affect your hormones, such as after childbirth or when you're lactating.

Irregular menstruation describes anything that's not a normal menstrual period. Some examples of an irregular period are:

- Periods that occur less than 21 days or more than 35 days apart
- Not having a period for three months (or 90 days)
- Menstrual flow that's much heavier or lighter than usual

- Period bleeding that lasts longer than seven days
- Periods that are accompanied by severe pain, cramping, nausea or vomiting
- Bleeding or spotting that happens between periods

REPRODUCTIVE SYSTEM IN FAMILY PLANNING

Reproductive health protects infant health by enabling birth spacing and birth limitation to be practiced through family planning.

Reproductive health care is defined as the constellation of methods, techniques and services that contribute to reproductive health and well-being by preventing and solving reproductive health problems. Reproductive health care saves lives and prevents significant levels of morbidity through family planning programmes, antenatal, delivery and post-natal services, prevention and management programmes for reproductive tract infections (including sexually transmitted diseases and HIV/AIDS), prevention of abortion and management of its complications, cancers of the reproductive system, and harmful practices that impact on reproductive function.

Reproductive health care needs are evident at all stages of the life cycle and account for a greater proportion of disability adjusted life years (DALYs) in girls and women than in boys and men. Reproductive health protects infant health by enabling birth spacing and birth limitation to be practiced through family planning. The prevention and early detection of reproductive tract infections, including sexually transmitted diseases and HIV, through the integration of preventive measures in family planning service delivery not only improves the quality of care provided but is also directly responsible for improvement in survival and health of infants.

Addressing harmful practices such as son preference, sex selection, sexual violence and female genital mutilation complements the positive impact of planned and spaced children through family planning services on infant mortality and the reproductive health of young girls and women. They are also in addition to prenatal, delivery and postnatal services, positive determinants of low maternal mortality and morbidity and are integral to the promotion of reproductive health in women of child bearing age. Reproductive tract infections, including sexually transmitted diseases and HIV contribute to significant level of ill-health in women of reproductive age and continue to pose a threat through the menopause which in turn brings with it increasing risk of cancers of the reproductive system.

BARRIER METHODS OF BIRTH CONTROL

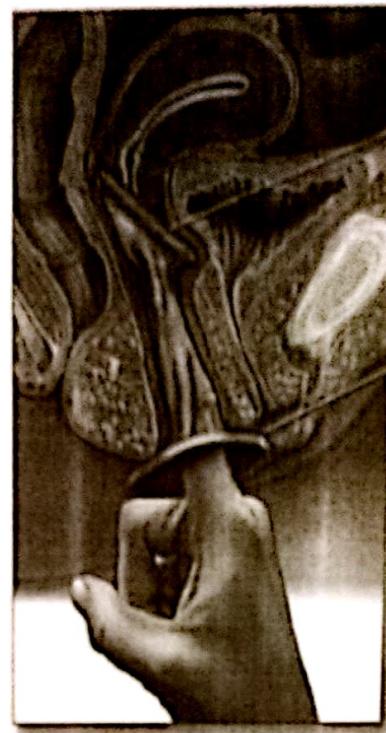
A **condom** is a thin latex or polyurethane sheath. The male condom is placed around the erect penis. The female condom is placed inside the vagina before intercourse.

A condom must be worn at all times during intercourse to prevent pregnancy.

Condoms can be bought in most drug and grocery stores. Some family planning clinics offer free condoms. You do not need a prescription to get condoms.

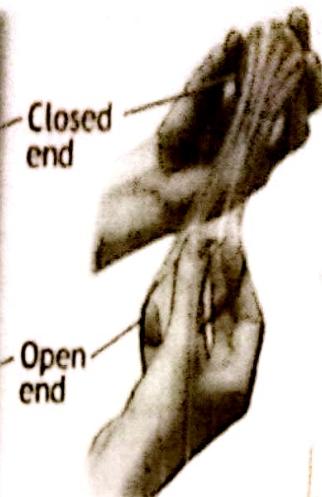


Rolled latex condom



Squeeze tip of condom so no air is trapped inside and continue to hold tip while unrolling condom to base of penis

©ADAM



Female condom

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A diaphragm is a flexible rubber cup that is filled with spermicidal cream or jelly.

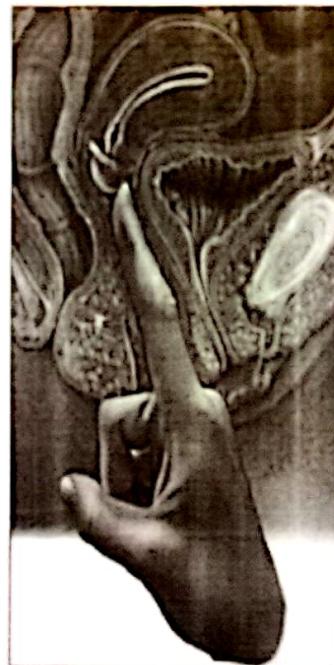
It is placed into the vagina over the cervix before intercourse, to prevent sperm from reaching the uterus.

It should be left in place for 6 to 8 hours after intercourse.



Barrier method:
The diaphragm fits over the cervical opening, preventing sperm from entering the uterus

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Barrier method:
The cervical cap fits snugly over the cervix, preventing sperm from entering the uterus

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Diaphragms must be prescribed by a woman's provider. The provider will determine the correct type and size of diaphragm for the woman.

About 5 to 20 pregnancies occur over 1 year in 100 women using this method, depending on proper use.

A similar, smaller device is called a cervical cap.

Risks include irritation and allergic reactions to the diaphragm or spermicide, and increased frequency of urinary tract infection and vaginal yeast infection. In rare cases, toxic shock syndrome may develop in women who leave the diaphragm in too long. A cervical cap may cause an abnormal Pap test.

Vaginal sponge

Vaginal contraceptive sponges are soft, and contain a chemical that kills or "disables" sperm.

The sponge is moistened and inserted into the vagina, to cover over the cervix before intercourse.

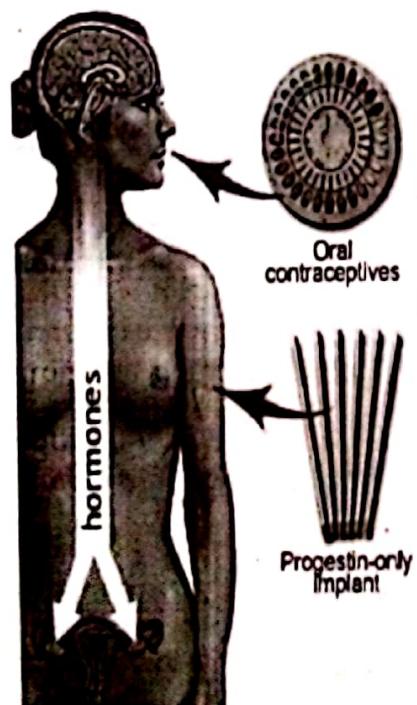
The vaginal sponge can be bought at your pharmacy without a prescription.

Hormonal methods of birth control

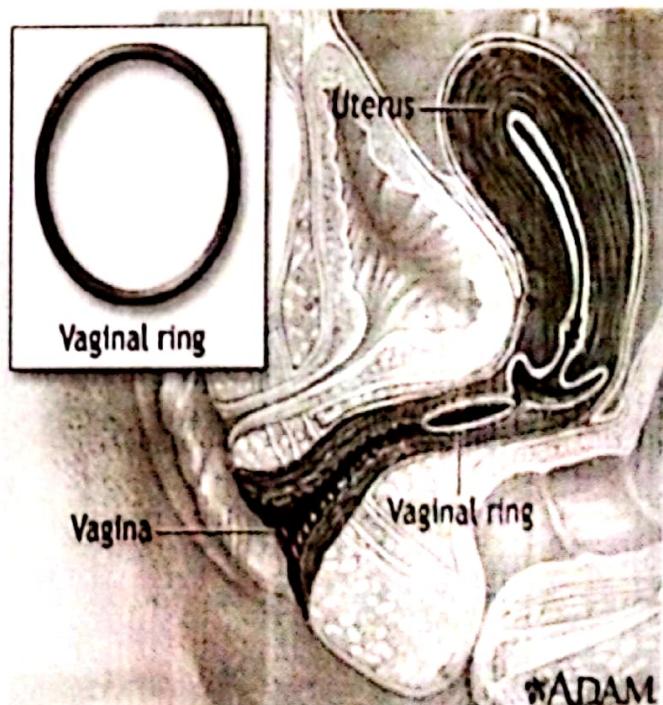
Some birth control methods use hormones. They will have either both an estrogen and a progestin, or a progestin alone. You need a prescription for most hormonal birth control methods.

Both hormones prevent a woman's ovary from releasing an egg during her cycle. They do this by affecting the levels of other hormones the body makes.

Progestins help prevent sperm from making their way to the egg by making mucus around a woman's cervix thick and sticky.



Combined estrogen-progestin birth control pills and progestin-only pills or implants prevent the pituitary gland's release of hormones that stimulate ovulation



Birth control pills: These may contain both estrogen and progestin, or only progestin.

Implants: These are small rods implanted beneath the skin. They release a continuous dose of hormone to prevent ovulation.

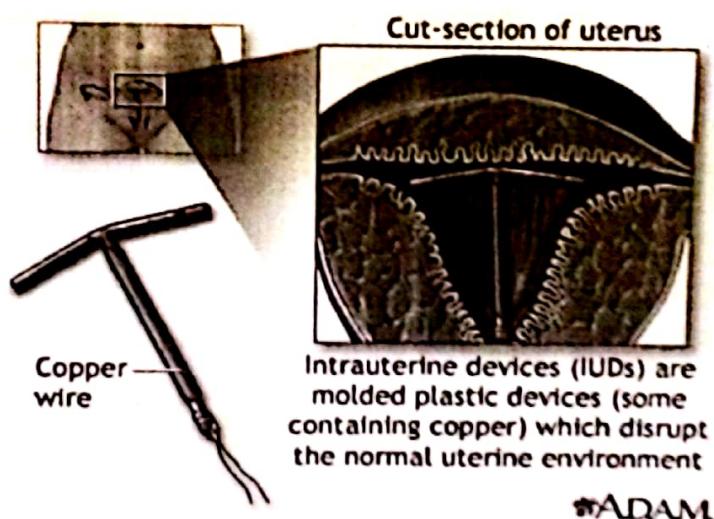
Progestin injections, such as Depo-Provera, that are given into the muscles of the upper arm or buttocks once every 3 months.

The skin patch, such as Ortho Evra, is placed on your shoulder, buttocks, or other place on the body. It releases a continuous dose of hormones.

The vaginal ring, such as NuvaRing, is a flexible ring about 2 inches (5 centimeters) wide. It is placed into the vagina. It releases the hormones progestin and estrogen.

Emergency (or "morning after") contraception: This medicine can be bought without a prescription at your drugstore.

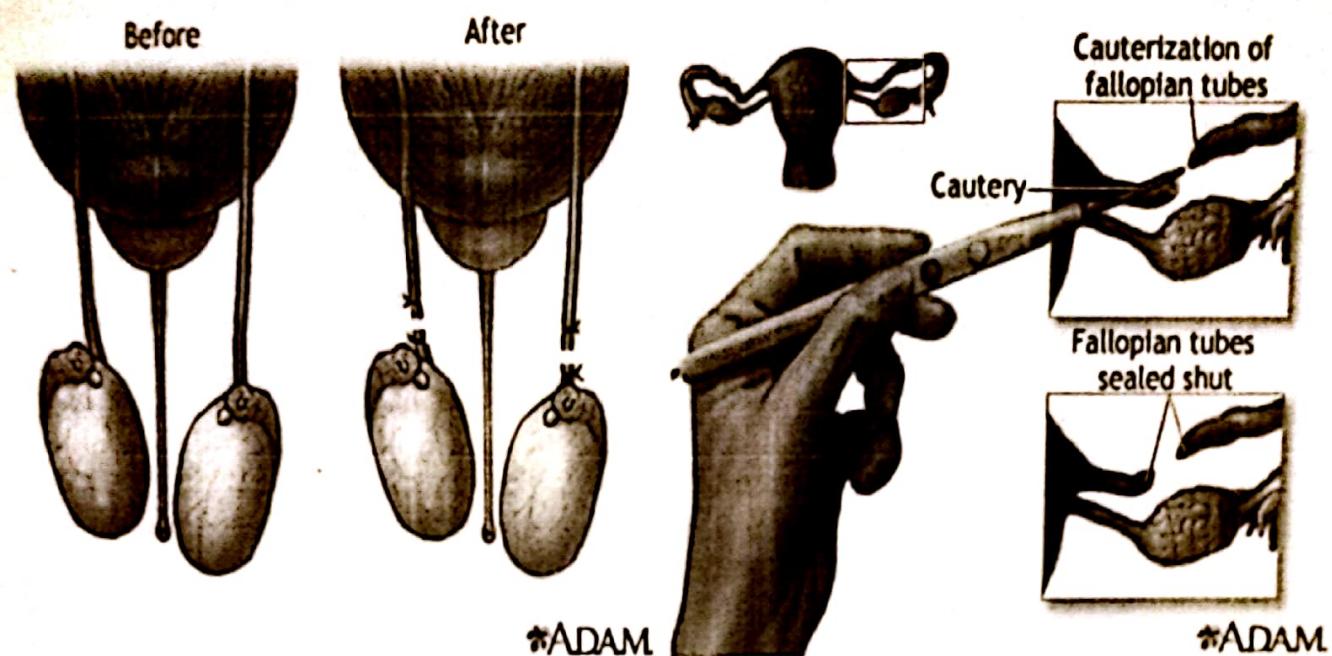
IUD (Intrauterine device):



- The IUD is a small plastic or copper device placed inside the woman's uterus by her provider. Some IUDs release small amounts of progestin. IUDs may be left in place for 3 to 10 years, depending on the device used.
- IUDs can be placed at almost any time.
- IUDs are safe and work well. Fewer than 1 out of 100 women per year will get pregnant using an IUD.
- IUDs that release progestin may be for treating heavy menstrual bleeding and reducing cramps. They may also cause periods to stop completely.

Permanent methods of birth control

These methods are best for men, women, and couples who feel certain they do not want to have children in the future. They include vasectomy and tubal ligation. These procedures can sometimes be reversed if a pregnancy is desired at a later time. However, the success rate for reversal is not high.



Birth control methods that do not work very well

Withdrawal of the penis from the vagina before ejaculation can still result in pregnancy. Some semen often escapes before full withdrawal. It can be enough to cause a pregnancy.

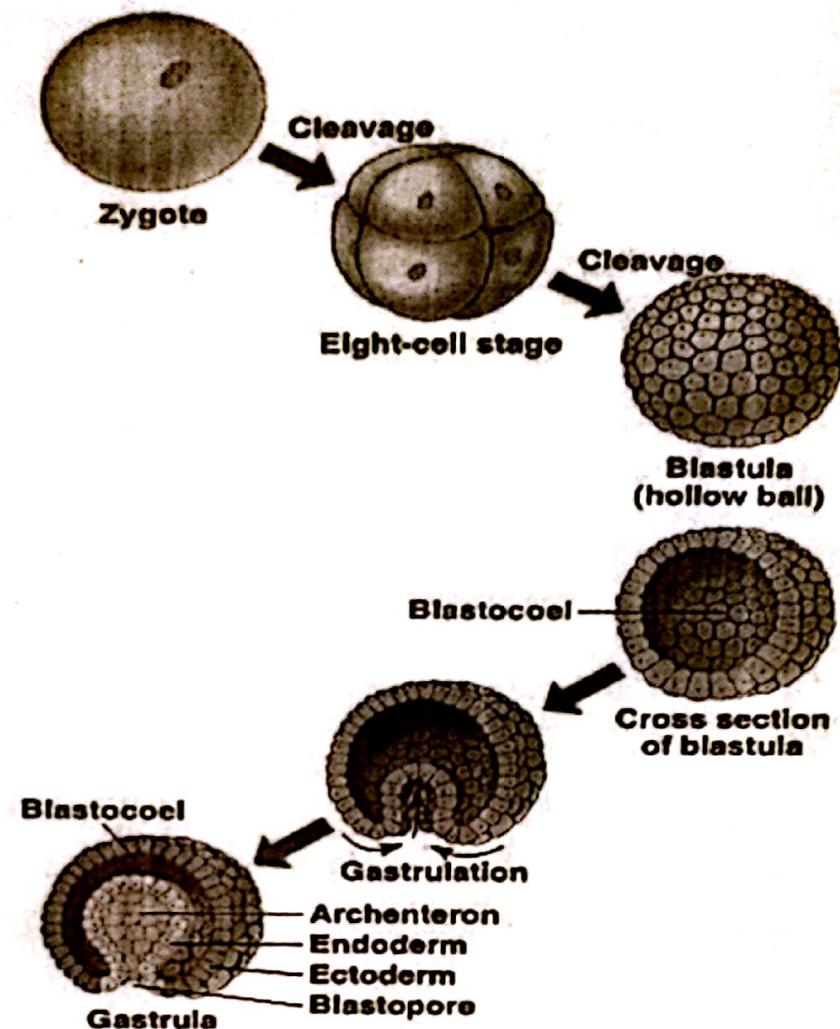
Douching shortly after sex is not likely to work. The sperm can make their way past the cervix within 90 seconds. Douching is never recommended because it can cause infections in the uterus and tubes.

Breastfeeding: Despite the myths, women who are breastfeeding can become pregnant.

Alternative Names

- Contraception
- Family planning and contraception
- Coitus interruptus

GASTRULATION



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The most characteristic event occurring during the third week of gestation is gastrulation.

Gastrulation is a formative process by which the three germ layers, which are precursors of all embryonic tissues, and the axial orientation are established in embryos.

During gastrulation, the bilaminar embryonic disc is converted into a trilaminar embryonic disc. Extensive cell shape changes, rearrangement, movement, and alterations in adhesive properties contribute to the process of gastrulation.

The embryo during this stage is called a gastrula.

Process of Gastrulation

Gastrulation begins with the formation of the primitive streak on the surface of the epiblast. Initially, the streak is vaguely defined, but in a 15- to a 16-day embryo, it is clearly visible as a narrow groove with slightly bulging regions on either side. The cephalic end of the streak, the primitive node, consists of a slightly elevated area surrounding the small primitive pit.

Cells of the epiblast migrate toward the primitive streak. Upon arrival in the region of the streak, they become flask-shaped, detach from the epiblast, and slip beneath it. This inward movement is known as invagination.

Once the cells have invaginated, some displace the hypoblast, creating the embryonic endoderm, and others come to lie between the epiblast and newly created endoderm to form mesoderm. Cells remaining in the epiblast then form ectoderm.

Thus, the epiblast, through the process of gastrulation, is the source of all of the germ layers, and cells in these layers will give rise to all of the tissues and organs in the embryo.

Each of the three germ layers (ectoderm, mesoderm, and endoderm) gives rise to specific tissues and organs:

- Embryonic ectoderm gives rise to the epidermis, central and peripheral nervous systems, eyes and internal ears, neural crest cells, and many connective tissues of the head.
- Embryonic endoderm is the source of the epithelial linings of the respiratory and alimentary (digestive) tracts, including the glands opening into the gastrointestinal tract, and glandular cells of associated organs such as the liver and pancreas.
- Embryonic mesoderm gives rise to all skeletal muscles, blood cells, the lining of blood vessels, all visceral smooth muscular coats, serosal linings of all body cavities, ducts and organs of the reproductive and excretory systems, and most of the cardiovascular system. In the body (trunk or torso), excluding the head and limbs, it is the source of all connective tissues, including cartilage, bones, tendons, ligaments, dermis, and stroma (connective tissue) of internal organs.

Factors controlling the process of Gastrulation

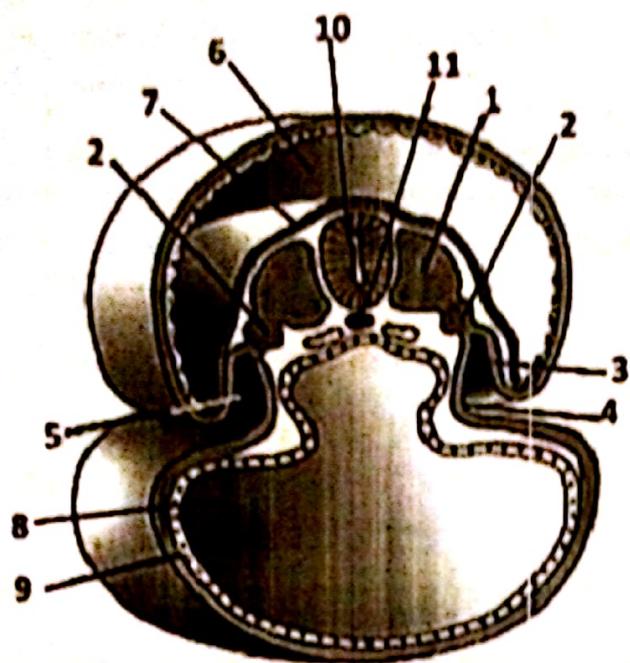
Cell migration and specific cation are controlled by fibroblast growth factor 8 (FGF8), which is synthesized by streak cells themselves. This growth factor controls cell movement by downregulating E-cadherin, a protein that normally binds epiblast cells together. FGF8 then controls cell specification into the mesoderm by regulating Brachyury (T) expression.

Consequences of Gastrulation

Gastrulation results in three important outcomes:

- The formation of the embryonic tissues called germ layers. The germ layers include the endoderm, ectoderm, and mesoderm. Each germ layer will later differentiate into different tissues and organ systems.
- The formation of the embryonic gut or archenteron.
- Gastrulation is the beginning of morphogenesis (development of body form). The appearance of the major body axes.

THE INTRAEMBRYONIC MESODERM



Intraembryonic mesoderm

1. Paraxial mesoderm
2. Intermediate mesoderm
3. Somatic/parietal layer of lateral plate mesoderm
4. Splanchnic/visceral layer of lateral plate mesoderm
5. Intra embryonic coelom
6. Amniotic cavity
7. Ectoderm
8. Yolk sac
9. Endoderm
- 10.Neural tube
- 11.Notochord

As the notochord and neural tube form, the intraembryonic mesoderm on each side forms longitudinal columns, the paraxial mesoderm, each in turn being continuous laterally with the intermediate mesoderm, and the latter gradually thinning out further laterally into the lateral mesoderm

PARAXIAL MESODERM AND SOMITE FORMATION: somite development begins about day 20 and is the result of segmentation of the paraxial mesoderm. The paraxial mesoderm thickens and fragments metamerically, dividing into paired cuboid bodies called somites which give rise to most of the axial skeleton and associated musculature as well as much of the dermis of the skin.

The first pair of somites develops just caudal to the cranial end of the notochord (future occipital area), and subsequent pairs form in a craniocaudal sequence after the appearance of the first somites. About 38 somite pairs form during days 20-30, the so-called somite period. Eventually about 42-44 somite pairs develop by the end of week 5. The somites form distinct surface elevations and are triangular in shape when seen in a transverse section. Each somite develops a slitlike cavity, the myocele, which eventually is occluded

Somites give origin to the sclerotome, whose cells condense around the notochord and give rise to the vertebral primordia and the myotome, which gives rise to the vertebral muscles. The myotome with the somatopleure gives origin to the muscles of the limbs and the anterior lateral body wall

INTERMEDIATE AND LATERAL PLATE MESODERM: Intermediate mesoderm gives rise to the nephrogenic cord from which the excretory apparatus originates. This mesodermal cell aggregation undergoes metamerlic segmentation parallel to the somites and forms nephrotomes. Segmentation, however, is never completed and never reaches the extreme caudal end of the nephrogenic cord

Lateral plate mesoderm splits into 2 layers:

- The intraembryonic splanchnopleure, which gives rise to muscle and connective tissue layers of the trunk, lines the entoderm and continues in the extraembryonic splanchnopleure
- The intraembryonic somatopleure or outer layer which lines the ectoderm and helps form the lateral and ventral trunk walls

The intraembryonic coelom first appears as many small isolated coelomic spaces in the lateral mesoderm and cardiogenic mesoderm (between the 2 layers of the lateral plate mesoderm) which coalesce to form a horseshoe-shaped cavity, the intraembryonic coelom, which is lined by flattened epithelial (mesothelial) cells. It will become the pleuropericardial-peritoneal cavity

THE COELOM DIVIDES the lateral mesoderm into 2 layers:

- A somatic (parietal) layer continuous with the extraembryonic mesoderm over the amnion and a
- A splanchnic (visceral) layer, which is continuous with the extraembryonic mesoderm over the yolk sac

Somatic mesoderm plus overlying embryonic ectoderm forms the body wall or somatopleure

Splanchnic mesoderm plus embryonic entoderm forms the wall of the primitive gut and is called the splanchnopleure

DURING THE SECOND MONTH, the intraembryonic coelom is divided into the body cavities, namely, the pericardial cavity, the pleural cavities, and the peritoneal cavity

DEVELOPMENT OF PLACENTA AND ITS ABNORMALITIES

The placenta is a temporary organ that forms in your uterus during pregnancy. It attaches to your uterine wall and provides nutrients and oxygen to your baby through the umbilical cord. Certain conditions of the placenta can cause pregnancy complications.

The placenta is a temporary organ that connects your baby to your uterus during pregnancy. The placenta develops shortly after conception and attaches to the wall of your uterus. Your baby is connected to the placenta by the umbilical cord. Together, the placenta and umbilical cord act as your baby's lifeline while in the uterus.

Functions of the placenta include:

- Provides your baby with oxygen and nutrients
- Removes harmful waste and carbon dioxide from your baby
- Produces hormones that help your baby grow
- Passes immunity from you to your baby
- Helps protect your baby

The placenta begins to form after a fertilized egg implants in your uterus around seven to 10 days after conception. It continues to grow throughout your pregnancy to support your baby. The placenta starts as a few cells and grows to be several inches long.

The placenta takes over hormone production by the end of the first trimester (12 weeks of pregnancy). Up until this time, the corpus luteum handles most of the hormone production. Many people's first-trimester symptoms of nausea and fatigue go away once the placenta takes over in the second trimester. The placenta appears to move only because the uterus expands as the pregnancy and fetus

grow. Your healthcare provider will look at the location of your placenta during your 20-week anatomy ultrasound and determine if its position may cause complications. Most placentas move to the top or side of the uterus by 32 weeks of pregnancy.

The placenta can form anywhere in your uterus. It develops wherever the fertilized egg implants into your uterine wall. Some of the positions of the placenta are:

- **Posterior placenta:** The placenta grows on the back wall of your uterus
- **Anterior placenta:** The placenta grows on the front wall of your uterus closest to your abdomen
- **Fundal placenta:** The placenta grows at the top of your uterus
- **Lateral placenta:** The placenta grows on the right or left wall of your uterus

The placenta can move up until about 32 weeks of pregnancy. It's common to have a placenta that moves upwards and away from your cervix as your baby gets bigger. It looks like a disc of bumpy tissue rich in blood vessels, making it appear dark red at term. Most of the mature placental tissue is made up of blood vessels. They connect with the baby through the umbilical cord and branch throughout the placenta disc like the limbs of a tree.

The placenta has two sides: the side attached to your uterus and the side closest to your baby.

- The side attached to your uterine wall is a deep reddish blue color
- The side facing your baby is gray

The placenta is about 10 inches long and 1 inch thick at its center. It weighs around 16 ounces (1 pound) by the time your baby is born.

CLINICAL RELEVANCE

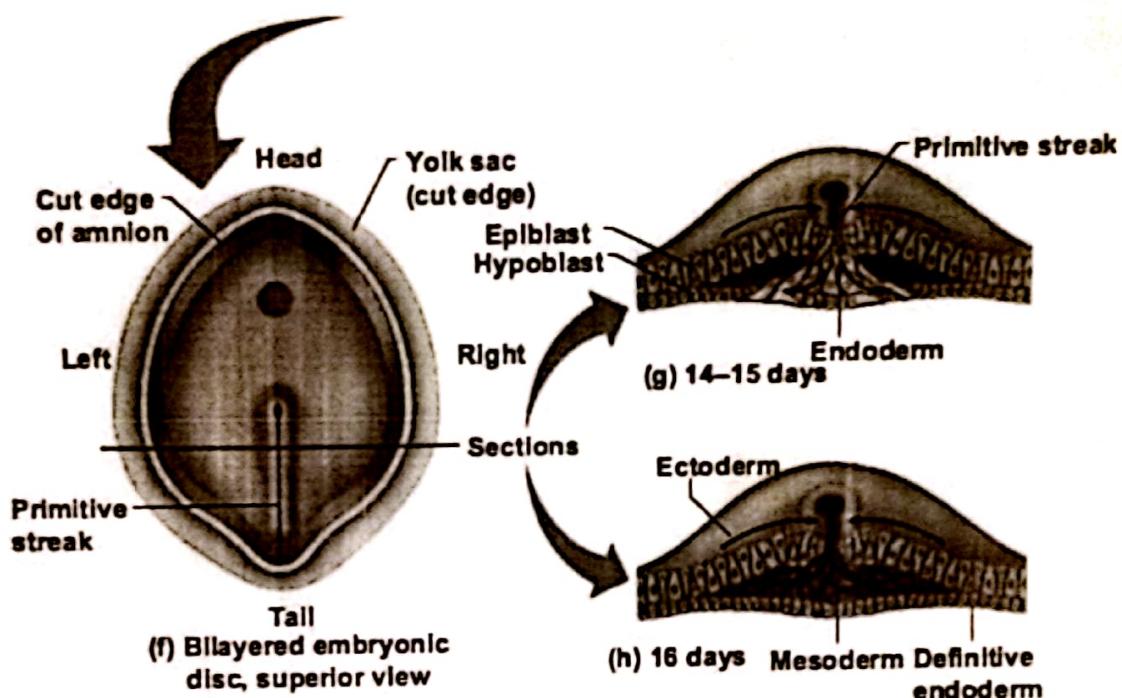
An issue with your placenta can be dangerous for both you and your baby. Some of the complications associated with the placenta are:

- **Placenta previa:** The placenta covers all or part of the cervix. It's sometimes called a low-lying placenta.
- **Placenta accreta:** The placenta attaches too deeply to the wall of your uterus.
- **Placental abruption:** A condition during pregnancy when the placenta separates from the uterus too early.
- **Placental insufficiency:** When the placenta isn't providing enough nutrients or oxygen to your baby.
- **Retained placenta:** When part of the placenta stays inside your uterus after pregnancy.

FURTHER DEVELOPMENT OF EMBRYONIC DISC

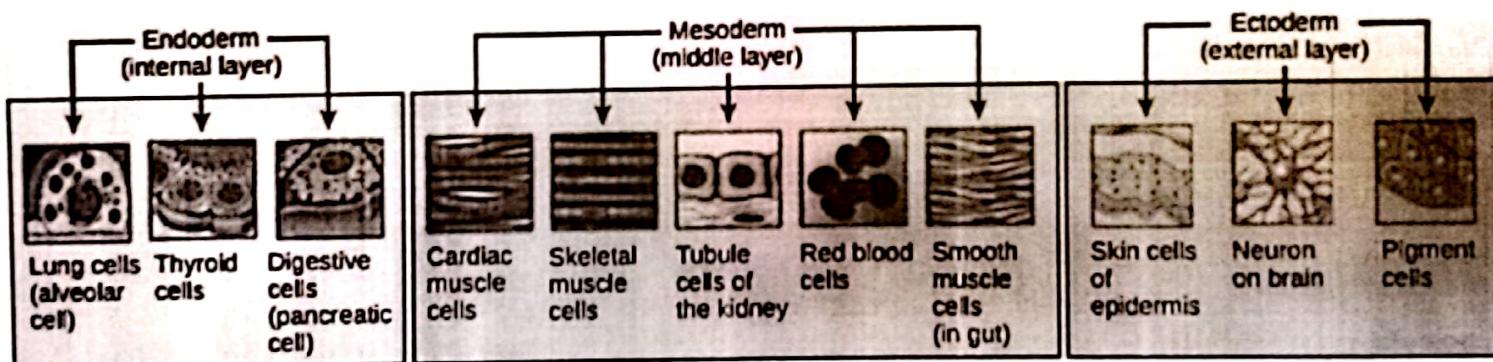
The typical blastula is a ball of cells. The next stage in embryonic development is the formation of the body plan. The cells in the blastula rearrange themselves spatially to form three layers of cells in a process known as gastrulation. During gastrulation, the blastula folds upon itself to form the three layers of cells. Each of these layers is called a germ layer, which differentiate into different organ systems.

Formation of the three primary germ layers



Human Anatomy and Physiology, 7e
by Elaine Marieb & Katja Hoehn

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Differentiation of germ layers: The three germ layers give rise to different cell types in the animal body: the ectoderm forms the nervous system and the outer layer of skin, the mesoderm gives rise to muscles and connective tissues, and the endoderm gives rise to the lining of the digestive system and other internal organs.

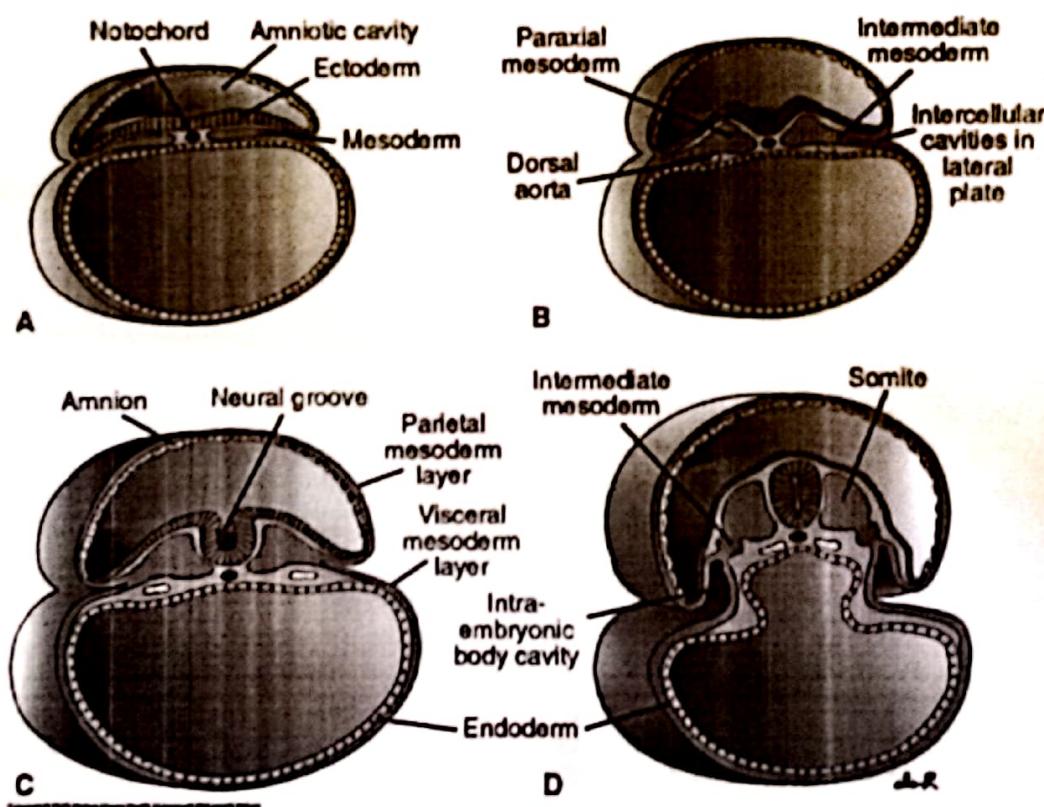
The three germ layers are the endoderm, the ectoderm, and the mesoderm.

- **Embryonic ectoderm** gives rise to the epidermis, central and peripheral nervous systems, eyes and internal ears, neural crest cells, and many connective tissues of the head.

- Embryonic endoderm is the source of the epithelial linings of the respiratory and alimentary (digestive) tracts, including the glands opening into the gastrointestinal tract, and glandular cells of associated organs such as the liver and pancreas.
- Embryonic mesoderm gives rise to all skeletal muscles, blood cells, the lining of blood vessels, all visceral smooth muscular coats, serosal linings of all body cavities, ducts and organs of the reproductive and excretory systems, and most of the cardiovascular system. In the body (trunk or torso), excluding the head and limbs, it is the source of all connective tissues, including cartilage, bones, tendons, ligaments, dermis, and stroma (connective tissue) of internal organs.

EMBRYONIC FOLDING

The flat trilaminar embryonic disk becomes a more cylindric embryo due to the longitudinal and transverse folding that occurs as a result of embryonic growth, especially of the neural tube. The foldings occur simultaneously and are not separate sequential events. Flexion, a process of curving, transforms the embryo into a sort of "tube" and isolates it from the embryonic membranes, to which it is eventually attached only by a thin stalk, the umbilical cord. The embryo increases rapidly in its long axis due to central growth being greater than peripheral growth, and the dorsal region of the embryo grows more rapidly than its ventral region, resulting in the embryo curving itself around the umbilical region. The dorsal region also thickens, especially in the midline, and the edges of the disk swing ventrally carrying the amnion with them. Thus, the embryo is surrounded by its amniotic cavity.



LONGITUDINAL FOLDING produces both head- and tailfolds, or flexion, and creates a cranial and caudal region to the embryo

Head fold: Neural folds (end of week 3) begin to develop into the brain and project dorsally into the amniotic cavity.

- ❖ The forebrain grows cranially beyond the oropharyngeal membrane and overhangs the primitive coelom. At the same time, the septum transversum (a mass of mesoderm cranial to the pericardial coelom), the heart, the pericardial coelom, and the oropharyngeal membrane turn under onto the ventral surface
 - During folding, part of the yolk sac is incorporated as the foregut (between brain and heart, ending blindly at the oropharyngeal membrane). The membrane separates the foregut from the stomodeum or primitive mouth cavity.
- ❖ After folding, the septum transversum lies caudal to the heart and develops into a major portion of the diaphragm.
- ❖ Before folding, the intraembryonic coelom is a flattened horseshoe-shaped cavity. After folding, the pericardial coelom lies ventrally and the pericardioperitoneal canals run dorsally over the septum transversum to join the peritoneal coelom which, on each side, communicates with the extraembryonic coelom

The tailfold (caudal end): takes place later than the headfold and results from the dorsal and caudal growth of the neural tube.

- ❖ As the embryo grows, the tail region projects over the cloacal membrane which eventually comes to lie ventrally
- ❖ During folding, part of the yolk sac is incorporated into the embryo as the hindgut, the terminal portion of which soon dilates and forms the cloaca, separated from the amniotic cavity by the cloacal membrane.
- ❖ Before folding, the primitive streak lies cranial to the cloacal membrane, but, after folding, lies caudal to it.
- ❖ The connecting stalk now attaches to the ventral embryonic surface, and the allantois is partly incorporated into the embryo

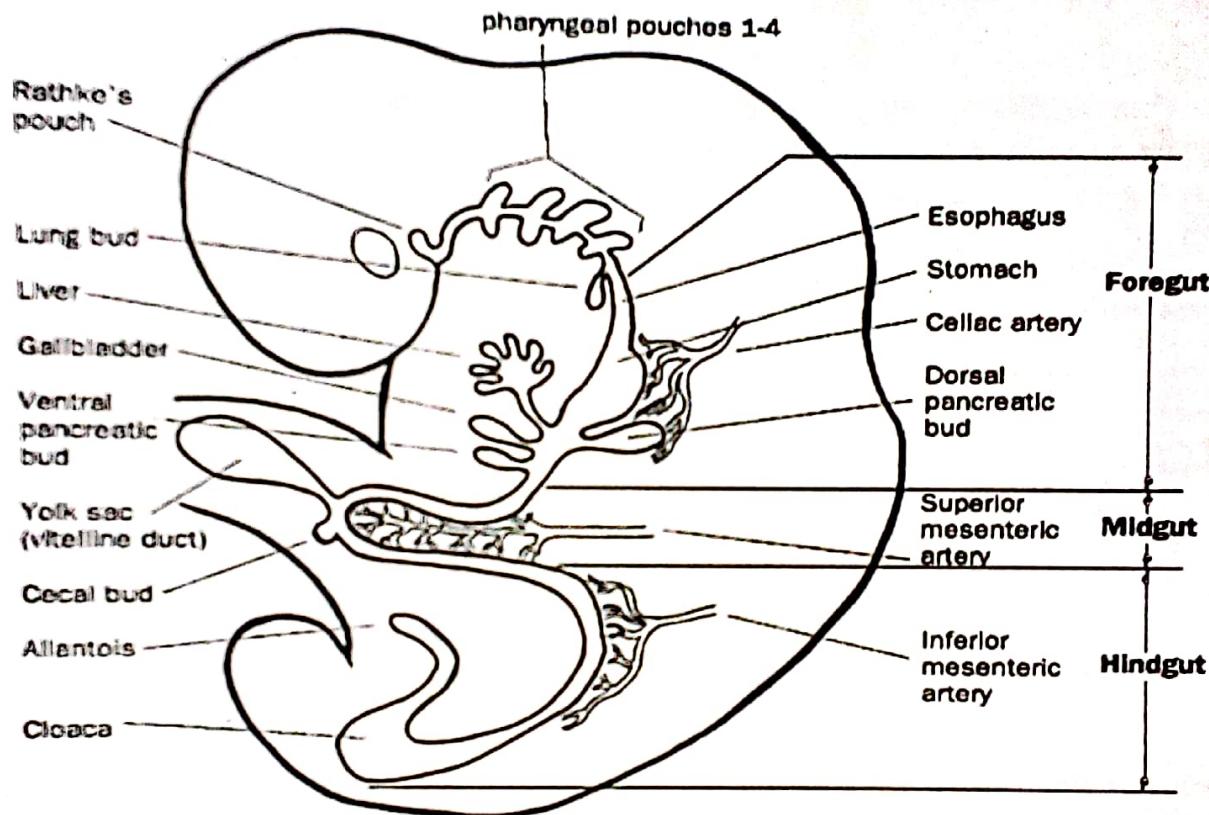
TRANSVERSE FOLDING (FLEXION) produces right and left lateral folds

- ❖ Each lateral body wall (somatopleure) folds toward the midline, rolling the edges of the embryonic disk ventrally to form a cylindric embryo.
- ❖ As lateral and ventral body walls form, part of the yolk sac is incorporated into the embryo as the midgut; simultaneously, the connection of the midgut with the yolk sac is reduced to a yolk stalk or vitelline duct.
- ❖ After folding, the area of the amnion attachment to the embryo is reduced to a narrow umbilicus on its ventral surface.
- ❖ As the midgut is separated from the yolk sac, it attaches to the dorsal abdominal wall via a thin dorsal mesentery
- ❖ As the umbilical cord forms, the ventral fusion of the lateral folds reduces the area of communication between the intra- and extraembryonic coelom.
- ❖ As the amniotic cavity enlarges and obliterates the extraembryonic coelom, the amnion forms an outer covering for the umbilical cord

EMBRYOLOGY OF GASTROINTESTINAL TRACT (GIT)

Germ layers, formed during gastrulation, are present by two weeks and include endoderm, mesoderm and ectoderm. In humans, the germ tissues are the basis of all tissues and organs.

- Endoderm - Epithelial lining and glands
- Mesoderm - Lamina propria, muscularis mucosae, submucosa
- muscularis externa and serosa
- Ectoderm - Enteric nervous system and posterior luminal digestive structures

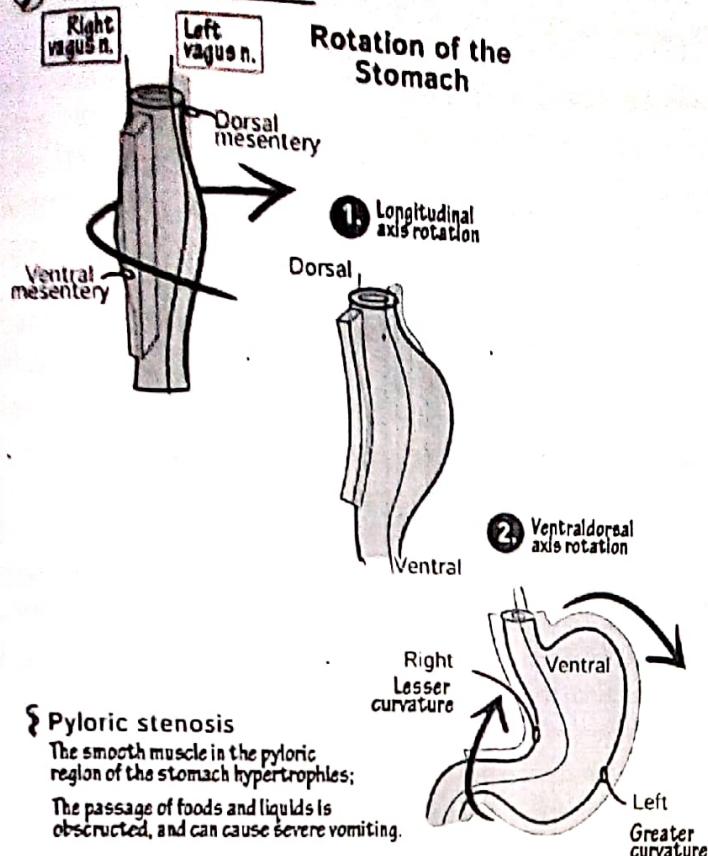


The Primitive gut tube develops during week 3-4 by incorporating the yolk sac during craniocaudal and lateral folding of the embryo. The tube is divided into 3 distinct sections; foregut, midgut and hindgut.

- Foregut gives rise to the esophagus, stomach, liver, gallbladder, bile ducts, pancreas and proximal duodenum.
- The midgut develops into the distal duodenum, jejunum, ileum, cecum, appendix, ascending colon, and proximal 2/3 of transverse colon.
- The hindgut becomes the distal 1/3 of the transverse colon, descending colon, sigmoid colon and the upper anal canal. Proliferation of the epithelial lining of the gut tube results in obliteration of the lumen by week 6.

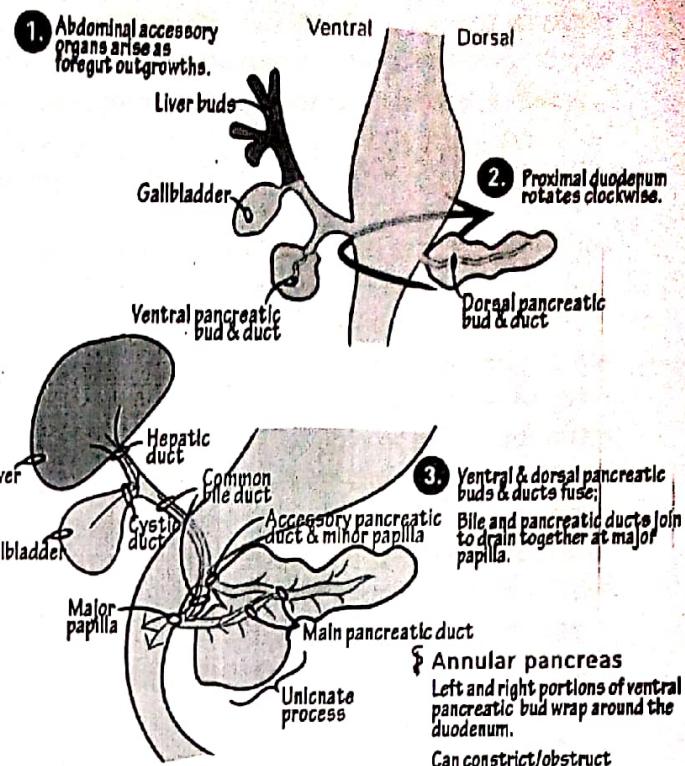
The central cells then degenerate and the tube is recanalized by week 8. Abnormalities in this process result in: stenosis, atresia, and duplications.

FOREGUT ROTATION



Rotation of the Stomach

Rotation of the Biliary & Pancreatic ducts



Foregut Formation

The foregut gives rise to the esophagus, stomach, liver, gallbladder, pancreas and the caudal portion of the duodenum.

Lateral grooves invaginate during week 4 on each side of the proximal foregut and fuse creating the tracheoesophageal septum. The septum separates the respiratory and digestive tracts with the ventral portion developing into respiratory system and dorsal into gastrointestinal tract. By week 16 the esophagus has stratified squamous epithelium and swallow can appreciated.

Failure of the tracheoesophageal septum development results in tracheoesophageal fistula and/or esophageal atresia.

The stomach develops from a fusiform dilation in the foregut during week 4. A 90 degree clockwise rotation creates the lesser peritoneal sac.

The liver develops from an endodermal outgrowth, hepatic diverticulum, at the cranoventral portion of the foregut. Mesoderm surrounds the diverticulum, septum transversum. Hepatic cells (hepatoblasts), both hematopoietic and endothelial precursor cells, then migrate into the septum transversum. The endothelial precursor cells, vitelline veins, are surrounded by hepatic cells forming the hepatic sinusoids. Bi-potential hepatoblasts give rise to both cholangiocytes and hepatocytes. The hepatoblasts in mesenchyme closest to the portal vein form a bi-layered structure, the ductal plate. These cells remodel to form bile ducts in the intrahepatic portal tracts. Abnormal development of intrahepatic bile ducts due

to ductal plate malformations are likely the underlying cause of congenital hepatic fibrosis and cystic kidney disease as well as ciliopathies such as Joubert syndrome, Meckel-Gruber and Ivemark syndrome.

Gallbladder and bile ducts begin as a cystic diverticulum. The gallbladder is initially solid and become cystic. Intrahepatic bile duct development starts at the hilum and progresses to the periphery of the liver. The common bile duct forms in an area of narrowing between the foregut and the hepatic diverticulum. At birth the most peripheral intrahepatic bile ducts are immature with persistence of ductal plate. Maturity of intrahepatic biliary tree is achieved by 4 weeks of life.

Pancreas development begins during the 4th-5th weeks of gestation as distinct dorsal and ventral buds arising from the endoderm of the caudal foregut, the proximal duodenum. The dorsal bud is larger than and slightly more cranial to the ventral bud. Each bud communicates with the foregut through a duct. Rotation of the duodenum causes the ventral pancreatic bud to rotate clockwise to the left of the duodenum and brings it posterior and inferior to the dorsal pancreatic bud. The two buds fuse to form the pancreas during the 7th week of gestation. The ventral bud forms the inferior part of the head of the pancreas and the uncinate process and the dorsal bud forms the superior part of the head, the body, and the tail of the pancreas. The ductal systems of the two buds fuse in the 8th week. The main pancreatic duct (duct of Wirsung) which enters the duodenum at the major duodenal papilla (ampulla of Vater) is formed by the longer dorsal duct draining into the proximal ventral duct to form. If the proximal portion of the dorsal duct remains, it forms an accessory duct (duct of Santorini) that opens into a minor accessory papilla located about 2 cm above the main duct. The accessory duct opens into a minor papilla in 33% of people and ends blindly in 8% of people. Fifty percent of people do not have an accessory duct. Endocrine cells (islets) are identifiable by the 8th week. Exocrine pancreatic development continues after birth with maturation of specific digestive enzymes.

Abnormal development of the pancreas results in several congenital anomalies to include pancreas divisum. This is the most common variant (10%) and results from non-fusion of dorsal and ventral ducts during the second month of gestation. Annular pancreas is another congenital anomaly. A band of pancreatic tissue encircles the duodenum and is typically associated with other anomalies to include Down's syndrome and duodenal atresia.

Midgut Formation

The distal duodenum, jejunum, ileum, cecum, appendix, ascending colon, and proximal 2/3 of transverse colon develop from the midgut, between the 6 and 10th weeks. The midgut loop herniates through the primitive umbilical ring during umbilical herniation at week 6. By ten weeks of development the abdomen has enlarged so that the entire length of the midgut can be accommodated. Following a 270 degree counterclockwise rotation around the superior mesenteric artery, the bowel returns to the abdominal cavity. The large intestine returns following the small intestine and does an additional 180 degree counterclockwise rotation. Colonic fixation occurs after the return to the abdomen. Cecum and appendix begin as a diverticulum around the 6th week. Unequal cecal growth leaves appendix medial to the cecum.

Clinical correlations include omphalocele which results from failure of the midgut loop to return to the abdomen. Some or all of the abdominal contents remain outside the abdominal wall covered with an outer amniotic and inner peritoneal sac. Meckel's diverticulum is a persistent remnant of vitelline duct, forming a blind pouch on the antimesenteric border of the ileum. The diverticula often contain ectopic gastric, pancreatic, thyroid or endometrial tissue. Malrotation occurs if the midgut undergoes only partial rotation. Incidence is about 1 in 500 live births and has been identified in 0.5% of autopsies.

Hindgut Formation

The distal 1/3 of the transverse colon, descending colon, sigmoid colon develop from the cranial end of the hindgut. The upper anal canal also develops from the terminal end of the hindgut with the urorectal septum dividing the upper anal canal and the urogenital sinus during the 6th week. By the 7th week, the urorectal septum fuses with the cloacal membrane, giving rise to the anal membrane and the urogenital membrane. The anal membrane ruptures during the 8th week allowing communication between the anal canal and the amniotic fluid. The superior 2/3 of the anal canal originates from hindgut and the inferior 1/3 is derived from proctodeum. The pectinate line is the junction of proctodeum ectoderm and hindgut endoderm.

Clinical correlation includes persistent cloaca resulting in fusion of rectum, vagina and urinary tract. The mesentery develops from the mesoderm and connects the primitive gut to the body wall. The ventral mesentery is present only between the liver and the stomach, and the liver and the duodenum. It forms the lesser omentum, between the liver and the stomach and duodenum, and the falciform ligament between the liver and the anterior body wall. The dorsal mesentery surrounds the rest of the primitive gut. It forms several organ ligaments and also becomes the greater omentum. Finally, the mesentery of the colon develops into the transverse mesocolon. During development some structures come to lie close to the posterior body wall and as the mesentery is absorbed the organ takes on a retroperitoneal position. Retroperitoneal organs include portion of the duodenum, the pancreas, the ascending and the descending colon.

Blood Supply

- Appropriate blood supply to the gastrointestinal tract and enteric organs is vital to health.
- Proximal Esophagus - Inferior Thyroid Artery
- Thoracic Esophagus - Terminal bronchial arteries
- Distal Esophagus - Left gastric and left phrenic arteries
- Stomach - Celiac artery
- Small intestine - Superior mesenteric artery
- Large intestine - Superior and Inferior mesenteric arteries

DEVELOPMENT OF GLANDS ASSOCIATED WITH GASTROINTESTINAL TRACT (GIT)

Glands contributing digestive juices include the salivary glands, the gastric glands in the stomach lining, the pancreas, and the liver and its adjuncts—the gallbladder and bile ducts. All of these organs and glands contribute to the physical and chemical breaking down of ingested food and to the eventual elimination of nondigestible wastes.

1. Salivary Gland:

Saliva, or salivary amylase, is a viscous, colourless, and opalescent liquid secreted by these glands.

It is released in minute amounts all over the buccal cavity to keep it wet.

Saliva is in charge of breaking down starch into maltose.

Saliva also has the following functions: It keeps the mouth and teeth in good shape, enhances the flavour of the food, acts as a solvent, increases the sensation of taste, acts as a lubricant, moistens the dry food, and makes swallowing easier.

2. Stomach:

Simple or branching tubular glands make up gastric glands.

In adults, these gastric glands release about 2-3 litres of gastric juice every day, and the secretion is regulated by both the neurological and hormonal systems.

Various gastric glands can be found on the stomach's wall. In the stomach mucosa, there are three main types of gastric glands.

Parietal cells—supply the stomach juice with hydrochloric acid. By providing H⁺, which activates pepsinogen, the precursor of pepsin, hydrochloric acid aids in the breakdown of proteins.

Chief cells in the body's gastric glands and the stomach's antrum secrete pepsinogen. Pepsin breaks down proteins into smaller pieces known as peptides or amino acids so they can finally be absorbed in the small intestine.

Mucin is secreted by mucous cells.

3. Liver:

The liver is the largest gland in the human body, weighing around 1.6 kg and placed on the right side of the upper abdominal cavity slightly beyond the diaphragm.

The liver is divided into two lobes: a bigger right lobe and a smaller left lobe with two smaller lobes. Behind the primary lobes are the quadrate lobe and the caudate lobe.

A pear-shaped structure called a gallbladder is found beneath the right lobe. The gallbladder acts as a reservoir for the bile juice generated by the liver.

The liver serves various important tasks in the human digestive system, including the liver, which is also in charge of lipogenesis. The liver is in charge of controlling blood sugar levels.

Bile is secreted by the liver and is responsible for emulsification. In the presence of the enzyme carotenes, the liver synthesizes vitamin A from beta carotene.

4. Pancreas:

The pancreas is a yellowish, elongated gland that lies horizontally in the duodenum's curvature behind the stomach.

The pancreas has both exocrine and endocrine functions. It consists of multiple branching tubules embedded in connective tissue containing blood and lymph arteries, nerves, and pancreatic ductules in exocrine tissue termed acini.

An alkaline pancreatic fluid secreted by the acinus assists in the digestion of carbohydrates, proteins, lipids, and nucleic acids.

The pancreas is responsible for two major functions: the pancreas is primarily involved in digestion in the human digestive system, the manufacture of hormones
Intestinal glands secrete pancreatic juice, which contains digestive enzymes.

In the mucosa of the small intestine, there are countless tiny glands. There are two kinds of them:
Lieberkuhn's Crypts release digestive enzymes and mucus.

These digestive fluids contain a variety of enzymes and are involved in the digestion of a wide range of foods.

ANOMALIES OF GIT

- Congenital atresias and stenoses of the digestive tract include:
- Esophageal atresia
- Congenital hypertrophic pyloric stenosis (pylorostenosis congenita)
- Atresia and stenosis of the small intestine
- Anal and rectal atresia
- Other congenital causes of intestinal obstruction include:
- Superior mesenteric artery syndrome
- Malrotation of the intestine and volvulus
- Meconium ileus
- Megacolon congenitum

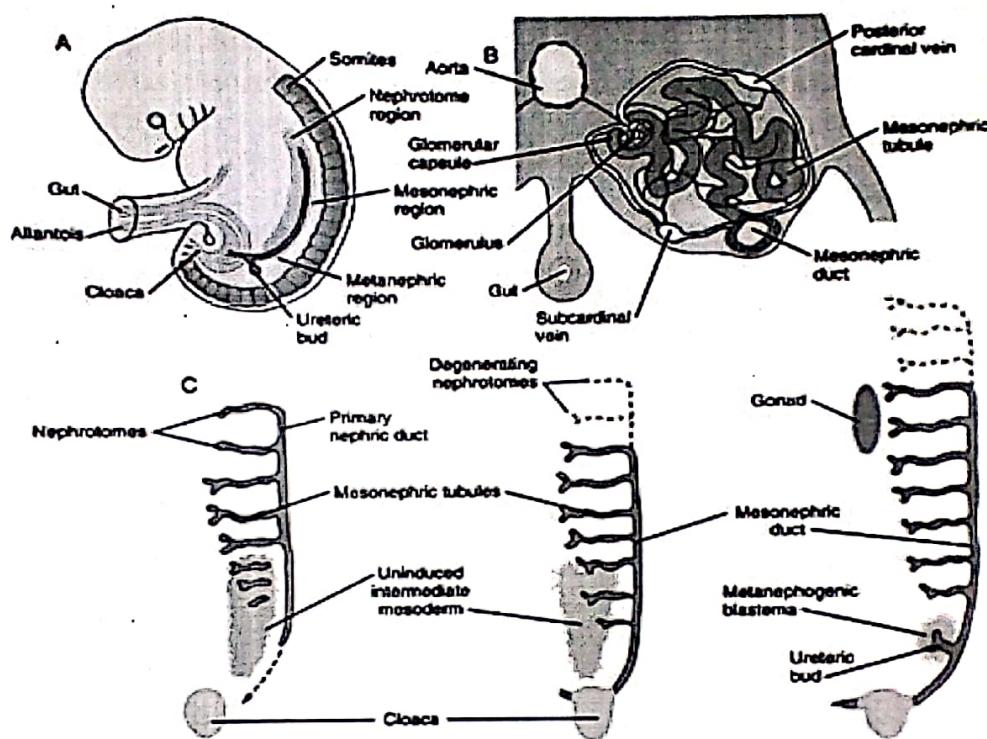
SUMMARY OF EVENTS

- Week 1-2 - Germ Layers develop
- Week 3-4 – Primitive gut tube forms
- Week 4 – Foregut organs begin to form
- Week 5 – Neural crest cells start migration to form ENS
- Week 6 – Midgut herniation
 - Week 7 – Urorectal septum begins to form
 - Week 7-8 - Primitive gut has re-canalized
 - Week 12-14- Appearance of primitive crypts
 - Week 13- Completed development of both circular and longitudinal muscle layers
 - Week 16- Epithelium develops along with muscularis mucosa
 - Week 16 – Esophageal swallowing can be appreciated
 - Week 20- Presence of well developed villi and crypts, along with lamina propria and specialized connective tissue

EMBRYOLOGY OF UROGENITAL SYSTEM

The urogenital system arises from intermediate mesoderm which forms a urogenital ridge on either side of the aorta. The urogenital ridge develops into three sets of tubular nephric structures (from head to tail):

- The pronephros
- The mesonephros
- The metanephros



The Pronephros

- Is the cranialmost set of tubes, which mostly regress

The mesonephros

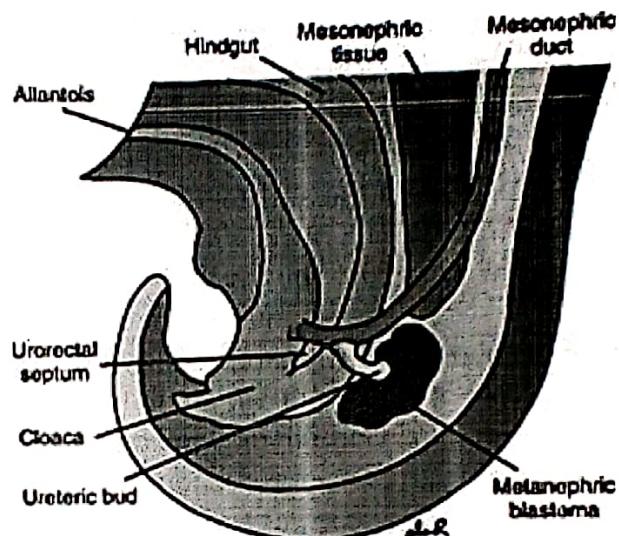
- Is located along the midsection of the embryo and develops into **mesonephric tubules** and the **mesonephric duct** (Wolffian duct).
- These tubules carry out some kidney function at first, but then many of the tubules regress. However, the **mesonephric duct persists and opens to the cloaca at the tail of the embryo**.

The metanephros

- Gives rise to the definitive adult kidney.
- Develops from an outgrowth of the caudal mesonephric duct, the **ureteric bud**, and from a condensation of nearby renogenic intermediate mesoderm, the **metanephric blastema**.

Steps in Renogenesis

- Involves a process of reciprocal induction, which is retinoic acid dependent
- Cranial-caudal patterning establishes a “renogenic” region within the intermediate mesoderm in the tail of the embryo –this renogenic mesoderm is the METANEPHRIC BLASTEMA
- The METANEPHRIC BLASTEMA secretes growth factors that induce growth of the URETERIC BUD from the caudal portion of the mesonephric duct.
- The URETERIC BUD proliferates and responds by secreting growth factors that stimulates proliferation and then differentiation of the metanephric blastema into glomeruli and kidney tubules (i.e. induces the blastema to undergo mesenchymal-to-epithelial transition).
- Perturbations in any aspect of these inductive events (e.g. mutations of either metanephric or ureteric factors or disruption of retinoic acid signaling) may cause inhibition of ureteric bud growth and renal hypoplasia or agenesis. Conversely, duplication or over-proliferation of structures can occur if there is a gain of function of the inductive factors.



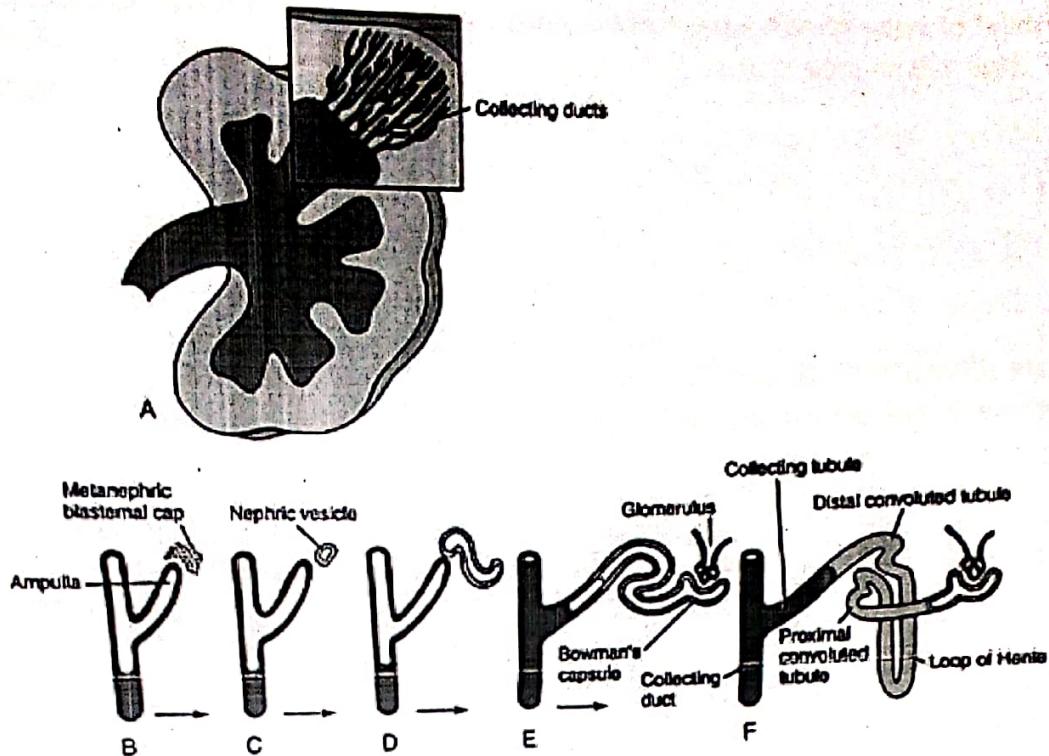
Derivatives of the ureteric bud and metanephric blastema in the adult kidney

A. Derivatives of the metanephric blastema:

- Podocytes covering glomerular capillaries
- Epithelial cells lining Bowman's capsule
- Proximal convoluted tubules
- Descending thick limbs of the loops of Henle
- Thin limbs of the loops of Henle
- Ascending thick limbs of the loop of Henle
- Distal convoluted tubules

B. Derivatives of the ureteric bud:

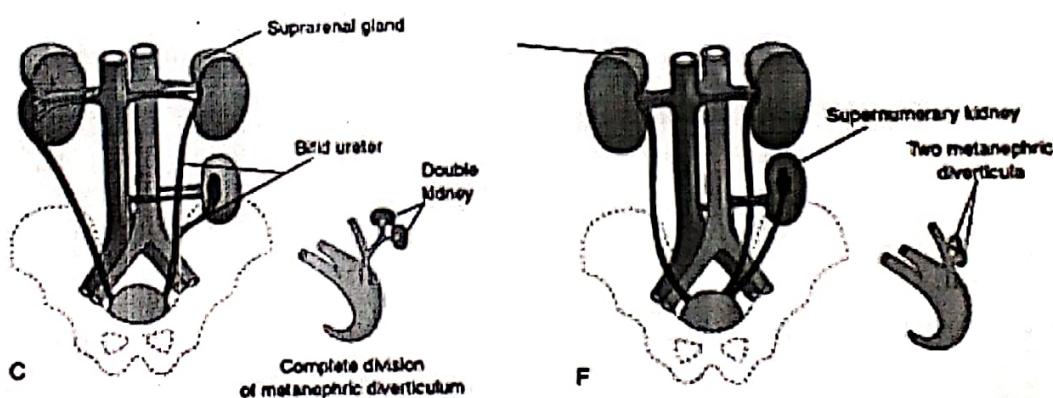
- Collecting tubules and ducts
- Minor and major calyces
- Ureters



Examples of perturbations in induction or differentiation of kidney tissue

A. Duplication of the urinary tract

- Occurs when the ureteric bud prematurely divides before penetrating the metanephric blastema
- Results in either a double kidney and/or a duplicated ureter and renal pelvis



B. Renal-Coloboma syndrome

- ❖ The Pax2 gene essential for metanephric mesenchyme to differentiate into epithelial tubules in response to inductive signals from ureteric bud, so mutations (even if HETEROZYGOUS) can produce renal defects. Patients typically exhibit the following symptoms:
 - Renal hypoplasia - due to reduced proliferation of the mesenchyme derived epithelia during development
 - Vesicouretral Reflux - most likely due to improper connection of the ureter to the bladder or possibly due to inherent defects in epithelial cells of the mature ureter

- **Colobomas** (ventral fissures in iris, retina, and/or optic nerve) - due to failure of the optic fissure to fuse (expression of Pax2 is observed in ventral part of the optic cup and optic stalk)

C. Nephroblastoma (Wilms Tumor)

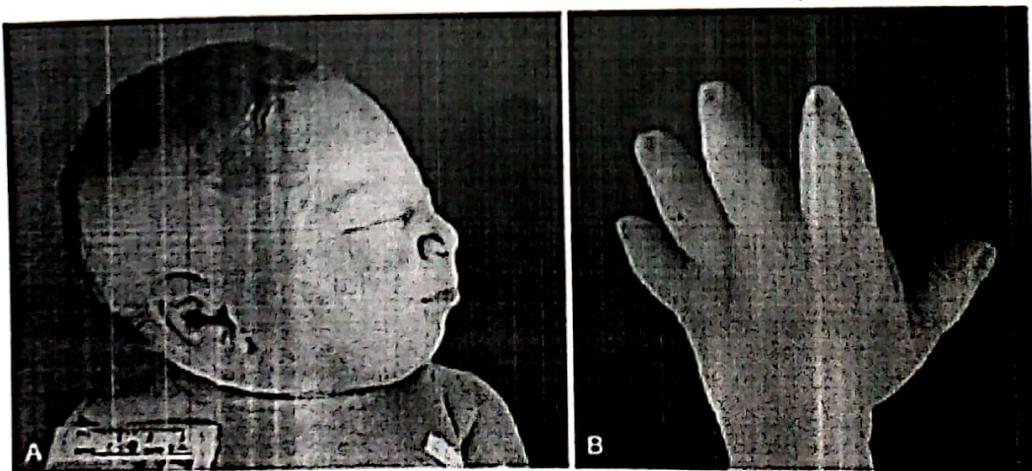
- found in infants from 0-24 months of age
- consists of blastemal, epithelial, and stromal cell types
- associated with mutations in genes related to kidney development (PAX2, WT1, etc.)
- essentially due to incomplete mesenchymal-to-epithelial transformation (i.e. the cells fail to fully differentiate and transform into cancerous cells).

D. Polycystic kidney disease

This condition can arise due to a variety of factors:

- Loss of polarity: aberrant differentiation of tubule cells results in inappropriate location of Na/K channels to the apical (rather than basal) domain of the cells. Na⁺ is pumped apically, water follows resulting in dilation of tubule lumens.
- Over proliferation: excessive growth of tubule epithelium can occlude the lumen causing blockage.

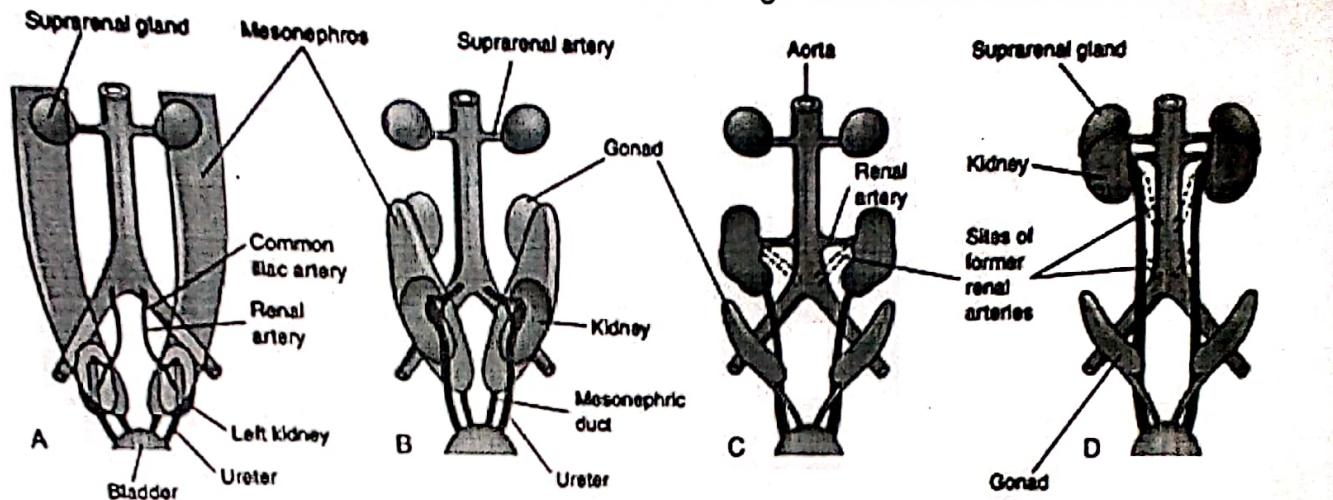
A hallmark of renal agenesis, hypoplasia, or dysfunction in utero is oligohydramnios (low amniotic fluid volume) since the amniotic fluid is produced by the kidneys. Reduced amniotic fluid volume causes increased pressure on the developing fetus, resulting in a sloped forehead, "parrot beak" nose, shortened fingers, and hypoplasia of internal organs, particularly the gut and lungs. Collectively, this sequence of anomalies is known as the Potter sequence.



Carson: Human Embryology and Developmental Biology, 4th Edition.
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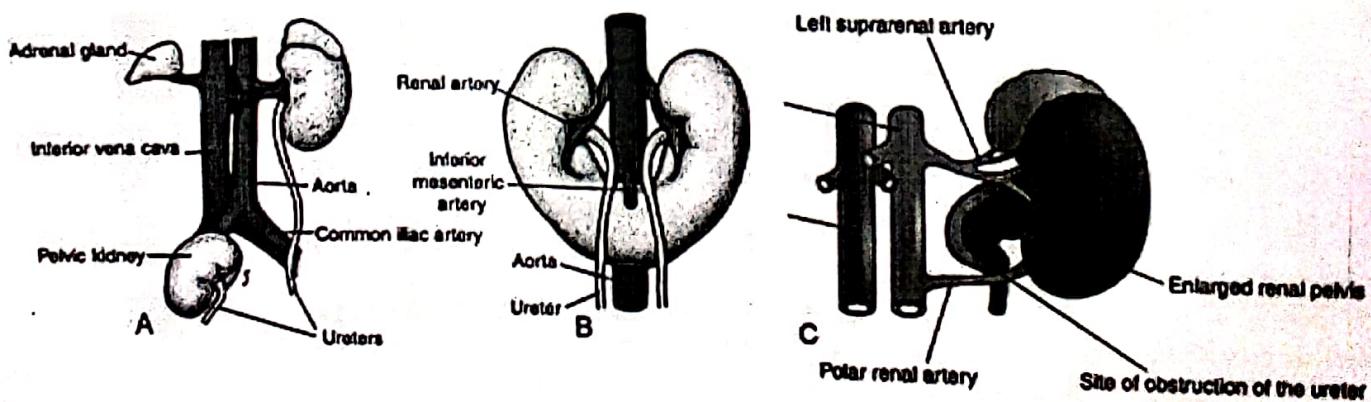
Ascent of the kidneys

- The kidneys initially form near the tail of the embryo.
- Vascular buds from the kidneys grow toward and invade the common iliac arteries.
- Growth of the embryo in length causes the kidneys to "ascend" to their final position in the lumbar region.
- Rather than "drag" their blood supply with them as they ascend, the kidneys send out new and slightly more cranial branches and then induce the regression of the more caudal branches.



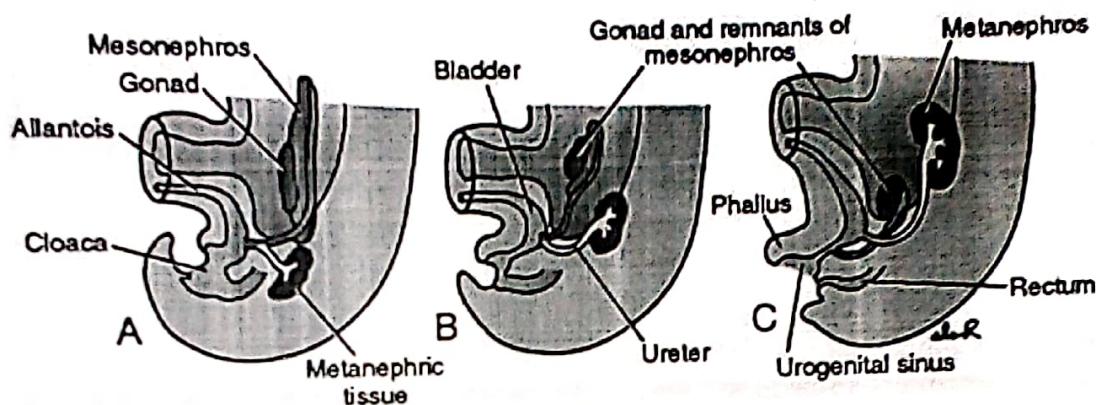
Malformations related to the ascent of the Kidneys

- Pelvic kidney (A):** one or both kidneys stay in the pelvis rather than ascending
- Horseshoe kidney (B):** the two developing kidneys fuse ventrally into a single, horseshoe shape that gets trapped in the abdomen by the inferior mesenteric artery.
- Supernumerary arteries (C):** can often have more than one renal artery per kidney, which is often asymptomatic but can sometimes compress the ureter causing a backup of fluid into the renal pelvis and kidney tubules (hydronephrosis)

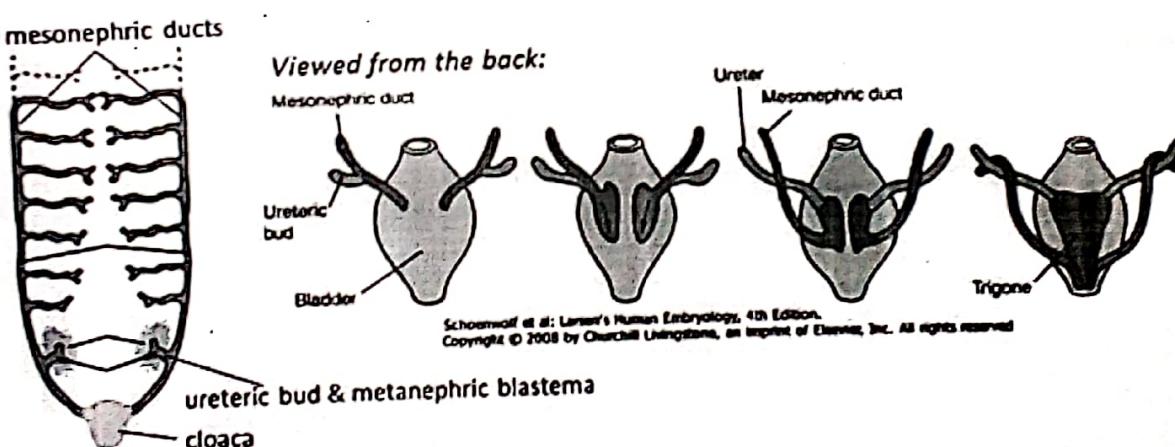


DEVELOPMENT OF THE BLADDER

- The terminal part of the hindgut ends in the CLOACA, which is an endoderm-lined chamber that contacts the surface ectoderm at the cloacal membrane and communicates with the allantois, which is a membranous sac that extends into the umbilicus alongside the vitelline duct.
- The cloaca is then divided by the URORECTAL SEPTUM
 - the DORSAL (inferior) portion develops into the RECTUM and ANAL CANAL
 - the VENTRAL (superior) portion develops into the BLADDER and UROGENITAL SINUS, which will give rise to the bladder and lower urogenital tracts (prostatic and penile urethrae in males; urethra and lower vagina in females).

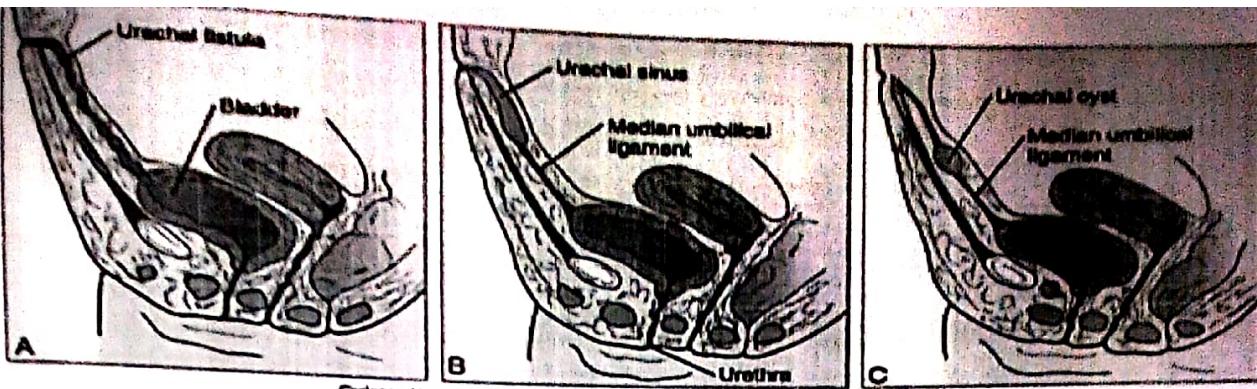


- As the bladder grows and expands, the distal ends of the mesonephric ducts are absorbed into the wall of the bladder as the TRIGONE.



Malformations related to the development of the Bladder

- Trigonitis:** As a MESONEPHRIC DUCT derivative, the trigone is sensitive to sex hormones and can undergo hormone-induced epithelial metaplasia (usually transformation from a transitional type to squamous type epithelium which can overproliferate and lead to urinary blockages).
- Abnormal attachment of the ureters:** the ureters can sometimes be attached to either to the urethra or parts of the reproductive tracts.
- Urachal fistulas, sinuses, and cysts:** occur when a remnant of the allantois persists and are found in the midline along the path from the umbilicus to the apex of the bladder (i.e. along the median umbilical ligament).



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DEVELOPMENT OF THE SUPRARENAL GLANDS

Development of the adrenal cortex

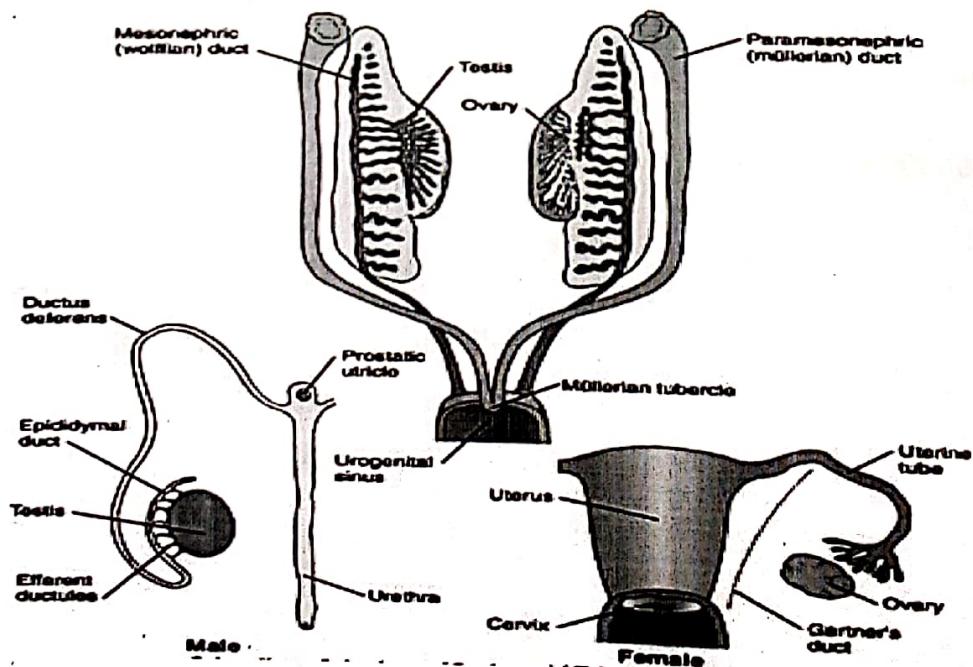
- Arises mostly from intermediate mesoderm in the lumbar region of the embryo.

Development of the adrenal medulla

- Trunk neural crest cells migrate into the center of the adrenal glands and develop into the chromaffin cells of the adrenal medulla. These cells are essentially postganglionic sympathetic neurons that release epinephrine or norepinephrine directly into the bloodstream as opposed to innervating a target organ.

DEVELOPMENT OF THE REPRODUCTIVE SYSTEMS

- ❖ The gonads arise from intermediate mesoderm within the urogenital ridges of the embryo
- ❖ The genital ducts arise from paired mesonephric and paramesonephric ducts
 - The mesonephric ducts give rise to MALE genital ducts
 - The paramesonephric ducts give rise to FEMALE genital ducts



- The gonads and reproductive tracts are indifferent up until 7 weeks of development; differentiation is influenced largely by the presence or absence of SRY (on the Y chromosome)
- If SRY+, then development proceeds along the male path
- If SRY-, then development proceeds along the female path

Development of the MALE reproductive tract

- Under the influence of SRY, the gonad develops into a TESTIS containing spermatogonia, Leydig cells, and Sertoli cells.
- Leydig cells produce TESTOSTERONE, which support growth of the mesonephric ducts. NOTE: without testosterone, the mesonephric ducts will REGRESS.
- Some testosterone is converted into Dihydroxytestosterone (DHT), which supports development of the prostate gland, penis, and scrotum.
- Sertoli cells produce ANTI-MÜLLERIAN HORMONE (aka Müllerian Inhibiting Substance, or MIS), which induces regression of the paramesonephric ducts. NOTE: in the absence of MIS, the paramesonephric ducts will PERSIST.

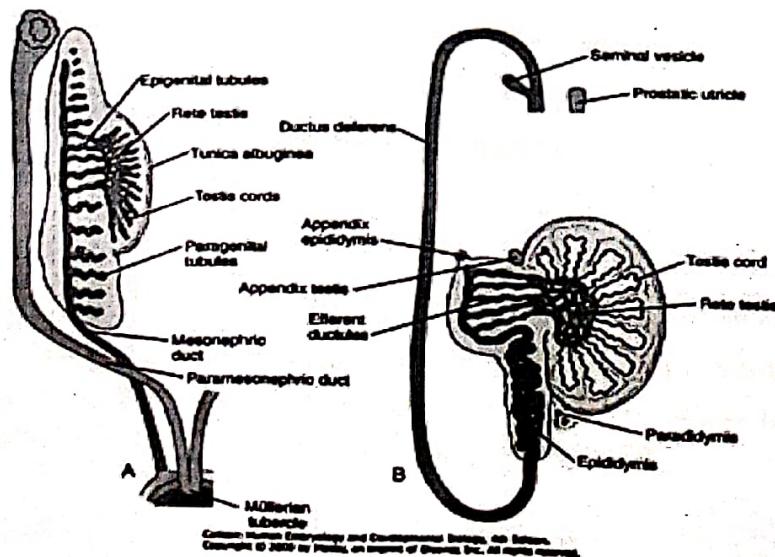
The development of the male gonad and upper reproductive tract is shown below - the red tube is the paramesonephric duct which regresses and the purple tube is the mesonephric duct, which develops into the epididymis and vas deferens:

Descent of the testes

- The testes arise in the lumbar region but then descend into pelvic cavity and through the inguinal canal to end up in the scrotum
- Descent of the testis is due to tethering of the testes to the anterior body wall by the gubernaculum. With growth and elongation of the embryo coupled with shortening of the gubernaculum, the testes are pulled through the body wall, then the inguinal canal, and finally into the scrotum.

Summary of male urogenital tract derivatives

- Ureteric bud:** ureter
- Mesonephric ducts:** rete testis, efferent ducts, epididymis, vas deferens, seminal vesicle, trigone of bladder
- Urogenital sinus:** bladder (except trigone), prostate gland, bulbourethral gland, urethra



Development of the FEMALE reproductive tract

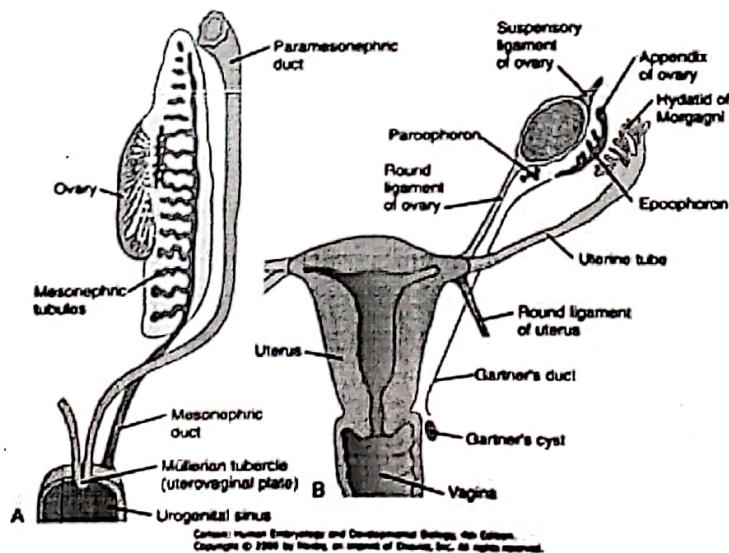
- In the absence of SRY, the gonad develops into an ovary with oogonia and stromal cells.
- Since no testosterone is produced, the mesonephric ducts regress.
- Since there is also no MIS, the paramesonephric ducts persist to give rise to the oviducts, uterus, and upper 1/3 of the vagina
- The urogenital sinus contributes to the formation of the bulbourethral glands and the lower 2/3 of the vagina

The development of the female gonad and upper reproductive tract is shown below - the red tube is the paramesonephric duct which becomes the oviduct and the purple tube is the mesonephric duct, which mostly regresses:

The development of the lower female reproductive tract is shown below - the uterus, cervix, and upper 1/3 of the vagina (derived from paramesonephric ducts) are shown in red and the lower 2/3 of the vagina, bulbourethral glands (purple buds appearing at the end of the movie), and vestibule (derived from urogenital sinus) is shown in yellow:

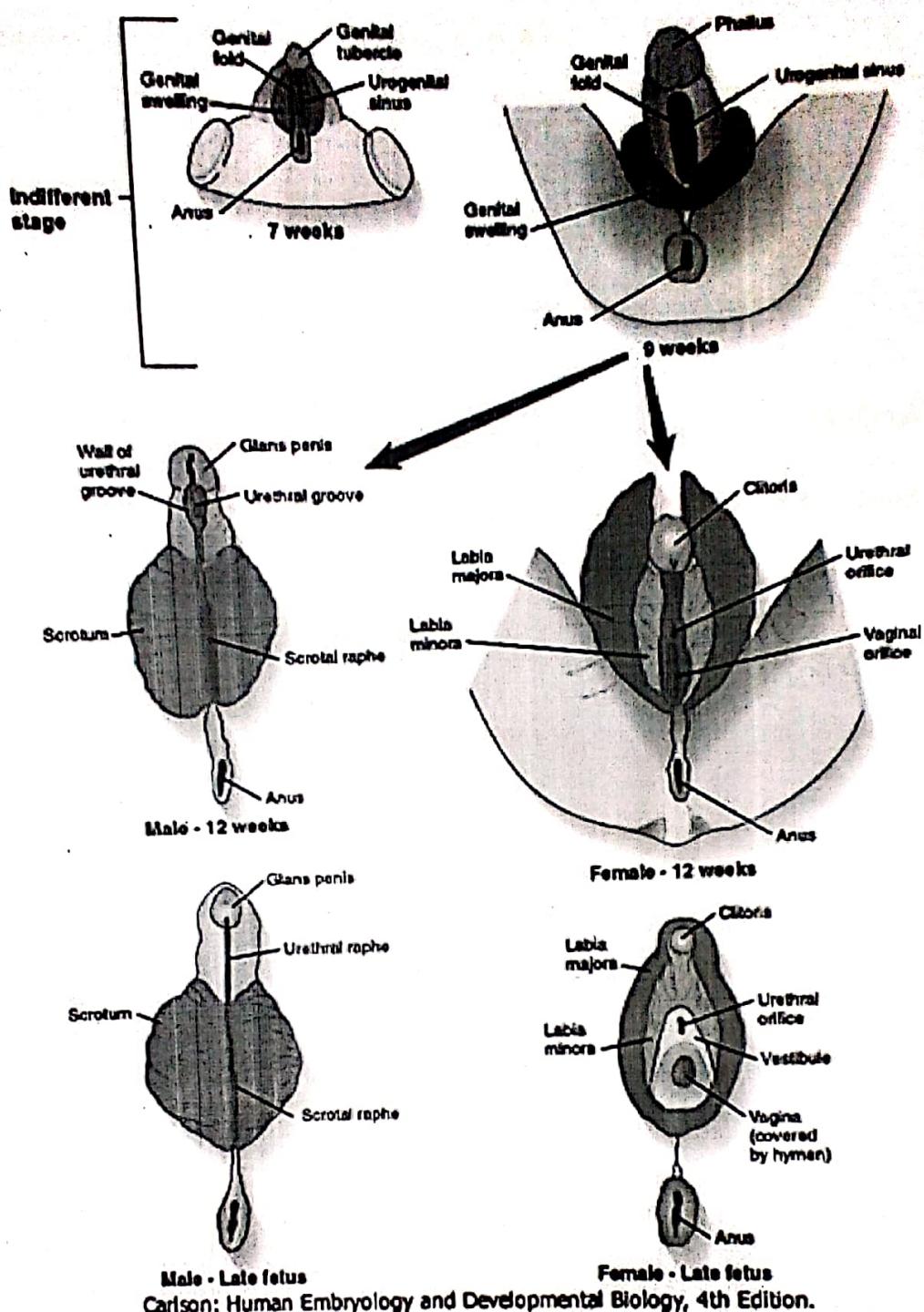
Summary of female urogenital tract derivatives

- Ureteric bud: ureter
- Mesonephric ducts: trigone of bladder
- Paramesonephric ducts: oviduct, uterus, upper 1/3 of vagina
- Urogenital sinus: bladder (except trigone), bulbourethral gland, urethra, lower 2/3 of vagina



Formation of the external genitalia

- Proliferation of mesoderm and ectoderm around the cloacal membrane produces primordial tissues of the external genitalia in both sexes: the genital tubercle, genital folds, and genital swellings. The primordia are indistinguishable up until about week 12.



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- In the MALE, the primordia differentiate as follows:

Genital Tubercle	Genital Folds	Genital Swellings
Body and glans of penis	Ventral aspect of penis	Scrotum
Corpora cavernosum & spongiosum	& Penile raphe	Scrotal raphe

- In the FEMALE, the primordia differentiate as follows:

Genital Tercle	Genital Folds	Genital Swellings
Body and glans of clitoris	Labia minora	Labia majora
		Mons pubis

ASSOCIATED UROGENITAL ANOMALIES

- Wide spectrum of disorders caused by defects in the development of kidneys or their outflow tracts
- Account for almost 25% of birth defects, and are a major cause of end-stage renal disease in children

Other names:

- Congenital abnormalities of kidney and urinary tract
- Congenital renal anomalies
- Hereditary renal disease
- Congenital renal and urinary tract malformations

Types

Anomalies of the Kidney

- ❖ renal agenesis or aplasia
- ❖ renal dysgenesis
 - renal dysplasia (dysplastic kidney)
 - renal hypoplasia (hypoplastic kidney)

Renal Cystic Anomalies

- Multicystic dysplastic kidney
- autosomal recessive polycystic kidney disease
- autosomal dominant polycystic kidney disease

Renal Ectopy (Ectopic Kidney)

Horseshoe Kidney

Anomalies of the Pelvis And Calyces

- Congenital hydronephrosis
- ureteropelvic junction obstruction

Anomalies of the Ureter

- Megaureter/ureterovesical junction obstruction
- vesicoureteral reflux
- Duplicated collecting system (duplex collecting system)
- ureterocele
- ectopic ureter

Anomalies of the Bladder

- Bladder exstrophy
- Congenital neurogenic bladder
- Bladder diverticulum
- prune belly syndrome
- urachal remnants

Anomalies of the Urethra

- Posterior urethral valves
- hypospadias
- Urethral stricture
- Urethral atresia or hypoplasia
- Epispadias

Anomalies of the Penis

- ❖ chordee
- ❖ penile torsion
- ❖ phimosis and paraphimosis
- ❖ inconspicuous penis
 - micropenis
 - concealed penis including buried penis and webbed penis