Medical Embryology

Alaa Hachem (DPhil)

Third Month to Birth: The Fetus and Placenta

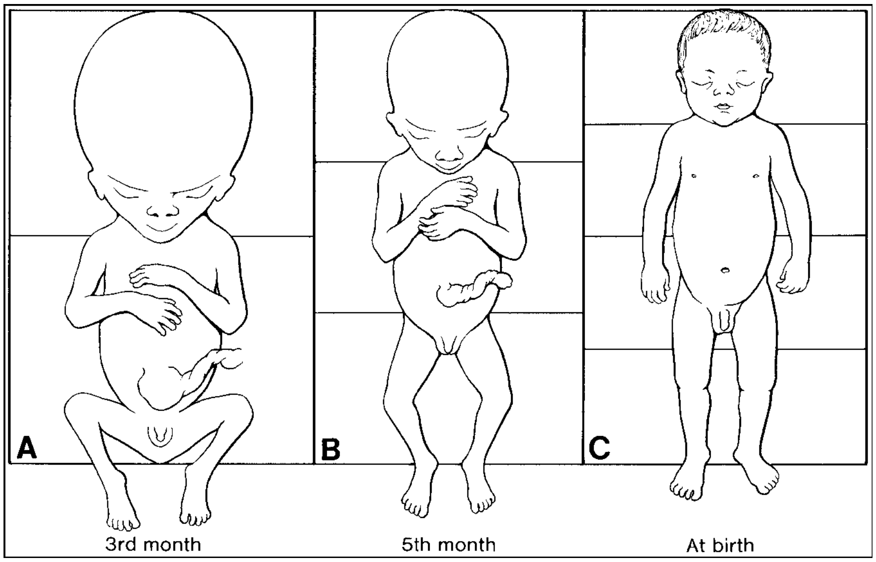
- **Development of the Fetus**

The period from the beginning of the ninth week to birth is known as the **fetal period.** It is characterized by maturation of tissues and organs and rapid growth of the body. The length of the fetus is usually indicated as the **crown-rump length** (CRL) (sitting height) or as the **crown-heel length** (CHL), the measurement from the vertex of the skull to the heel (standing height). These measurements, expressed in centimeters, are correlated with the age of the fetus in weeks or months. In general, **the length of pregnancy is considered to be 280 days, or 40 weeks after the onset of the last normal menstrual period (LNMP) or more accurately, 266 days or 38 weeks after fertilization.** For the purposes of the following discussion, age is calculated from the time of fertilization and is expressed in weeks or calendar months.

- **MONTHLY CHANGES**

One of the most striking changes taking place during fetal life is the relative slowdown in growth of the head compared with the rest of the body. At the beginning of the third month the head constitutes approximately half of the CRL (Figs. 6.1 and 6.2). By the beginning of the fifth month, the size of the head is about one-third of the CHL, and at birth it is approximately one-fourth of the CHL (Fig. 6.2). Hence, over time, growth of the body accelerates but that of the head slows down.

During the **third month** the face becomes more human looking. The eyes, initially directed laterally, move to the ventral aspect of the face, and the ears come to lie close to their definitive position at the side of the head. The limbs reach their relative length in comparison with the rest of the body, although the lower limbs are still a little shorter and less well developed than the upper extremities. **Primary ossification centers** are present in the long bones and skull by the 12th week. Also by the 12th week, external genitalia develop to such a degree that the sex of the fetus can be determined by external examination (ultrasound). During the 6th week **intestinal loops cause a large swelling (herniation) in the umbilical cord,** but by the 12th week the loops withdraw into the abdominal cavity. At the end of the third month, reflex activity can be evoked in aborted fetuses, indicating muscular activity.



During the **fourth** and **fifth months** the fetus lengthens rapidly, and at the end of the first half of intrauterine life its CRL is approximately 15 cm, that is, about half the total length of the newborn. The weight of the fetus increases little during this period and by the end of the fifth month is still less than 500 g. The fetus is covered with fine hair, called **lanugo hair;** eyebrows and head hair are also visible. **During the fifth month movements of the fetus can be felt by the mother.**

During the **second half of intrauterine life,** weight increases considerably, particularly during the last 2.5 months, when 50% of the full-term weight (approximately 3200 g) is added. During the **sixth month,** the skin of the fetus is reddish and has a wrinkled appearance because of the lack of underlying connective tissue. A fetus born early in the sixth month has great difficulty surviving. Although several organ systems are able to function, the respiratory system and the central nervous system have not differentiated sufficiently, and coordination between the two systems is not yet well established. By 6.5 to 7 months, the fetus has a length of about 25 cm and weighs approximately 1100 g. If born at this time, the infant has a 90% chance of surviving.

During the last 2 months, the fetus obtains well-rounded contours as the result of deposition of subcutaneous fat. By the end of intrauterine life, the skin is covered by a whitish, fatty substance (**vernix caseosa**) composed of secretory products from sebaceous glands.

At the end of the **ninth month** the skull has the largest circumference of all parts of the body, an important fact with regard to its passage through the birth canal. At the time of birth the weight of a normal fetus is 3000 to 3400 g; its CRL is about 36 cm; and its CHL is about 50 cm. Sexual characteristics are pronounced, and the testes should be in the scrotum.

TIME OF BIRTH

The date of birth is most accurately indicated as 266 days, or 38 weeks, after fertilization. The oocyte is usually fertilized within 12 hours of ovulation. However, sperm deposited in the reproductive tract up to 6 days prior to ovulation can survive to fertilize oocytes. Thus, most pregnancies occur when sexual intercourse occurs within a 6-day period that ends on the day of ovulation. A pregnant woman usually will see her obstetrician when she has missed two successive menstrual bleeds.

The obstetrician calculates the date of birth as 280 days or 40 weeks from the first day of the LNMP. In women with regular 28-day menstrual periods the method is fairly accurate, but when cycles are irregular, substantial miscalculations may be made. An additional complication occurs when the woman has some bleeding about 14 days after fertilization as a result of erosive activity by the implanting blastocyst. Hence the day of delivery is not always easy to determine. Most fetuses are born within 10 to 14 days of the calculated delivery date. If they are born much earlier, they are categorized as **premature;** if born later, they are considered **postmature.**

Occasionally the age of an embryo or small fetus must be determined. By combining data on the onset of the last menstrual period with fetal length, weight, and other morphological characteristics typical for a given month of development, a reasonable estimate of the age of the fetus can be formulated. A valuable tool for assisting in this determination is **ultrasound,** which can provide an accurate (1 to 2 days) measurement of CRL during the 7th to 14th weeks. Measurements commonly used in the 16th to 30th weeks are **biparietal diameter (BPD),** head and abdominal circumference, and femur length. An accurate determination of fetal size and age is important for managing pregnancy, especially if the mother has a small pelvis or the baby has a birth defect.

C L I N I C A L C O R R E L A T E S

Low Birth Weight

There is considerable variation in fetal length and weight, and sometimes these values do not correspond with the calculated age of the fetus in months or weeks. Most factors influencing length and weight are genetically determined, but environmental factors also play an important role.

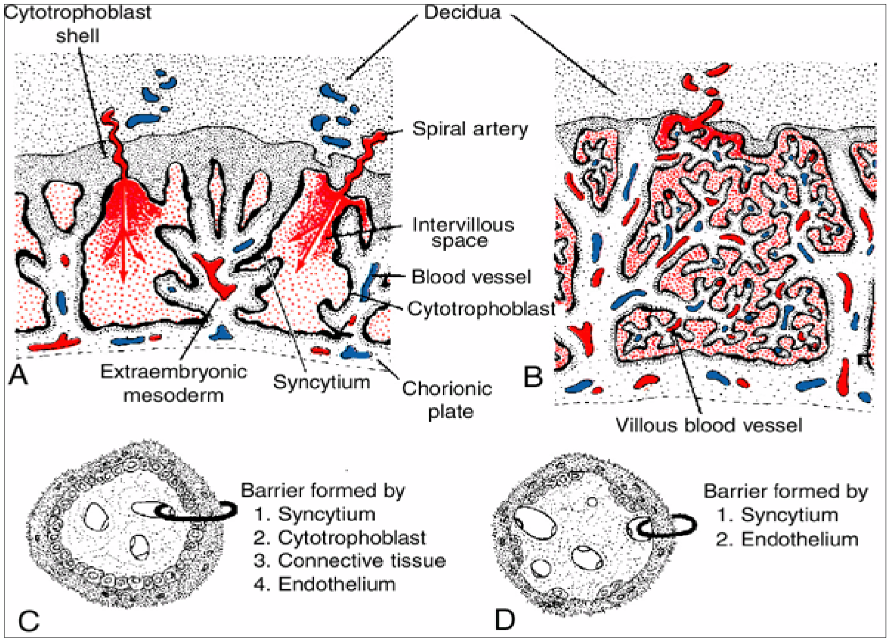
Intrauterine growth restriction (IUGR) is a term applied to infants who are at or below the 10th percentile for their expected birth weight at a given gestational age. Fetuses that weigh less than 500 g seldom survive, while those that weigh 500 to 1000 g may live if provided with expert care. However, approximately 50% of babies born weighing less than 1000 g who survive will have severe neurological deficits. Infants may be full term, but small because of IUGR or small because they are born prematurely.

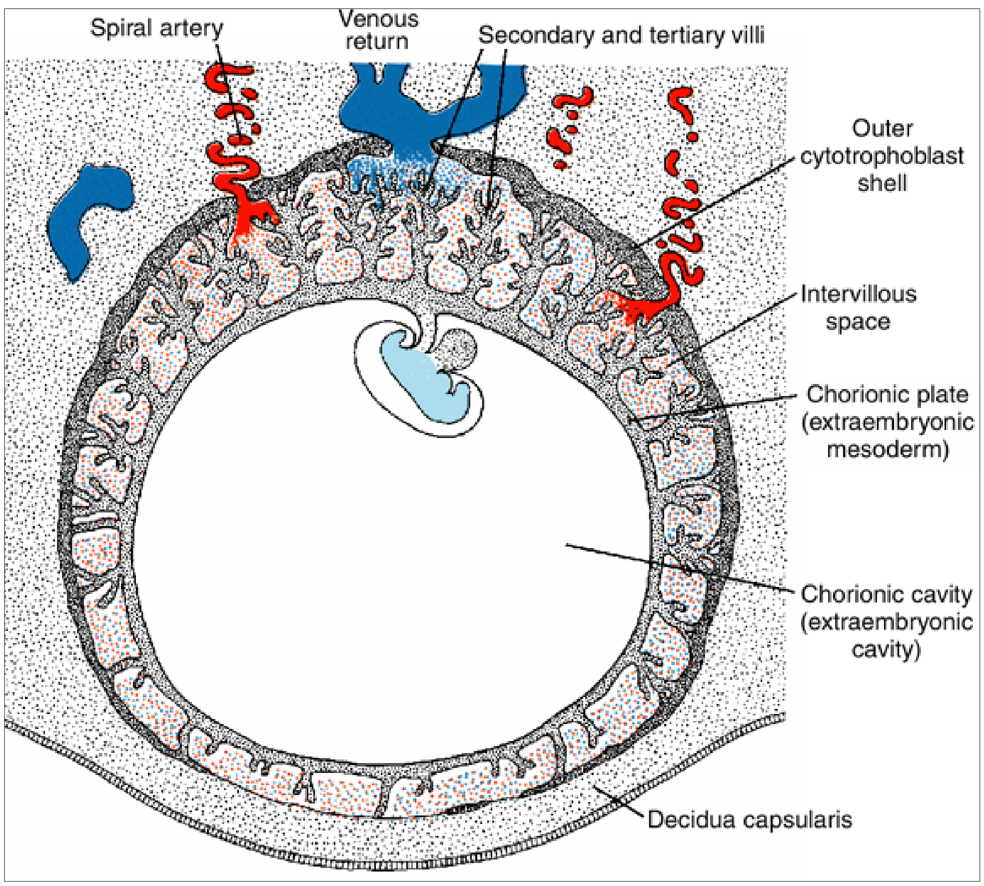
Fetal Membranes and Placenta

As the fetus grows, its demands for nutritional and other factors increase causing major changes in the placenta. Foremost among these is an increase in surface area between maternal and fetal components to facilitate exchange. The disposition of fetal membranes is also altered as production of amniotic fluid increases.

CHANGES IN THE TROPHOBLAST

By the beginning of the second month, the **trophoblast** is characterized by a great number of secondary and tertiary villi that give it a radial appearance. The villi are anchored in the mesoderm of the **chorionic plate** and are attached peripherally to the maternal decidua by way of the outer **cytotrophoblast shell.** The surface of the villi is formed by the syncytium, resting on a layer of cytotrophoblastic cells that in turn cover a core of vascular mesoderm. The capillary system developing in the core of the villous stems soon comes in contact with capillaries of the chorionic plate and connecting stalk, thus giving rise to the extraembryonic vascular system.


Cytotrophoblast shell
Decidua
Spiral artery
Intervillous space
Blood vessel
Cytotrophoblast
A
Extraembryonic mesoderm
Syncytium
Chorionic plate
B
Villous blood vessel
Barrier formed by
1. Syncytium
2. Cytotrophoblast
3. Connective tissue
4. Endothelium
C
Barrier formed by
1. Syncytium
2. Endothelium
D

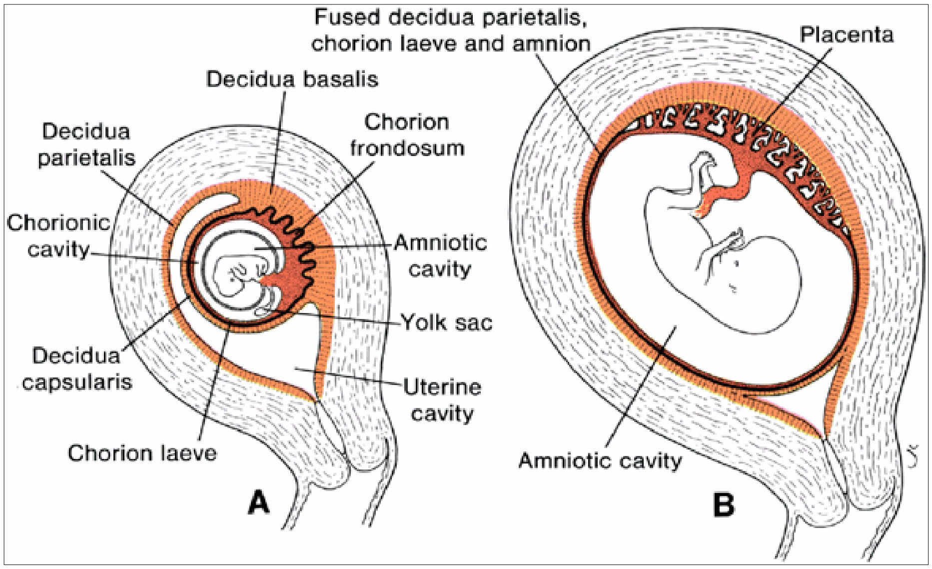

Spiral artery
Venous return
Secondary and tertiary villi
Outer cytotrophoblast shell
Intervillous space
Chorionic plate (extraembryonic mesoderm)
Chorionic cavity (extraembryonic cavity)
Decidua capsularis

During the following months, numerous small extensions sprout from existing villous stems into the surrounding **lacunar** or **intervillous spaces.** Initially these newly formed villi are primitive, but by the beginning of the fourth month, cytotrophoblastic cells and some connective tissue cells disappear. The syncytium and endothelial wall of the blood vessels are then the only layers that separate the maternal and fetal circulations. Frequently the syncytium becomes very thin, and large pieces containing several nuclei may break off and drop into the intervillous blood lakes. These pieces, known as **syncytial knots,** enter the maternal circulation and usually degenerate without causing any symptoms. Disappearance of cytotrophoblastic cells progresses from the smaller to larger villi, and although some always persist in large villi, they do not participate in the exchange between the two circulations.

CHORION FRONDOSUM AND DECIDUA BASALIS

In the early weeks of development, villi cover the entire surface of the chorion. As pregnancy advances, villi on the embryonic pole continue to grow and expand, giving rise to the **chorion frondosum** (bushy chorion). Villus on the abembryonic pole degenerate and by the third month this side of the chorion, now known as the chorion laeve, is smooth.

The difference between the embryonic and abembryonic poles of the chorion is also reflected in the structure of the **decidua,** the functional layer of the endometrium, which is shed during parturition. The decidua over the chorion frondosum, the **decidua basalis,** consists of a compact layer of large cells, **decidual cells,** with abundant amounts of lipids and glycogen. This layer, the **decidual plate,** is tightly connected to the chorion. The decidual layer over the abembryonic pole is the **decidua capsularis**. With growth of the chorionic vesicle, this layer becomes stretched and degenerates. Subsequently, the chorion laeve comes into contact with the uterine wall (**decidua parietalis**) on the opposite side of the uterus and the two fuse, obliterating the uterine lumen. Hence the only portion of the chorion participating in the exchange process is the chorion frondosum, which, together with the deciduas basalis, makes up the **placenta.** Similarly, fusion of the amnion and chorion to form the **amniochorionic membrane** obliterates the chorionic cavity. It is this membrane that ruptures during labor (breaking of the water).



Structure of the Placenta

By the beginning of the fourth month, the placenta has two components: (*a*) a **fetal portion,** formed by the chorion frondosum; and (*b*) a **maternal portion,** formed by the decidua basalis. On the fetal side, the placenta is bordered by the **chorionic plate**; on its maternal side, it is bordered by the decidua basalis, of which the **decidual plate** is most intimately incorporated into the placenta. In the **junctional zone,** trophoblast and decidua cells intermingle. This zone, characterized by decidual and syncytial giant cells, is rich in amorphous extracellular material. By this time most cytotrophoblast cells have degenerated. Between the chorionic and decidual plates are the intervillous spaces, which are filled with maternal blood. They are derived from lacunae in the syncytiotrophoblast and are lined with syncytium of fetal origin. The villous trees grow into the intervillous blood lakes.

During the fourth and fifth months the decidua forms a number of **decidual septa,** which project into intervillous spaces but do not reach the chorionic plate. These septa have a core of maternal tissue, but their surface is covered by a layer of syncytial cells, so that at all times a syncytial layer separates maternal blood in intervillous lakes from fetal tissue of the villi. As a result of this septum formation, the placenta is divided into a number of compartments, or **cotyledons**. Since the decidual septa do not reach the chorionic plate, contact between intervillous spaces in the various cotyledons is maintained.

As a result of the continuous growth of the fetus and expansion of the uterus, the placenta also enlarges. Its increase in surface area roughly parallels that of the expanding uterus and throughout pregnancy it covers approximately 15 to 30% of the internal surface of the uterus. The increase in thickness of the placenta results from arborization of existing villi and is not caused by further penetration into maternal tissues.

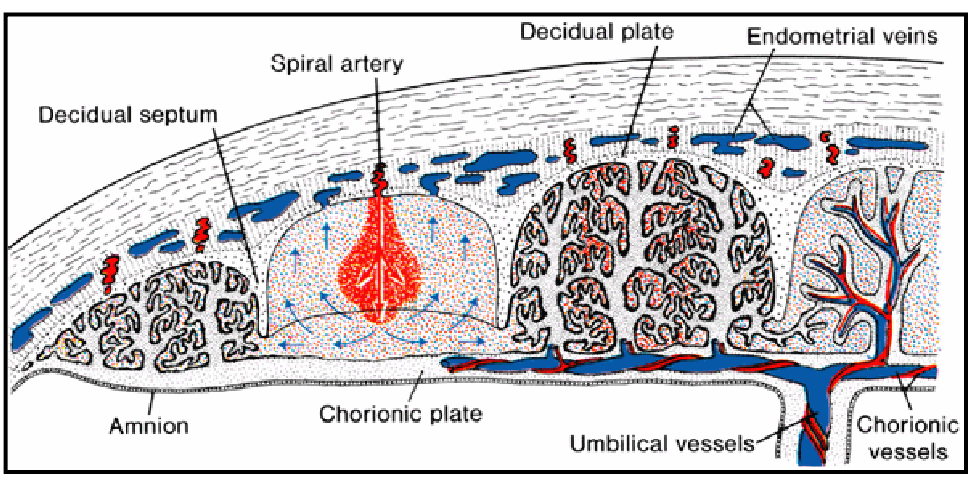
FULL-TERM PLACENTA

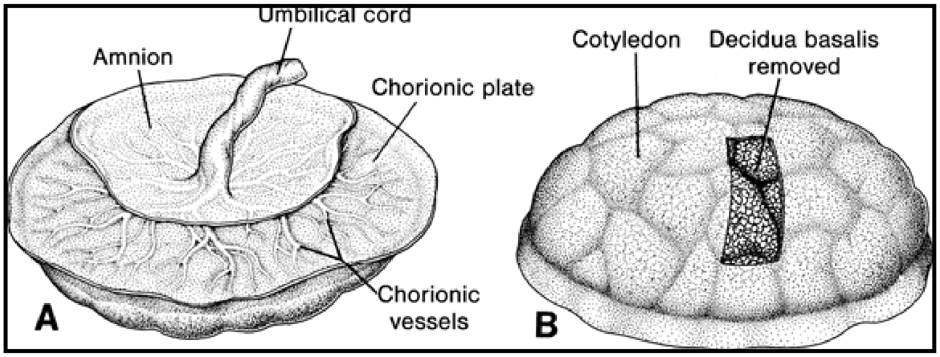
At full term, the placenta is discoid with a diameter of 15 to 25 cm, is approximately 3 cm thick, and weighs about 500 to 600 g. At birth, it is torn from the uterine wall and, approximately 30 minutes after birth of the child, is expelled from the uterine cavity. After birth, when the placenta is viewed from the **maternal side,** 15 to 20 slightly bulging areas, the **cotyledons,** covered by a thin layer of decidua basalis, are clearly recognizable. Grooves between the cotyledons are formed by decidual septa.

The **fetal surface** of the placenta is covered entirely by the chorionic plate. A number of large arteries and veins, the **chorionic vessels,** converge toward the umbilical cord. The chorion, in turn, is covered by the amnion. Attachment of the umbilical cord is usually eccentric and occasionally even marginal. Rarely, however, does it insert into the chorionic membranes outside the placenta (**velamentous insertion**).

CIRCULATION OF THE PLACENTA

Cotyledons receive their blood through 80 to 100 spiral arteries that pierce the decidual plate and enter the intervillous spaces at more or less regular intervals. The lumen of the spiral artery is narrow, so blood pressure in the intervillous space is high. This pressure forces the blood deep into the intervillous spaces and bathes the numerous small villi of the villous tree in oxygenated blood. As the pressure decreases, blood flows back from the chorionic plate toward the decidua, where it enters the endometrial veins. Hence, blood from the intervillous lakes drains back into the maternal circulation through the endometrial veins.





Collectively, the intervillous spaces of a mature placenta contain approximately 150 ml of blood, which is replenished about 3 or 4 times per minute. This blood moves along the chorionic villi, which have a surface area of 4 to 14 m2. However, placental exchange does not take place in all villi, only in those whose fetal vessels are in intimate contact with the covering syncytial membrane. In these villi, the syncytium often has a brush border consisting of numerous microvilli, which greatly increases the surface area and consequently the exchange rate between maternal and fetal circulations. The **placental membrane,** which separates maternal and fetal blood, is initially composed of four layers: (*a*) the endothelial lining of fetal vessels; (*b*) the connective tissue in the villus core; (*c*) the cytotrophoblastic layer; and (*d*) the syncytium. From the fourth month on, however, the placental membrane thins, since the endothelial lining of the vessels comes in intimate contact with the syncytial membrane, greatly increasing the rate of exchange. Sometimes called the **placental barrier,** the placental membrane is not a true barrier, since many substances pass through it freely. Because the maternal blood in the intervillous spaces is separated from the fetal blood by a chorionic derivative, the human placenta is considered to be of the **hemochorial** type.

FUNCTION OF THE PLACENTA

Main functions of the placenta are (*a*) **exchange of metabolic and gaseous products** between maternal and fetal bloodstreams and (*b*) **production of hormones.**

1. **Exchange of Gases**

Exchange of gases, such as oxygen, carbon dioxide, and carbon monoxide, is accomplished by simple diffusion. At term, the fetus extracts 20 to 30 ml of oxygen per minute from the maternal circulation and even a short-term interruption of the oxygen supply is fatal to the fetus. Placental blood flow is critical to oxygen supply, since the amount of oxygen reaching the fetus primarily depends on delivery, not diffusion.

2. **Exchange of Nutrients and Electrolytes**

Exchange of nutrients and electrolytes, such as amino acids, free fatty acids, carbohydrates, and vitamins, is rapid and increases as pregnancy advances.

3. **Transmission of Maternal Antibodies**

Immunological competence begins to develop late in the first trimester, by which time the fetus makes all of the components of **complement.** Immunoglobulins consist almost entirely of **maternal immunoglobulin G (IgG)** that begins to be transported from mother to fetus at approximately 14 weeks. In this manner, the fetus gains passive immunity against various infectious diseases. Newborns begin to produce their own IgG, but adult levels are not attained until the age of 3 years.

4. **Hormone Production**

By the end of the fourth month the placenta produces **progesterone** in sufficient amounts to maintain pregnancy if the corpus luteum is removed or fails to function properly. In all probability, all hormones are synthesized in the syncytial trophoblast. In addition to progesterone, the placenta produces increasing amounts of **estrogenic hormones,** predominantly **estriol,** until just before the end of pregnancy, when a maximum level is reached. These high levels of estrogens stimulate uterine growth and development of the mammary glands.

During the first two months of pregnancy, the syncytiotrophoblast also produces **human chorionic gonadotropin (hCG),** which maintains the corpus luteum. This hormone is excreted by the mother in the urine, and in the early stages of gestation, its presence is used as an indicator of pregnancy. Another hormone produced by the placenta is **somatomammotropin** (formerly **placental lactogen**). It is a growth hormone-like substance that gives the fetus priority on maternal blood glucose and makes the mother somewhat diabetogenic. It also promotes breast development for milk production.

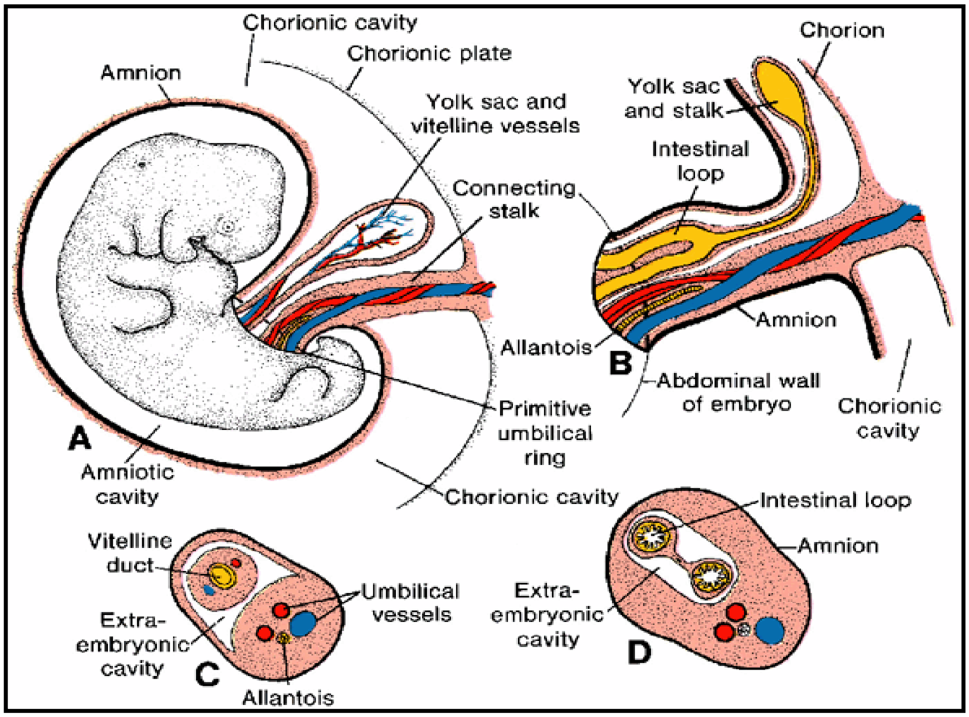
Amnion and Umbilical Cord

The oval line of reflection between the amnion and embryonic ectoderm (**amnio-ectodermal junction**) is the **primitive umbilical ring.** At the fifth week of development, the following structures pass through the ring: (*a*) the **connecting stalk,** containing the allantois and the umbilical vessels, consisting of two arteries and one vein; (*b*) the **yolk stalk** (**vitelline duct**), accompanied by the vitelline vessels; and (*c*) the **canal connecting the intraembryonic and extraembryonic cavities**. The yolk sac proper occupies a space in the **chorionic cavity,** that is, the space between the amnion and chorionic plate.

During further development, the amniotic cavity enlarges rapidly at the expense of the chorionic cavity, and the amnion begins to envelop the connecting and yolk sac stalks, crowding them together and giving rise to the **primitive umbilical cord**. Distally the cord contains the yolk sac stalk and umbilical vessels. More proximally it contains some intestinal loops and the remnant of the allantois. The yolk sac, found in the chorionic cavity, is connected to the umbilical cord by its stalk. At the end of the third month, the amnion has expanded so that it comes in contact with the chorion, obliterating the chorionic cavity. The yolk sac then usually shrinks and is gradually obliterated.

The abdominal cavity is temporarily too small for the rapidly developing intestinal loops and some of them are pushed into the extraembryonic space in the umbilical cord. These extruding intestinal loops form a **physiological umbilical hernia**. At approximately the end of the third month, the loops are withdrawn into the body of the embryo and the cavity in the cord is obliterated. When the allantois and the vitelline duct and its vessels are also obliterated, all that remains in the cord are the umbilical vessels surrounded by the **jelly of Wharton.** This tissue, which is rich in proteoglycans, functions as a protective layer for the blood vessels. The walls of the arteries are muscular and contain many elastic fibers, which contribute to a rapid constriction and contraction of the umbilical vessels after the cord is tied off.

Figure: 6.15



C L I N I C A L C O R R E L A T E S

- **Umbilical Cord Abnormalities**

At birth, the umbilical cord is approximately 2 cm in diameter and 50 to 60 cm long. It is tortuous, causing **false knots.** An extremely long cord may encircle the neck of the fetus, usually without increased risk, whereas a short one may cause difficulties during delivery by pulling the placenta from its attachment in the uterus.

Normally there are two arteries and one vein in the umbilical cord. In 1 in 200 newborns, however, only one artery is present, and these babies have approximately a 20% chance of having cardiac and other vascular defects. The missing artery either fails to form (agenesis) or degenerates early in development.

- **Amniotic Bands**

Occasionally, tears in the amnion result in **amniotic bands** that may encircle part of the fetus, particularly the limbs and digits. Amputations, **ring constrictions,** and other abnormalities, including craniofacial deformations, may result. Origin of the bands is probably from infection or toxic insults that involve either the fetus, fetal membranes, or both. Bands then form from the amnion, like scar tissue, constricting fetal structures.

Placental Changes at the End of Pregnancy

At the end of pregnancy, a number of changes that occur in the placenta may indicate reduced exchange between the two circulations. These changes include (*a*) an increase in fibrous tissue in the core of the villus, (*b*) thickening of basement membranes in fetal capillaries, (*c*) obliterative changes in small capillaries of the villi, and (*d*) deposition of fibrinoid on the surface of the villi in the junctional zone and in the chorionic plate. Excessive fibrinoid formation frequently causes infarction of an intervillous lake or sometimes of an entire cotyledon. The cotyledon then assumes a whitish appearance.

Amniotic Fluid

The amniotic cavity is filled with a clear, watery fluid that is produced in part by amniotic cells but is derived primarily from maternal blood. The amount of fluid increases from approximately 30 ml at 10 weeks of gestation to 450 ml at 20 weeks to 800 to 1000 ml at 37 weeks. During the early months of pregnancy, the embryo is suspended by its umbilical cord in this fluid, which serves as a protective cushion. The fluid (*a*) absorbs jolts, (*b*) prevents adherence of the embryo to the amnion, and (*c*) allows for fetal movements. The volume of amniotic fluid is replaced every 3 hours. From the beginning of the fifth month, the fetus swallows its own amniotic fluid and it is estimated that it drinks about 400 ml a day, about half of the total amount. Fetal urine is added daily to the amniotic fluid in the fifth month, but this urine is mostly water, since the placenta is functioning as an exchange for metabolic wastes. During childbirth, the amnio-chorionic membrane forms a hydrostatic wedge that helps to dilate the cervical canal.

C L I N I C A L C O R R E L A T E S

- **Amniotic Fluid**

Hydramnios or **polyhydramnios** is the term used to describe an excess of amniotic fluid (1500–2000 ml), whereas **oligohydramnios** refers to a decreased amount (less than 400 ml). Both conditions are associated with an increase in the incidence of birth defects. Primary causes of hydramnios include idiopathic causes (35%), maternal diabetes (25%), and congenital malformations, including central nervous system disorders (e.g., anencephaly) and gastrointestinal defects (atresias, e.g., esophageal) that prevent the infant from swallowing the fluid. Oligohydramnios is a rare occurrence that may result from renal agenesis.

Premature rupture of the amnion, the most common cause of preterm labor, occurs in 10% of pregnancies. Furthermore, clubfoot and lung hypoplasia may be caused by **oligohydramnios** following amnion rupture. Causes of rupture are largely unknown, but in some cases trauma plays a role.

Fetal Membranes in Twins

Arrangement of fetal membranes in twins varies considerably, depending on the type of twins and on the time of separation of **monozygotic twins.**

- **DIZYGOTIC TWINS**

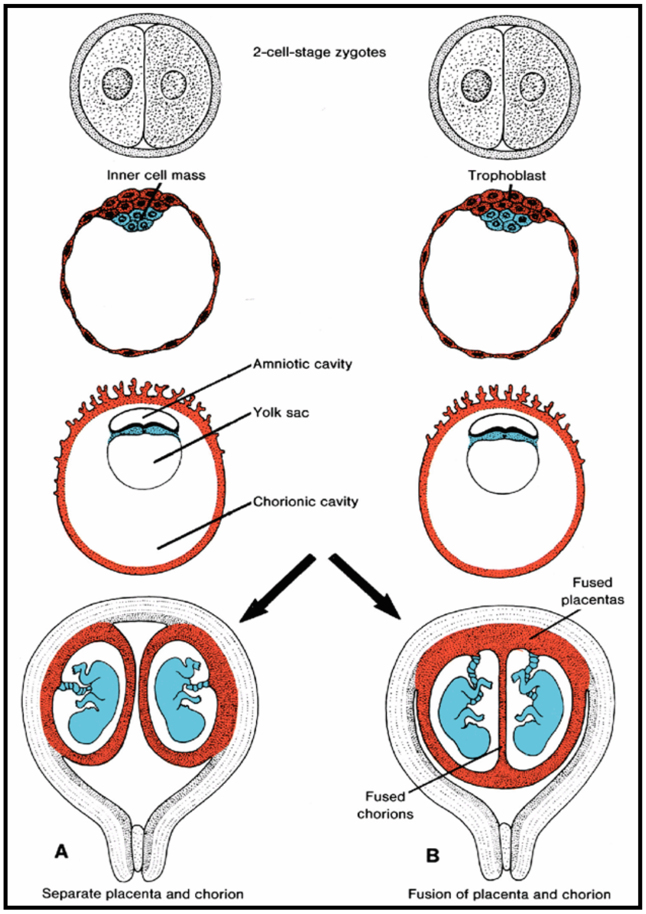
Approximately two-thirds of twins are **dizygotic,** or **fraternal,** and their incidence of 7 to 11 per 1000 births increases with maternal age. They result from simultaneous shedding of two oocytes and fertilization by different spermatozoa. Since the two zygotes have totally different genetic constitutions, the twins have no more resemblance than any other brothers or sisters. They may or may not be of different sex. The zygotes implant individually in the uterus, and usually each develops its own placenta, amnion, and chorionic sac.

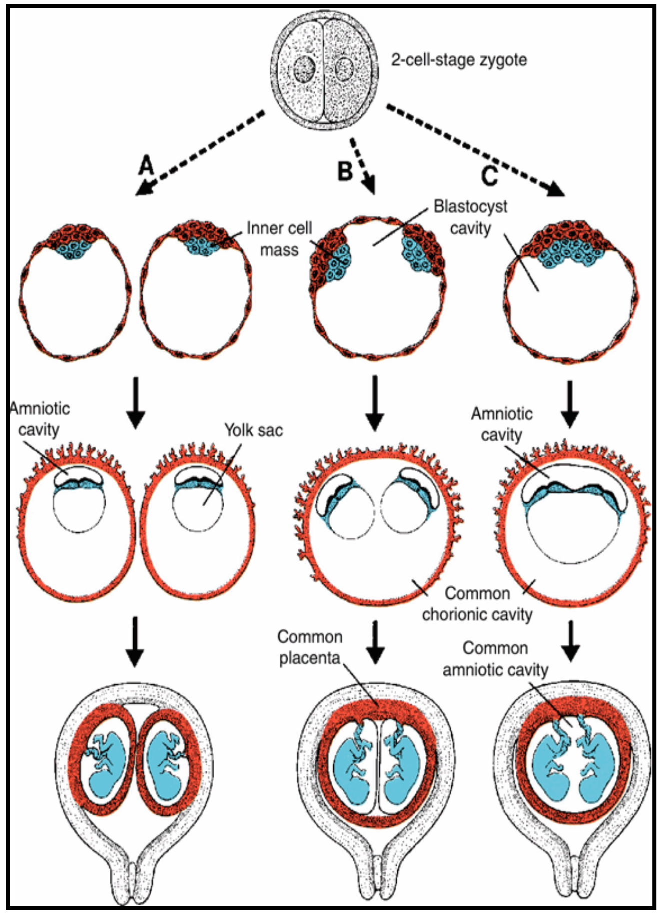
Sometimes, however, the two placentas are so close together that they fuse. Similarly, the walls of the chorionic sacs may also come into close apposition and fuse. Occasionally, each dizygotic twin possesses red blood cells of two different types (**erythrocyte mosaicism**), indicating that fusion of the two placentas was so intimate that red cells were exchanged.

- **MONOZYGOTIC TWINS**

The second type of twins, which develops from a single fertilized ovum, is **monozygotic,** or **identical, twins.** The rate for monozygotic twins is 3 to 4 per 1000. They result from splitting of the zygote at various stages of development. The earliest separation is believed to occur at the two-cell stage, in which case two separate zygotes develop. The blastocysts implant separately, and each embryo has its own placenta and chorionic sac. Although the arrangement of the membranes of these twins resembles that of dizygotic twins, the two can be recognized as partners of a monozygotic pair by their strong resemblance in blood groups, fingerprints, sex, and external appearance, such as eye and hair color.

Splitting of the zygote usually occurs at the early blastocyst stage. The inner cell mass splits into two separate groups of cells within the same blastocyst cavity. The two embryos have a common placenta and a common chorionic cavity, but separate amniotic cavities. In rare cases the separation occurs at the bilaminar germ disc stage, just before the appearance of the primitive streak. This method of splitting results in formation of two partners with a single placenta and a common chorionic and amniotic sac. Although the twins have a common placenta, blood supply is usually well balanced. Although triplets are rare (about 1/7600 pregnancies), birth of quadruplets, quintuplets, and so forth is rarer. In recent years multiple births have occurred more frequently in mothers given gonadotropins (fertility drugs) for ovulatory failure.





C L I N I C A L C O R R E L A T E S

- **Twin Defects**

Twin pregnancies have a high incidence of perinatal mortality and morbidity and a tendency toward preterm delivery. Approximately 12% of premature infants are twins and twins are usually small at birth. Low birth weight and prematurity place infants of twin pregnancies at great risk, and approximately 10 to 20% of them die, compared with only 2% of infants from single pregnancies.

The incidence of twinning may be much higher, since twins are conceived more often than they are born. Many twins die before birth and some studies indicate that only 29% of women pregnant with twins actually give birth to two infants. The term **vanishing twin** refers to the death of one fetus. This disappearance, which occurs in the first trimester or early second trimester, may result from resorption or formation of a **fetus papyraceus**. Another problem leading to increased mortality among twins is the **twin transfusion syndrome,** which occurs in 5 to 15% of monochorionic monozygotic pregnancies. In this condition, placental vascular anastomoses, which occur in a balanced arrangement in most monochorionic placentas, are formed so that one twin receives most of the blood flow and flow to the other is compromised. As a result, one twin is larger than the other. The outcome is poor, with the death of both twins occurring in 60 to 100% of cases.

At later stages of development, partial splitting of the primitive node and streak may result in formation of **conjoined (Siamese) twins.** These twins are classified according to the nature and degree of union as **thoracopagus** (*pagos*, fastened); **pygopagus;** and **craniopagus**. Occasionally, monozygotic twins are connected only by a common skin bridge or by a common liver bridge. The type of twins formed depends upon when and to what extent abnormalities of the node and streak occurred. Many conjoined twins have survived.

➢ Parturition (Birth)

For the first 34 to 38 weeks of gestation, the uterine myometrium does not respond to signals for **parturition (birth)**. However, during the last 2 to 4 weeks of pregnancy, this tissue undergoes a transitional phase in preparation for the onset of **labor.** Ultimately, this phase ends with a thickening of themyometrium in the upper region of the uterus and a softening and thinning of the lower region and cervix.

Labor itself is divided into three stages: 1) **effacement** (thinning and shortening) and dilatation of the cervix; this stage ends when the cervix is fully dilated; 2) **delivery**

of the fetus; and 3) **delivery of the placenta and fetal membranes.** Stage 1 is produced by uterine contractions that force the amniotic sac against the cervical canal like a wedge or, if the membranes have ruptured, then pressure will be exerted by the presenting part of the fetus, usually the head. Stage 2 is also assisted by uterine contractions, but the most important force is provided by increased intra-abdominal pressure from contraction of abdominal muscles. Stage 3 requires uterine contractions and is aided by increasing intra-abdominal pressure.

As the uterus contracts, the upper part retracts creating a smaller and smaller lumen, while the lower part expands, thereby producing direction to the force. Contractions usually begin about 10 minutes apart; then, during the second stage of labor, they may occur less than 1 minute apart and last from 30 to 90 seconds. Their occurrence in pulses is essential to fetal survival, since they are of sufficient force to compromise uteroplacental blood flow to the fetus.

C L I N I C A L C O R R E L A T E S

- ### Preterm Birth

Factors initiating labor are not known and may involve: **"retreat from maintenance of pregnancy"** in which pregnancy supporting factors (e.g., hormones, etc.) are withdrawn; or **active induction** caused by stimulatory factors targeting the uterus. Probably, components of both phenomena are involved.

Unfortunately, a lack of knowledge about these factors has restricted progress in preventing **preterm birth.** Preterm birth (delivery before 34 weeks) of premature infants is the second leading cause of infant mortality in the United States and also contributes significantly to morbidity. It is due to premature rupture of the membranes, premature onset of labor, or pregnancy complications requiring premature delivery. Maternal hypertension and diabetes as well as abruption placenta are risk factors. Maternal infections, including bacterial vaginosis, are also associated with an increased risk.