Third Month to Birth

The Fetus & Placenta

Development Of The Fetus

Fetal period

- 9th week to birth
- tissues & organs maturation
- rapid growth of the body

- **crown rump length (CRL)** (sitting height)
- **crown-heel length (CHL)** (standing height)

TABLE 8.1 *Growth in Length and Weight During the Fetal Period*

Age (Wk)	CRL (cm)	Weight (g)
9–12	5–8	10–45
13–16	9–14	60–200
17–20	15–19	250–450
21–24	20–23	500–820
25–28	24–27	900–1,300
29–32	28–30	1,400–2,100
33–36	31–34	2,200–2,900
37–38	35–36	3,000–3,400

- Growth in length third, 4th , 5th months
- Weight increase in during the last 2 months of gestation

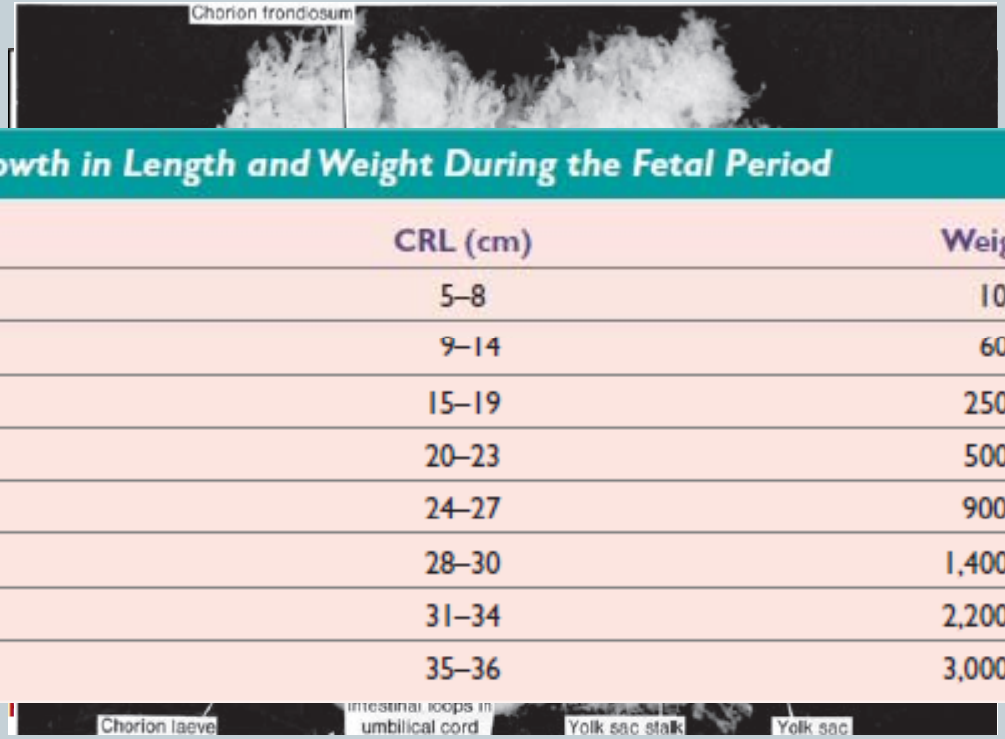
pregnancy length;

- **280 days, or 40 weeks after** LNMP
- **266 days or 38 weeks after fertilizationes**

Monthly Changes

Head growth slowdown

- third month begining, the head half of the CRL
- 5th month beginning, the head about 1/3 of the CHL
- at birth, head about 1/4 of the CHL



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21–24	20–23	500–820
25–28	24–27	900–1,300
29–32	28–30	1,400–2,100
33–36	31–34	2,200–2,900
37–38	35–36	3,000–3,400

Monthly Changes

third month, the face becomes more human looking (Figs. 8.3 and 8.4). The

- Eyes
- Ears
- The limbs length

the 12th week.

- **Primary ossification centers** (long bones & skull)
- external genitalia development (ultrasound)
- **intestinal loops have** withdrawn into the abdominal cavity
- muscular activity.

During the **4th & 5th months, the** fetus lengthens rapidly

- CRL at end of first half of intrauterine life, 15 cm
- end of the 5th month 500 g weight
- **lanugo hair; eyebrows**
- **During the 5th month, fetus movements felt by mother**
- **weight increases** during the last 2.5 months,

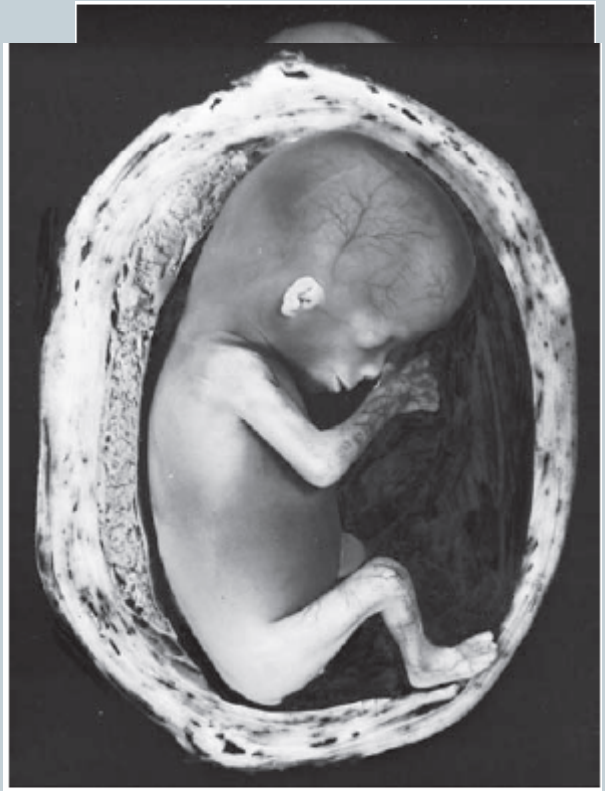


Figure 8.4 A 12-week fetus in utero. Note the extremely thin skin and underlying blood vessels. The face has all of the human characteristics, but the ears are still primitive. Movements begin at this time but are usually not felt by the mother.

Monthly Changes

During the sixth month

- reddish & wrinkled fetus skin, lack of underlying connective tissue
- the respiratory system & CNS have not differentiated sufficiently

During the last 2 months

- fetus obtains well-rounded contours
- Deposition of subcutaneous fat

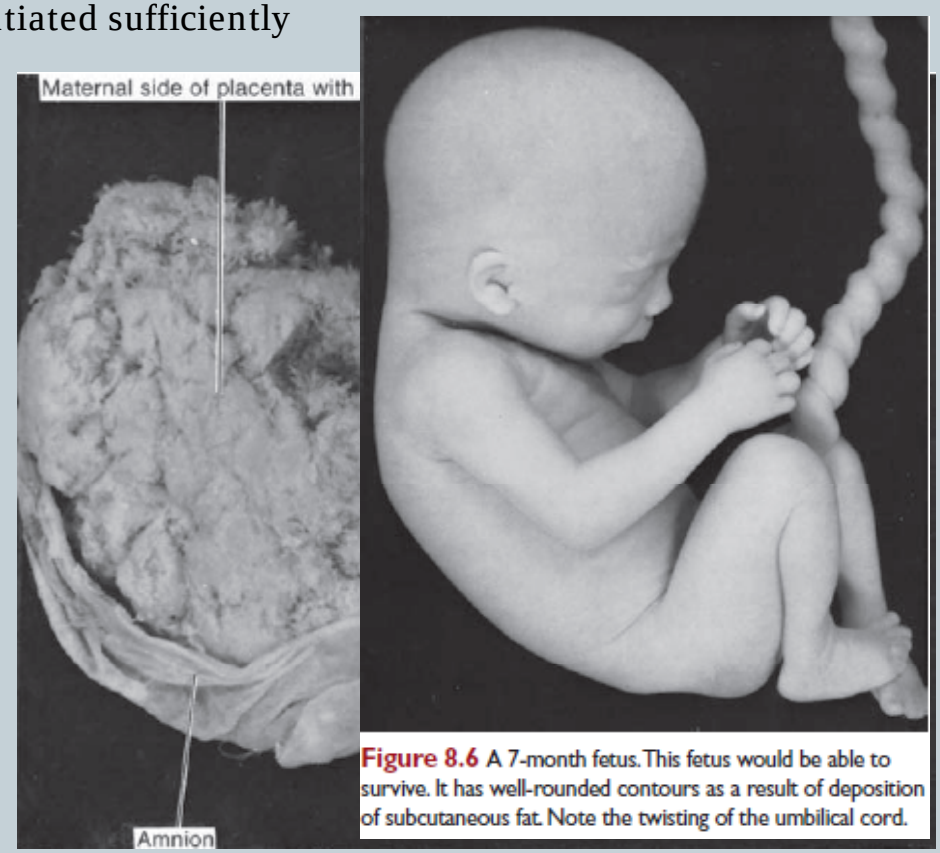


Figure 8.6 A 7-month fetus. This fetus would be able to survive. It has well-rounded contours as a result of deposition of subcutaneous fat. Note the twisting of the umbilical cord.

vernix caseosa

- sebaceous glands secretory products

end of the ninth month

- the skull (largest circumference of the body

At the time of birth
normal fetus

- weight 3,000 to 3,400 gr
- CRL is about 36 cm
- CHL is about 50 cm
- Pronounced Sexual characteristics and the testes should be in the scrotum.

TABLE 8.2 *Developmental Horizons During Fetal Life Event*

	Age (Wk)
Taste buds appear	7
Swallowing	10
Respiratory movements	14–16
Sucking movements	24
Some sounds can be heard	24–26
Eyes sensitive to light[a]	28

[a]Recognition of form and color occurs postnatally.

Time of Birth

- 266 days, or 38 weeks, after fertilization
- **280 days or 40 weeks from the first day of the LNMP**
- bleeding about 14 days after fertilization

- Most fetuses are born within 10 to 14 days
- **premature;**
- **postmature.**

during the 7th to 14th weeks

- **ultrasound** (1 to 2 days) CRL measurement

16th to 30th weeks are

- **biparietal diameter (BPD)**
- **Head** circumference
- **Abdominal** circumference
- **femur length**

Clinical points

Low birth weight (gestational age independent)

- 2500-4000 gr
- 51 Cm
- Preterm

Clinical points

IUGR or SGA (gestational age dependent)

- 10%
- Neurological problems
- Congenital malformation
- Meconium aspiration
- Hypoglycemia & hypocalcemia
- Respiratory distress syndrome (RDS)

After birth (Barkers hypothesis)

- Metabolic disorders (obesity, hypertension, hypercholesterolemia, cardiovascular d., diabetes 2

Higher in black people

Causes:

- Chromosomal abnormalities
- Teratogens
- Congenital infections (rubella, cytomegalovirus, toxoplasmosissyphlis)
- Poor maternal health (hypertension, renal & cardiac diseases)
- Mothers nutrition & socioeconomic levels
- Cigarettes & alcohol & drugs
- Placental insufficiency
- Multiple birth

Clinical points

Fetal Period

- Growth promoting factor
- Insulin like growth factor 1 (IGF-1)
- IGF-1 gene mutation cause IUGR
- Permanent

After birth

- GH
- GH-GHR produce IGF-1
- GHR mutation Laron dwarfism
- No IUGR

Fetal membrane & placenta

Placenta

- Facilitate nutrients & gas exchange

Beginning of 9th week

- Major changes
- Increase in surface area between fetus & mother

Fetal membrane status change:

- Increase in amniotic fluid production

Change in the trophoblast

fetal part of Placenta

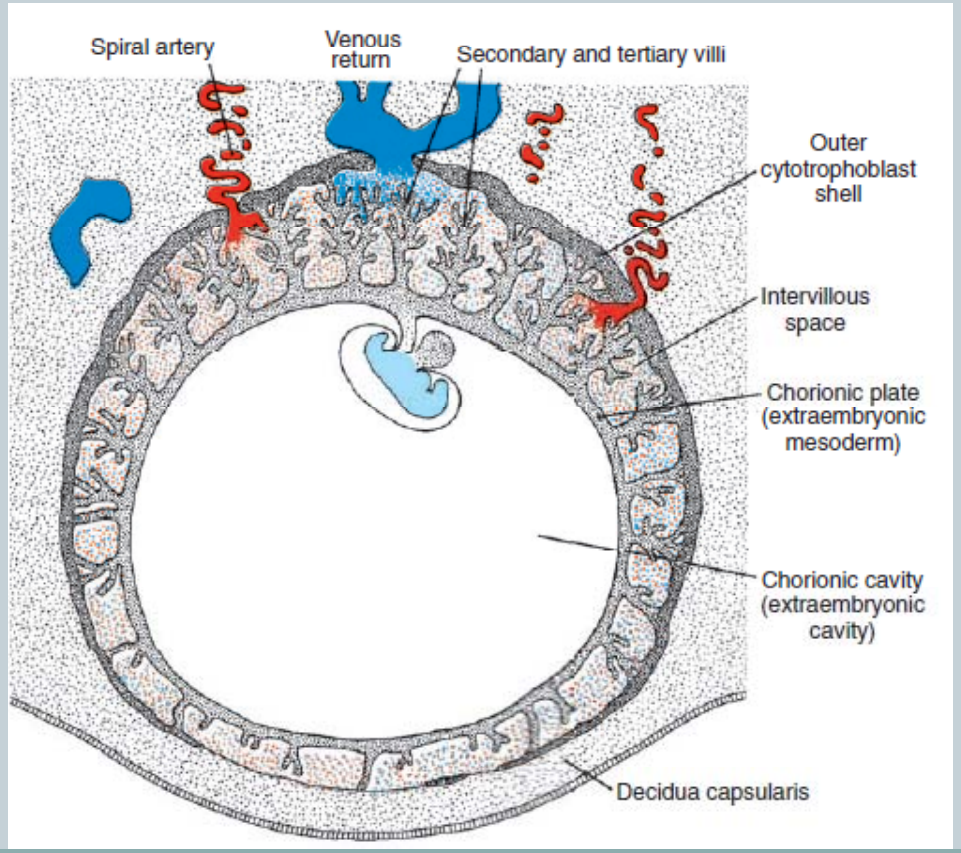
- Trophoblast
- Extraembryonic mesoderm (chorionic plate)

Maternal part of Placenta

- Uterus endometrium

Beginning of second month

- secondary & tertiary villi
- (radial appearance)



Change in the trophoblast

- **Beginning of 4th month**

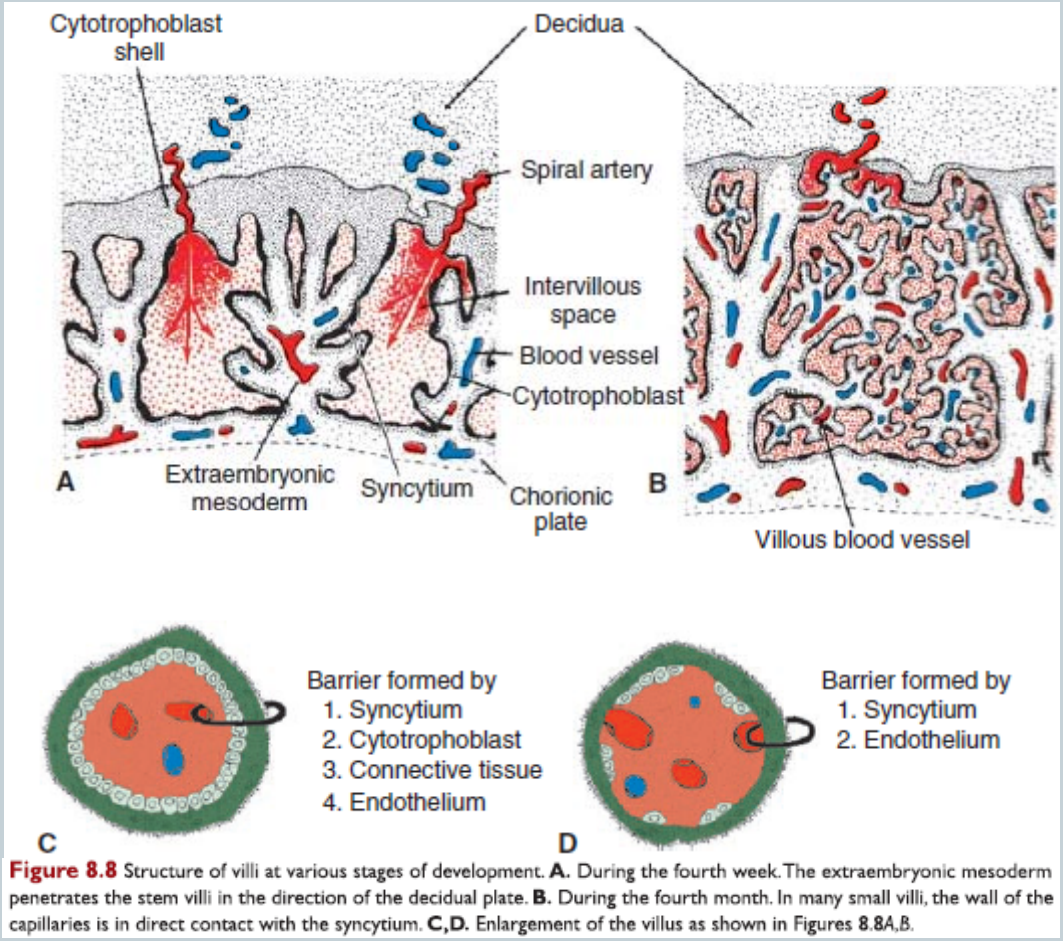


Figure 8.8 Structure of villi at various stages of development. **A.** During the fourth week. The extraembryonic mesoderm penetrates the stem villi in the direction of the decidual plate. **B.** During the fourth month. In many small villi, the wall of the capillaries is in direct contact with the syncytium. **C,D.** Enlargement of the villus as shown in Figures 8.8*A,B*.

Clinical point (preeclampsia)

Maternal hypertension

Proteinuria

5%

Eclampsia (seizures)

Suddenly 20th week

- Fetal growth retardation
- Fetal death
- Mother death
- Early delivery (preterm birth)

Unknown

Trophoblast disorder (Incomplete differentiation of cytotrophoblast from epithelial to endothelial)

- Preeclampsia in previous pregnancy
- Nulliparity (First pregnancy)
- Obesity family history
- Multiple gestation
- Mother medical conditions (hypertension & diabets)
- Commonly in women with hydatiidform moles

Chorion frondosum & desidua basalis

Embryonic part of Placenta

Embryonic pole

- Chorion frondosum

Mother part of placenta

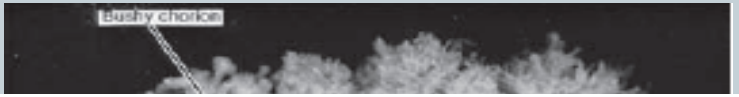
Abembryonic pole

- Chorion laeve (third month)

Decidua

- Desid Decidua basalis (embryonic pole)
- Decidua capsularis (abembryonic pole)
- Decidua parietalis

Amniochorionic membrane



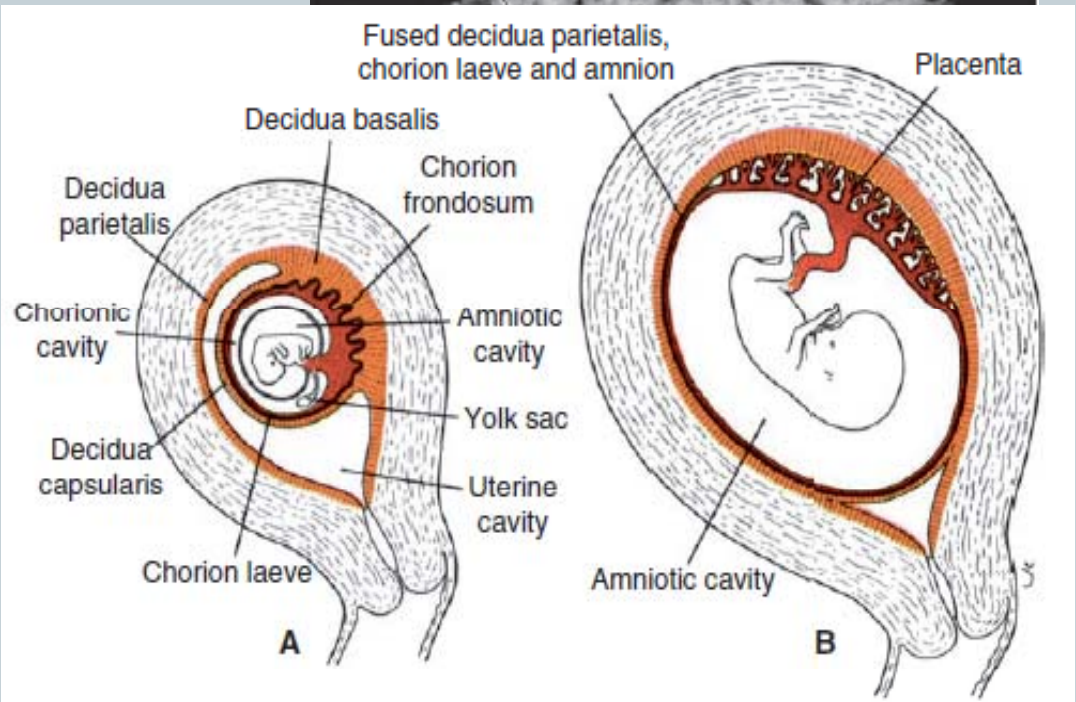


Figure 8.10 Relation of fetal membranes to wall of the uterus. **A.** End of the second month. Note the yolk sac in the chorionic cavity between the amnion and chorion. At the abembryonic pole, villi have disappeared (chorion laeve). **B.** End of the third month. The amnion and chorion have fused, and the uterine cavity is obliterated by fusion of the chorion laeve and the decidua parietalis.

the embryonic pole in contrast to small villi at the abembryonic pole. Note the connecting stalk and yolk sac with its extremely long vitelline duct.

Structure of the placenta

Beginning of 4th month

Placenta:

(1) **fetal portion** (chorion frondosum)

(2) **maternal portion** (decidua basalis)

4th & 5th month

Decidual septa

Cotyledons

Placenta 15-30% uterus

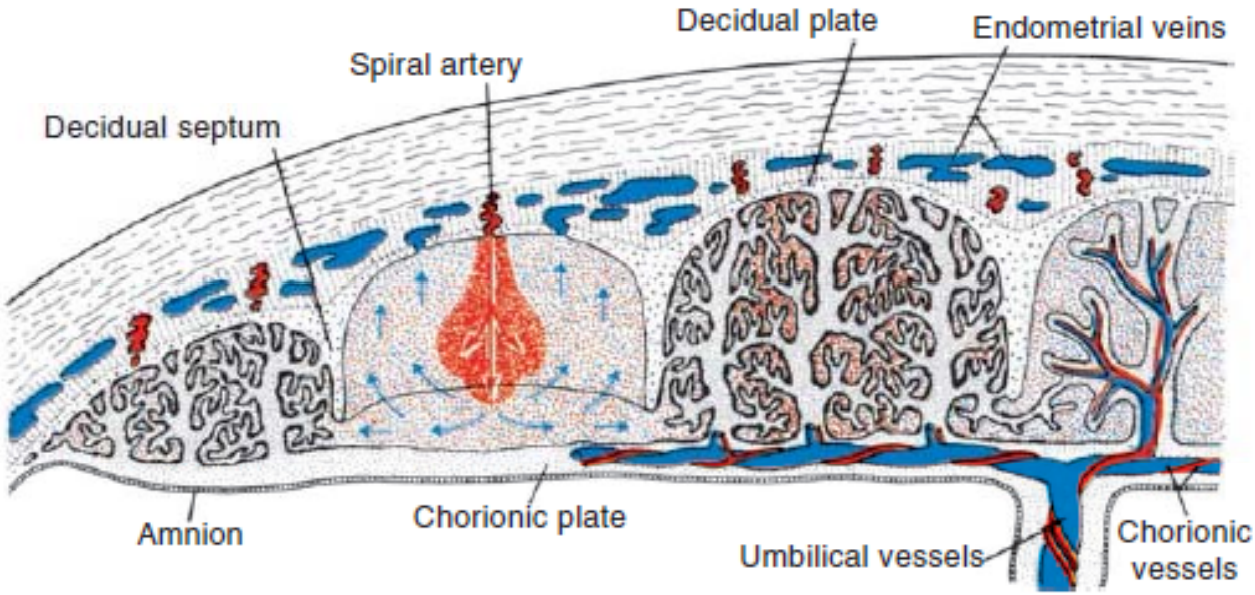


Figure 8.13 The placenta in the second half of pregnancy. The cotyledons are partially separated by the decidual (maternal) septa. Most of the intervillous blood returns to the maternal circulation by way of the endometrial veins. A small portion enters neighboring cotyledons. The intervillous spaces are lined by syncytium.

Full-Term Placenta

- Discoid
- 15 to 25 cm
- 3 cm thick
- 500 to 600 g weight

maternal side

- 15 to 20 slightly cotyledons
- covered by a thin layer of decidua basalis

fetal surface

- Covered by the chorionic plate

- Eccentric or marginal

junction of umbilical cord

velamentous insertion

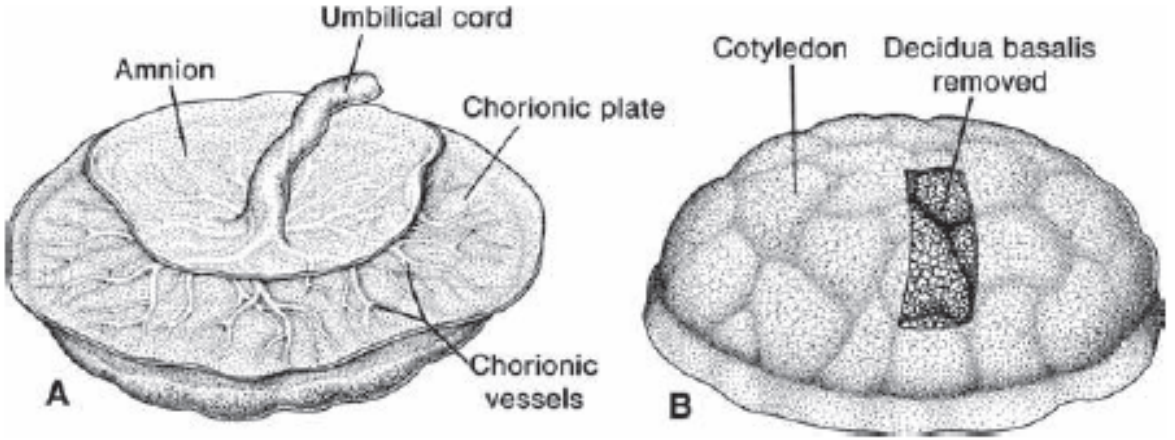


Figure 8.14 A full-term placenta. **A.** Fetal side. The chorionic plate and umbilical cord are covered by amnion. **B.** Maternal side showing the cotyledons. In one area, the decidua has been removed. The maternal side of the placenta is always carefully inspected at birth, and frequently one or more cotyledons with a whitish appearance are present because of excessive fibrinoid formation and infarction of a group of intervillous lakes.

Circulation of the Placenta

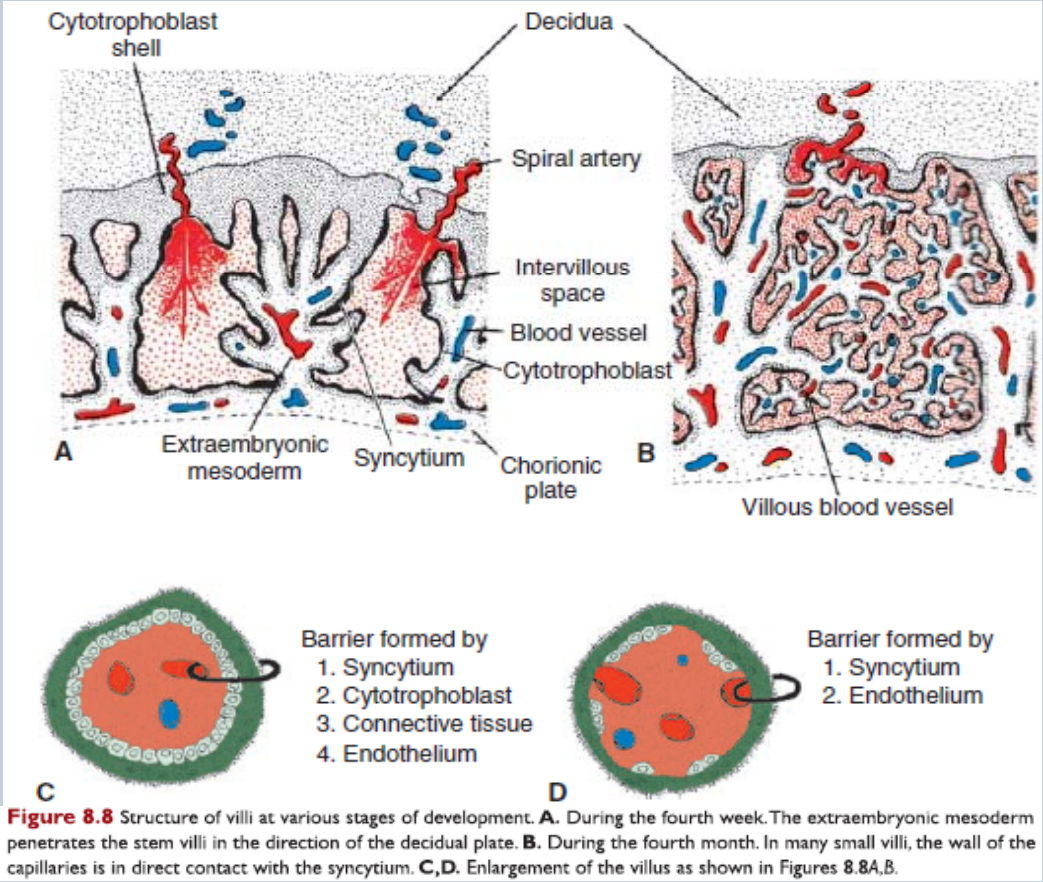
- 80 to 100 spiral arteries pierce the decidual plate
- enter the intervillous spaces
- approximately 150 mL
- 3 or 4 times in min
- 4-14 m^2

Placental membrane

1. Endothelial linning of fetal vessel
2. Connective tissue
3. Cytotriphoblast
4. Syncytiotrophoblast

- Placental barrier

- **Hemochorial type**



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Function of the placenta

1. Metabolit exchange (nutrient, IgG on 14th week)
   (embryo produce compelement end of thid month. IgG after birth but not enough until 3 years)

2. Gas exchange (20-30 ml O2/min)

3. Hormone production (syncytiotrophoblast)

- Progesteron(end of 4th month)
- Esteriol (uterine growth & mammary glands development)
- hCG (first 2 monthes)
- Somatomammotropin (placental lactogen)

Embryo priority for glucose consumption

Breast development for milk production

Clinical Correlates

Erythroblastosis Fetalis and Fetal Hydrops

Because some fetal blood cells escape across the placental barrier, there is a potential for these cells to elicit an antibody response by the mother's immune system. The basis for this response is the fact that more than 400 red blood cell antigens have been identified, and although most do not cause problems during pregnancy, some can stimulate a maternal antibody response against fetal blood cells. This process is an example of **isoimmunization**, and if the maternal response is sufficient, the antibodies will attack and hemolyze fetal red blood cells, resulting in **hemolytic disease of the fetus and newborn**. Previously, the disease was called **erythroblastosis fetalis** because in some cases severe hemolysis stimulated an increase in production of fetal blood cells called **erythroblasts**. However, this severity of anemia occurs only in a few cases such that hemolytic disease of the fetus and newborn is a more appropriate terminology. In rare cases, the anemia becomes so severe that **fetal hydrops** (edema and effusions into the body cavities) occurs, leading to fetal death (Fig. 8.15). Most severe cases are caused by antigens from the **CDE (Rhesus)** blood group system. The D or **Rh antigen** is the most dangerous, because immunization can result from a single exposure and occurs earlier and with greater severity with each succeeding pregnancy. The maternal antibody response occurs in cases when the fetus is D(Rh) positive and the mother is D(Rh) negative and is elicited when fetal red blood cells enter the maternal system because of small areas of bleeding at the surface of placental villi or at birth. This condition can be prevented by screening women at their first prenatal visit for Rh blood type and for the presence of anti-D antibodies to determine if she has been sensitized previously. In Rh-negative women without anti-D antibodies, recommendations include treatment with Rh immunoglobulin at 28 weeks' gestation; following times when fetal-maternal mixing of blood may have occurred (e.g., after amniocentesis or pregnancy loss); and after delivery if the newborn is found to be Rh positive. Since the introduction of Rh immunoglobulin in 1968, hemolytic disease in the fetus and newborn in the United States has almost been eliminated.

Antigens from the **ABO blood group** can also elicit an antibody response, but the effects are much milder than those produced by the CDE group. About 20% of all infants have an ABO maternal incompatibility, but only 5% will be clinically affected. These can be effectively treated postnatally.

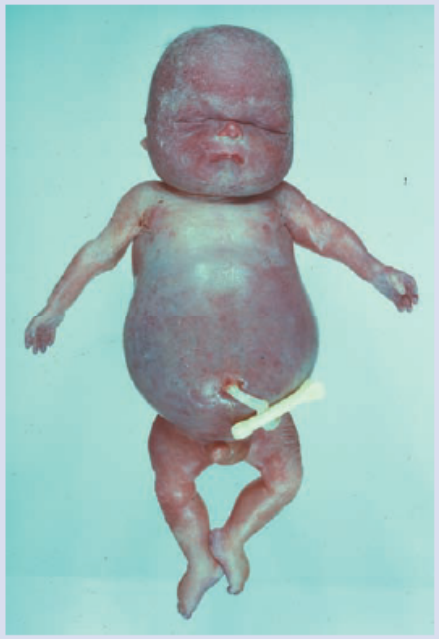

Figure 8.15 Fetal hydrops caused by the accumulation of fluid in fetal tissues.

Clinical Correlates

The Placental Barrier

Maternal steroidal hormones readily cross the placenta. Other hormones, such as thyroxine, do so only at a slow rate. Some synthetic progestins rapidly cross the placenta and may masculinize female fetuses. Even more dangerous was the use of the synthetic estrogen **diethylstilbestrol (DES)**, which easily crosses the placenta. This compound produced clear-cell carcinoma of the vagina and abnormalities of the cervix and uterus in females and in the testes of males in individuals who were exposed to the compound during their intrauterine life (see Chapter 9).

Although the placental barrier is frequently considered to act as a protective mechanism against damaging factors, many viruses—such as rubella, cytomegalovirus, Coxsackie, variola, varicella, measles, and poliomyelitis virus—traverse the placenta without difficulty. Once in the fetus, some viruses cause infections, which may result in cell death and birth defects (see Chapter 9).

Unfortunately, most drugs and drug metabolites traverse the placenta without difficulty, and many cause serious damage to the embryo (see Chapter 9). In addition, maternal use of heroin and cocaine can cause habituation in the fetus.

Amnion & umbilical cord

On 5th week

Primitive ambilical ring

(1)Connecting stalk (allantois ,two arteries & one vein)

(2) yolk stalk (vitelline duct)

(3) the connecting canal (Intra & extraembryonic cavities)

Primitive umbilical cord

1 & 2

Umbilical vessels & Wharton's jelly

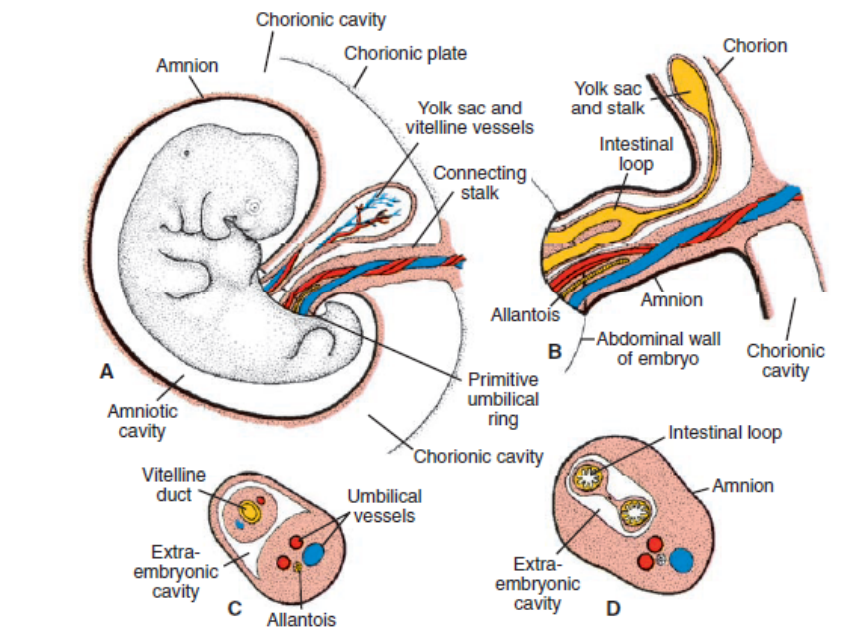

Figure 8.16 **A.** A 5-week embryo showing structures passing through the primitive umbilical ring. **B.** The primitive umbilical cord of a 10-week embryo. **C.** Transverse section through the structures at the level of the umbilical ring. **D.** Transverse section through the primitive umbilical cord showing intestinal loops protruding in the cord.

Placental changes at the & of pregnancy

Exchange reduction

1. Increase in fibrous tissue in villus core
2. thickening of basement membrane in fetal capillaries
3. Obliterative changes in villus capillaries
4. Fibrinoid deposition on villus sueface

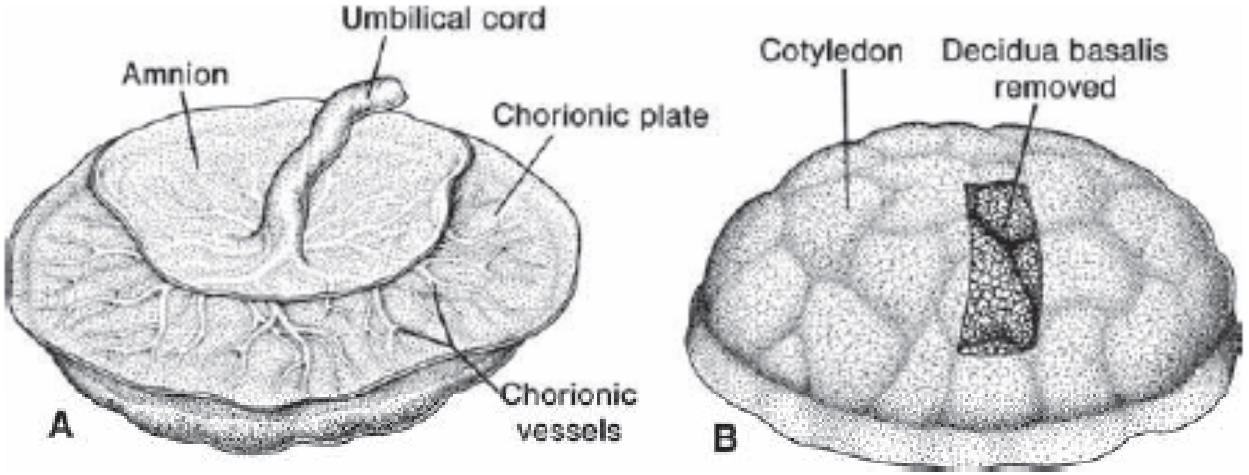

Figure 8.14 A full-term placenta. **A.** Fetal side. The chorionic plate and umbilical cord are covered by amnion. **B.** Maternal side showing the cotyledons. In one area, the decidua has been removed. The maternal side of the placenta is always carefully inspected at birth, and frequently one or more cotyledons with a whitish appearance are present because of excessive fibrinoid formation and infarction of a group of intervillous lakes.

Amniotic fluid

- Amniotic cells
- Maternal blood

- 10th week: 30 ml
- 20th week: 450 ml
- 37th week: 800-1000 ml

Functions:

1. Absorb jolts
2. Prevention of embryo adherence to amnion
3. Fetal movement

fluid replacement: Each 3 h

Beginning of 5th month

Fetus swallows amniotic fluid (400ml)

5th month urine added to amniotic fluid

Clinical Correlates

Umbilical Cord Abnormalities

At birth, the umbilical cord is approximately 1 to 2 cm in diameter and 50 to 60 cm long. It is tortuous, causing **false knots**. Length of a cord reflects the amount of intrauterine movement of the fetus, and shortened cords have been observed in fetal movement disorders and with intrauterine constraint. 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 one in 200 newborns, however, only a **single umbilical 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 (Fig. 8.17). Origin of the bands is unknown.

Amniotic Fluid

Hydramnios or **polyhydramnios** is the term used to describe an excess of amniotic fluid (1,500 to 2,000 mL), whereas **oligohydramnios** refers to a decreased amount (<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. The lack of fluid in the amniotic cavity may constrict the fetus and cause club foot or there may be too little fluid for the fetus to "breathe" into its lungs resulting in lung hypoplasia.

Premature rupture of the membranes (PROM) refers to rupture of the membranes before uterine contractions begin and occurs in 10% of pregnancies. **Preterm** PROM occurs before 37 completed weeks of pregnancy, occurs in 3% of pregnancies, and is a common cause of preterm labor. Causes of preterm PROM are unknown, but risk factors include a previous pregnancy affected by prematurity or PROM, black race, smoking, infections, and severe polyhydramnios.

(continued on following page)

Clinical Correlates

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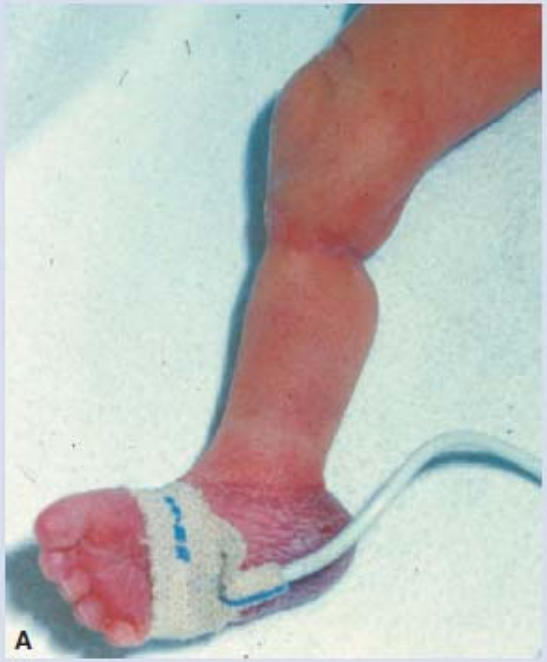

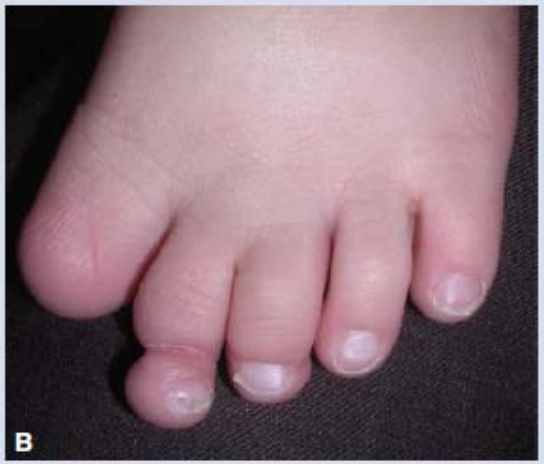

Hydraminos

- More than 1500- 2000 ml
- 35% idiopathic
- 25% maternaldiabetes
- Central nervous sys. Defects (anancephaly)
- Gastrointestinal defects (osophageal atresia)

Oligohydraminos

- rare
- Renal agenesia

Club foot

Little fluid for breath (lung hypoplasia)

Premature rupture of membrane (PROM)

- 10%

Preterm PROM

- before 37 weeks
- 3%
- Common cause of preterm labor
- Unknown
- Previous pregnancy with PROM
- Black race
- Smoking
- Infection
- Severe hydraminos

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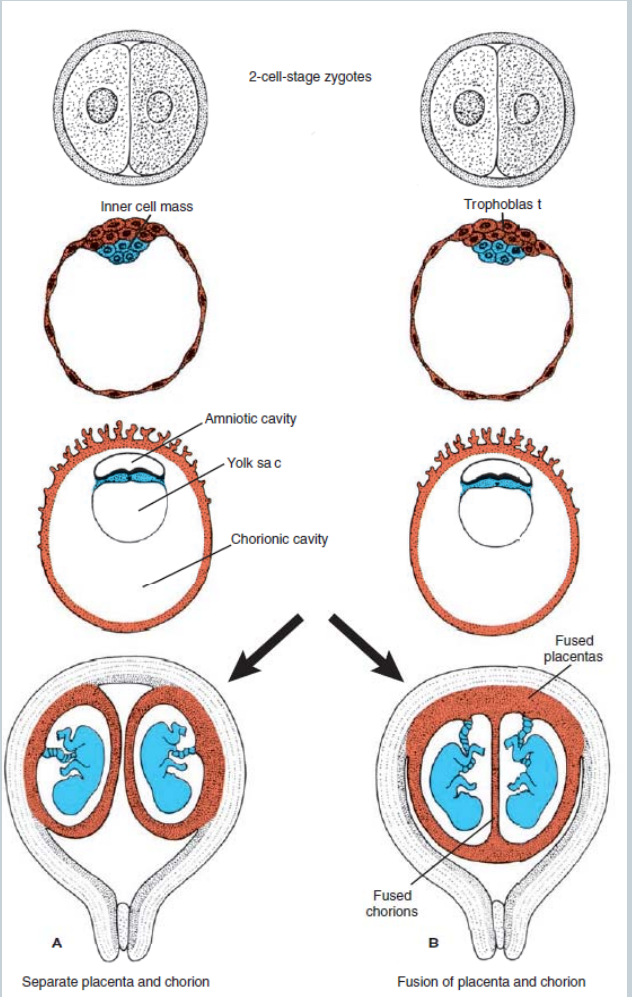
Fetal membrane in twins

- 90% dizygotic (fraternal)

Increas in dizygotic twins:

- Maternal age increase
- ART

- Erythrocyte mosaicism



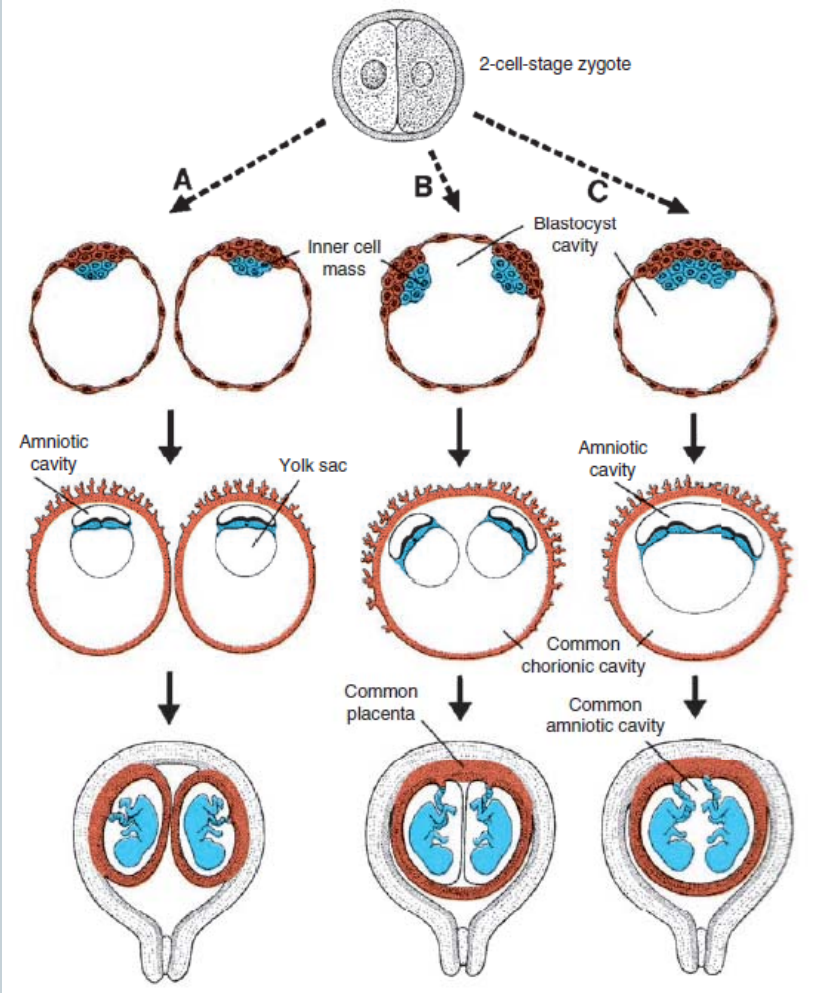
Fetal membrane in twins

- Monozygotic (identical)
- 3-4 in 1000

1. 2 cells embryo (A)
2. Blastocyst (more common) (B)
3. Bilaminar disc (C)

Triplet

1 in 7,600



Clinical Correlates

Abnormalities Associated with Twins

Twin pregnancies have a high incidence of perinatal mortality and morbidity and an increased risk for preterm delivery. Approximately 60% of twins are born preterm and also have a high incidence of being low birth weight. Both of these factors put twin pregnancies at great risk and twin pregnancies have an infant mortality rate three times higher than that for singletons.

The incidence of twinning may be much higher than the number observed at birth because 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 the early second trimester, may result from resorption or formation of a fetus papyraceus (Fig. 8.20).

Another problem leading to increased mortality among twins is twin–twin transfusion syndrome, which occurs in 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 (Fig. 8.21). The outcome is poor, with the death of both twins occurring in 50% to 70% of cases.

At later stages of development, partial splitting of the primitive node and streak may result in formation of conjoined twins. These twins are classified according to the nature and degree of their union (Figs. 8.22 and 8.23). Occasionally, monozygotic twins are connected only by a common skin bridge or by a common liver bridge. The type of twins formed depends on when and to what extent abnormalities of the node and streak occurred. Misexpression of genes, such as Goosecoid, may also result in conjoined twins. Many conjoined twins have survived, including the most famous pair, Chang and Eng, who were joined at the abdomen and who traveled to England and the United States on exhibitions in the mid-1800s. Finally settling in North Carolina, they farmed and fathered 21 children with their two wives.

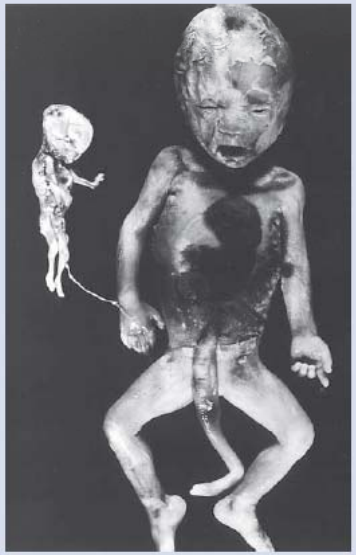


Figure 8.20 Fetus papyraceus. One twin is larger, and the other has been compressed and mummified, hence the term *papyraceus*.

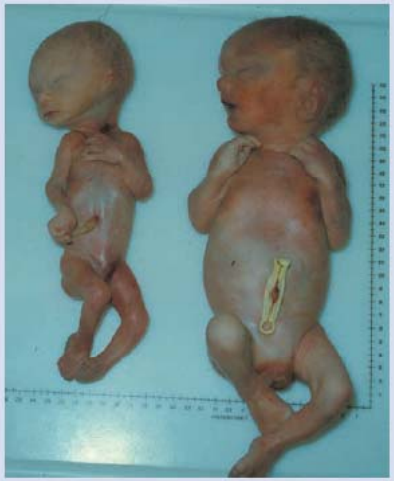


Figure 8.21 Monozygotic twins with twin transfusion syndrome. Placental vascular anastomoses produced unbalanced blood flow to the two fetuses.

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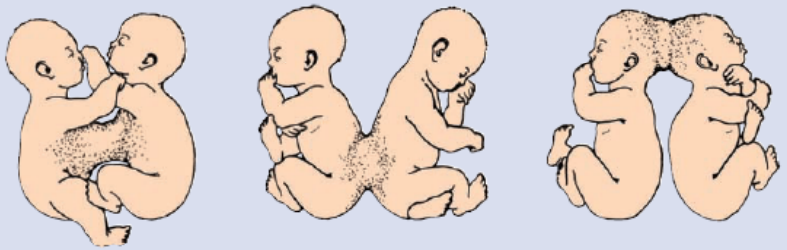
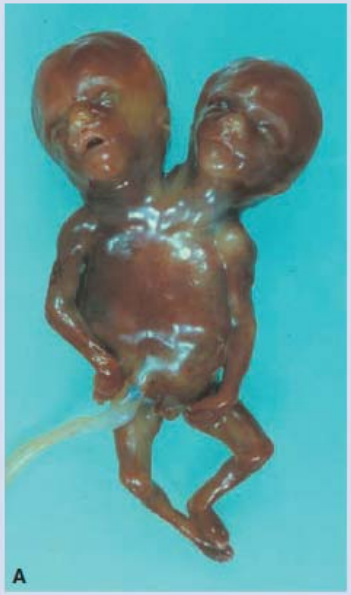


Figure 8.22 Thoracopagus, pygopagus, and craniopagus twins (*pagus;* fastened). Conjoined twins can be separated only if they have no vital parts in common.



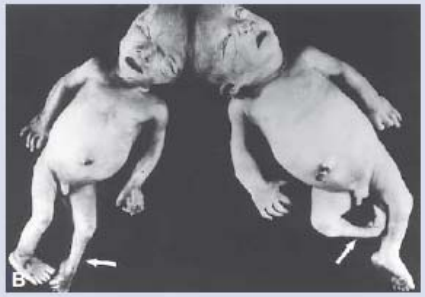


Figure 8.23 Examples of conjoined twins. **A.** Dicephalus (two heads). **B.** Craniopagus (joined at the head and thorax).

In brother sister pairs of dizygotic twins, testosterone from the male twin can affect development of the female. Thus, females in such pairs tend to have square jaws, larger teeth, perform better on spacial-ability tests and have better ball skills than most girls. They are 15% less likely to get married and they have fertility problems, producing 25% fewer children.

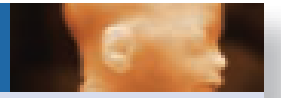
Parturition (birth)

- During last 2 to 4 weeks of pregnancy

Labor:

1. Effacement (cervix thining, shortening & dilatation)
2. Fetus delivery
3. Placenta & fetal membrane delivery

Clinical Correlates



Preterm Birth

Factors initiating labor are not known and may involve "**retreat from maintenance of pregnancy**," in which pregnancy-supporting factors (e.g., hormones) 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 37 completed weeks) of **premature infants** occurs in approximately 12% of births in the United States and is a leading cause of infant mortality and also contributes significantly to morbidity. It is caused by preterm PROM, premature onset of labor, or pregnancy complications requiring premature delivery. Risk factors include previous preterm birth, black race; multiple gestations; infections, such as periodontal disease and bacterial vaginosis; and low maternal body-mass index.