

# Third Month to Birth



## The Fetus & Placenta

# Development Of The Fetus



## Fetal period

- 9<sup>th</sup> week to birth
- tissues & organs amaturation
- rapid growth of the body
  
- **crown rump length (CRL)** (sitting height)
- **crown-heel length (CHL)** (standing height)
  
- Growth in length during 3<sup>rd</sup> , 4<sup>th</sup> , 5<sup>th</sup> month
- Increase weight during the last 2 months of gestation

## pregnancy length;

- 280 days, or 40 weeks after LNMP
- 266 days or 38 weeks after fertilization

**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

# Monthly Changes



## Head growth slowdown

- beginning at the third month = the head half of the CRL
- beginning at the 5<sup>th</sup> month the head = about 1/3 of the CHL
- at birth = head about 1/4 of the CHL



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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

A

Fig

# Monthly Changes

## *third month, the face becomes more human looking*

- The Eyes = initially directed laterally, move to the ventral aspect of the face
- the ears = come to lie close to their definitive position at the side of the head
- The limbs length increase

## *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- intestinal loops have withdrawn into the abdominal cavity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 4<sup>th</sup> & 5<sup>th</sup> months, the fetus lengthens rapidly*

- CRL at end of first half of intrauterine life, 15 cm
- end of the 5<sup>th</sup> month 500 g weight
- **lanugo hair; eyebrows**
- **During the 5<sup>th</sup> 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 because lack of underlying connective tissue
- the respiratory system & CNS have not differentiated sufficiently

## During the last 2 months

- fetus obtains well-rounded contours  
Because Deposition of subcutaneous fat
- **vernix caseosa** :  
sebaceous glands secretion products

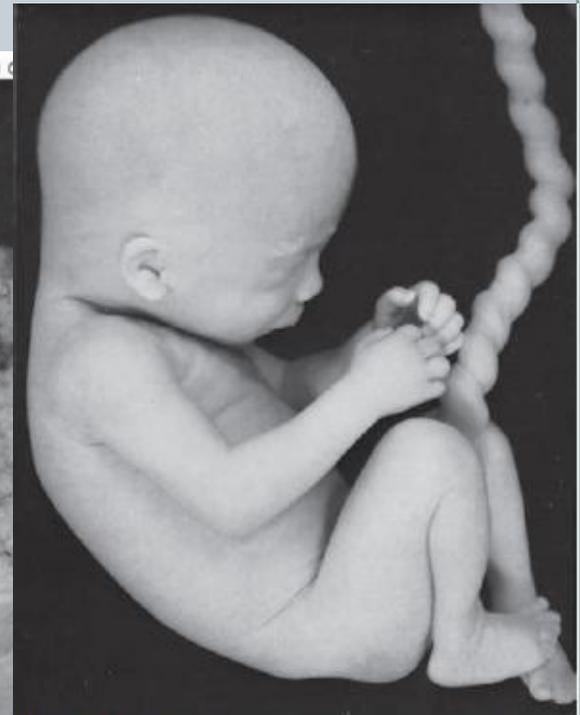
## end of the ninth month

- 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.



**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.

**TABLE 8.2** *Developmental Horizons During Fetal Life Event*

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

<sup>a</sup>Recognition of form and color occurs postnatally.

# Time of Birth

- 266 days, or 38 weeks, after fertilization
- The oocyte is usually fertilized within 12 hours of ovulation
- Sperm can survive up to 6 days in female tract
  
- 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 of the calculated delivery date
- premature
- post mature

## during the 7th to 14th weeks :

- ❖ **Ultrasound** can determine CRL measurement

## 16th to 30th weeks are:

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

## Clinical Correlates



### 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.

The average size of a newborn is 2,500 to 4,000 g (6 to 9 lb) with a length of 51 cm (20 in). The term **low birth weight (LBW)** refers to a weight <2,500 g, regardless of gestational age. Many infants weigh <2,500 g because they are **preterm** (born before 37 weeks of gestation). In contrast, the terms **intrauterine growth restriction (IUGR)** and **small for gestational age (SGA)** take into account gestational age.

**IUGR** is a term applied to infants who do not attain their optimal intrauterine growth. These infants are pathologically small and at risk for poor outcomes. Infants who are **SGA** have a birth weight that is below the 10th percentile for their gestational age. These babies may be pathologically small (they may have IUGR) or they may be constitutionally small (healthy, but smaller in size). The challenge is to differentiate the two conditions so that healthy, but small babies are not subjected to high-risk protocols used for babies with IUGR.

Approximately 1 in 10 babies have IUGR and therefore have an increased risk of neurological problems, congenital malformations, meconium aspiration, hypoglycemia, hypocalcemia, and respiratory distress syndrome (RDS). There are also long-term effects on these infants. For

example, babies with IUGR have been shown to have a greater chance as adults to develop a metabolic disorder later in life, such as obesity, hypertension, hypercholesterolemia, cardiovascular disease, and type 2 diabetes (called **Barker's hypothesis**).

The incidence of IUGR is higher in blacks than in whites. Causative factors include chromosomal abnormalities; teratogens; congenital infections (rubella, cytomegalovirus, toxoplasmosis, and syphilis); poor maternal health (hypertension and renal and cardiac disease); the mother's nutritional status and socioeconomic level; her use of cigarettes, alcohol, and other drugs; placental insufficiency; and multiple births (e.g., twins, triplets).

The major growth-promoting factor during development before and after birth is **insulin-like growth factor-I (IGF-I)**, which has **mitogenic and anabolic effects**. Fetal tissues express IGF-I, and serum levels are correlated with fetal growth. Mutations in the *IGF-I* gene result in IUGR, and this growth retardation is continued after birth. In contrast to the prenatal period, postnatal growth depends on **growth hormone (GH)**. This hormone binds to its receptor (GHR), activating a signal transduction pathway and resulting in synthesis and secretion of IGF-I. Mutations in the GHR result in **Laron's dwarfism**, which is characterized by marked short stature, and sometimes blue sclera. These individuals show little or no IUGR, because IGF-I production does not depend on GH during fetal development.

# *Fetal membrane & placenta*



## **Placenta**

- Facilitate nutrients & gas exchange

## **Beginning of 9<sup>th</sup> week**

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

## **Fetal membrane**

- Increase in amniotic fluid production

# Change in the trophoblast

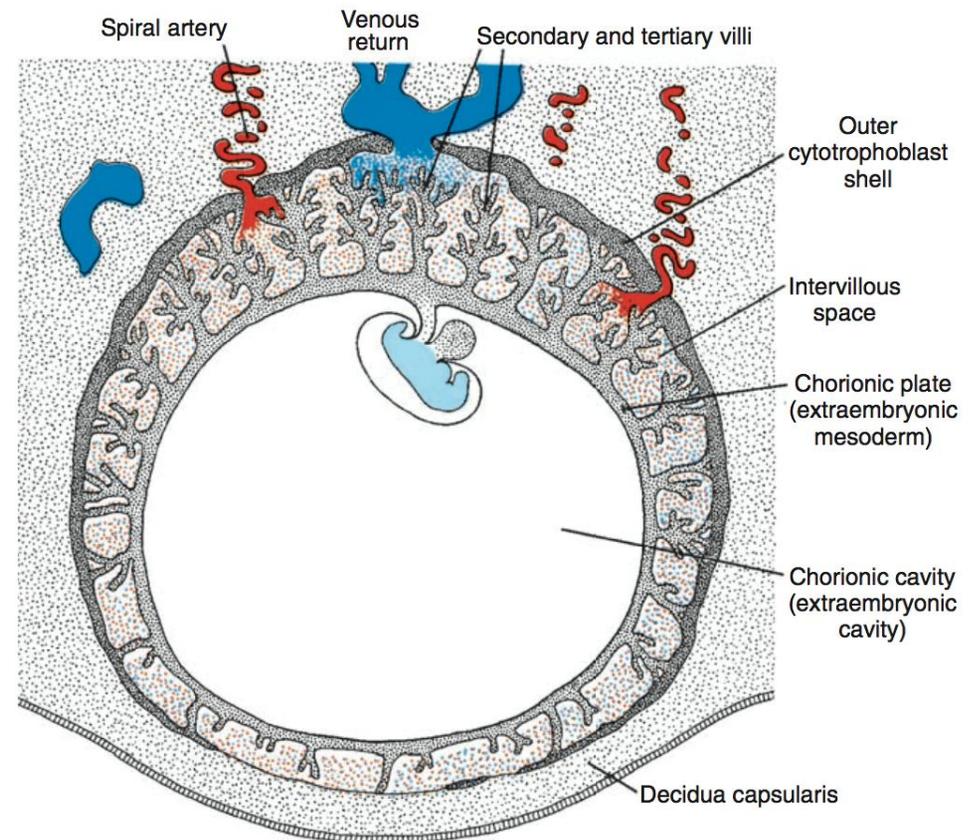
## Beginning of second month :

### *fetal part of Placenta*

- Trophoblast (secondary & tertiary villi / radial appearance)
- Extraembryonic mesoderm (chorionic plate)

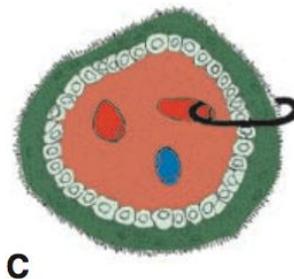
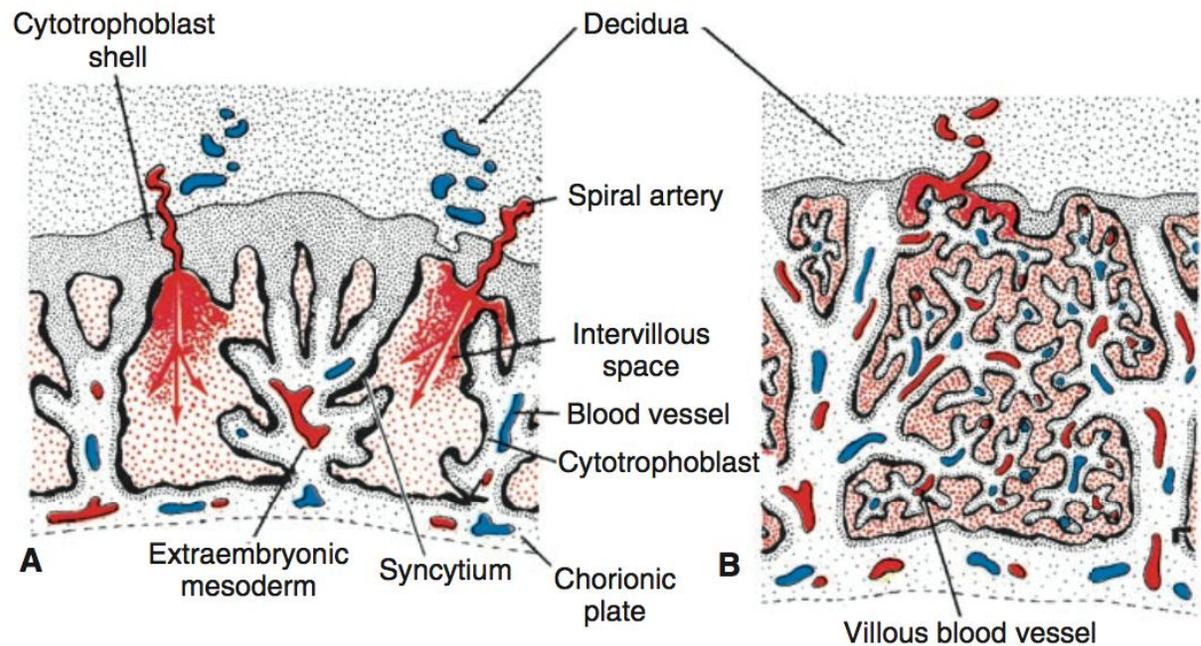
### *Maternal part of Placenta*

- Uterus endometrium

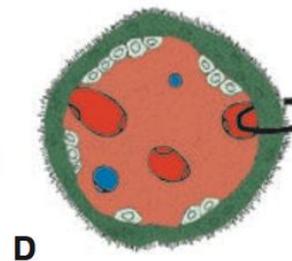


# Change in the trophoblast

- Beginning of 4<sup>th</sup> month



- Barrier formed by
1. Syncytium
  2. Cytotrophoblast
  3. Connective tissue
  4. Endothelium



- Barrier formed by
1. Syncytium
  2. Endothelium

## Clinical Correlates



**Preeclampsia** is a condition characterized by maternal hypertension and proteinuria due to reduced organ perfusion and occurs in approximately 5% of pregnancies. The condition may progress to eclampsia, which is characterized by seizures. Preeclampsia begins suddenly anytime from approximately 20 weeks' gestation to term and may result in fetal growth retardation, fetal death, or death of the mother. In fact, preeclampsia is a leading cause of maternal mortality in the United States and is completely reversible by delivery of the baby. However, delivery too early puts the infant at risk for complications related to preterm birth. Despite many years of research, the cause of preeclampsia is unknown. The condition

appears to be a trophoblastic disorder related to failed or incomplete differentiation of cytotrophoblast cells, many of which do not undergo their normal epithelial-to-endothelial transformation. As a result, invasion of maternal blood vessels by these cells is rudimentary. How these cellular abnormalities lead to hypertension and other problems is not clear. Risk factors for preeclampsia include, preeclampsia in a previous pregnancy, nulliparity (first pregnancy), obesity, family history of preeclampsia, multiple gestation (twins or more), and medical conditions, such as hypertension and diabetes. Preeclampsia also commonly occurs in women with hydatidiform moles (see Chapter 4, p. 48) in which case it occurs early in pregnancy.

# Chorion frondosum & desidua basalis

## Embryonic pole

- Chorion frondosum

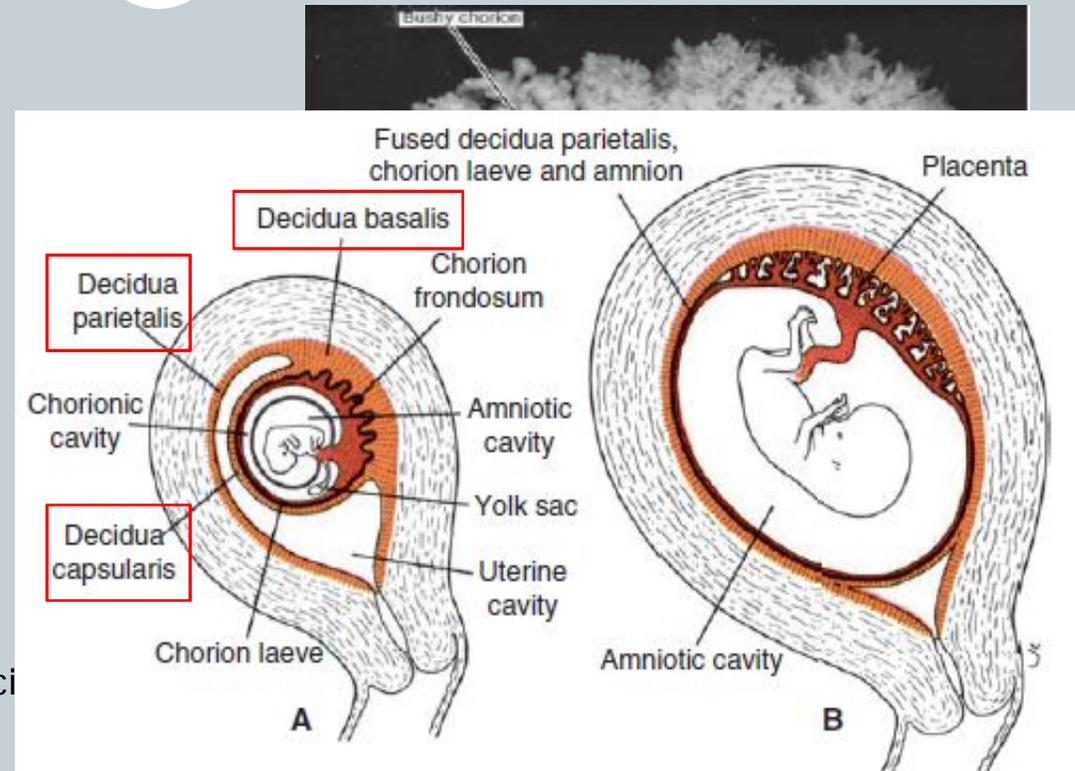
## Abembryonic pole

- Chorion laeve

## Decidua

- Decidua basalis (Embryonic pole)
- Decidua capsularis (Abembryonic pole)
- Decidua parietalis ( wall of uterus )
- **Placenta** = Chorion frondosum + Decidua basalis

**Amniochorionic membrane = fusion of amnion + chorion**



**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.

showing the bushy appearance of the trophoblast at 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 4<sup>th</sup> month

Placenta:

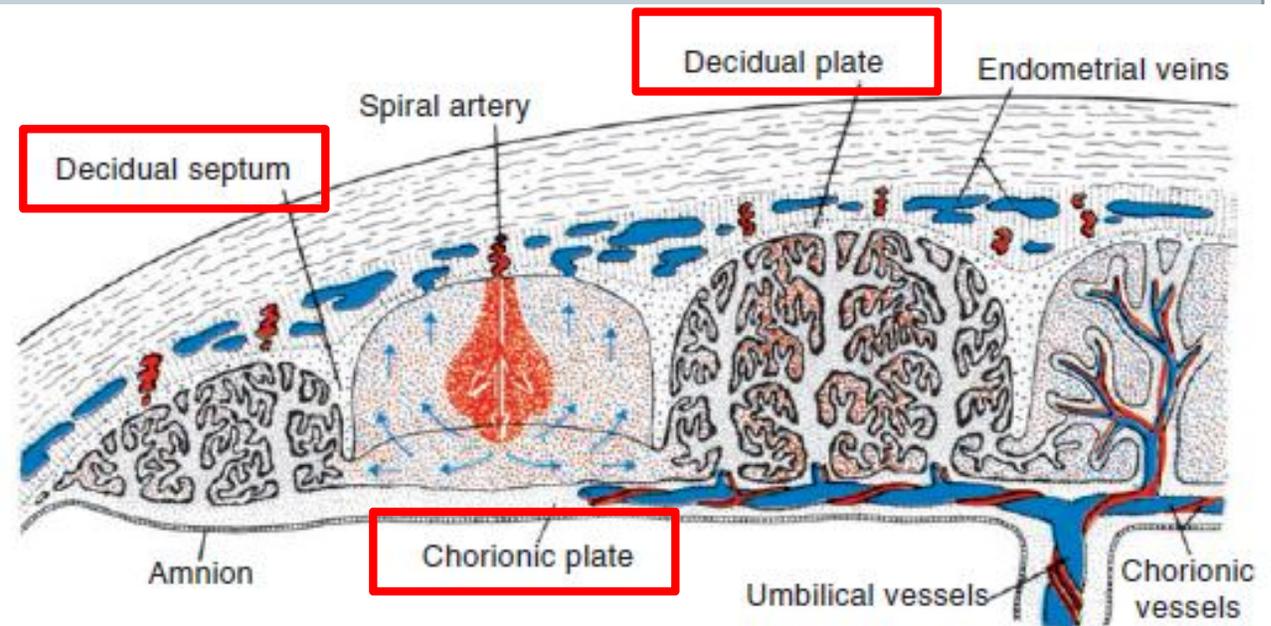
- (1) **fetal portion** (chorion frondosum)
- (2) **maternal portion** (decidua basalis)

4<sup>th</sup> & 5<sup>th</sup> month

**Decidual septa =**

- Maternal tissue in central part
- Syncytium cell in outer part

**Cotyledons**



**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

## Placenta is disc like shape:

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

## velamentous insertion:

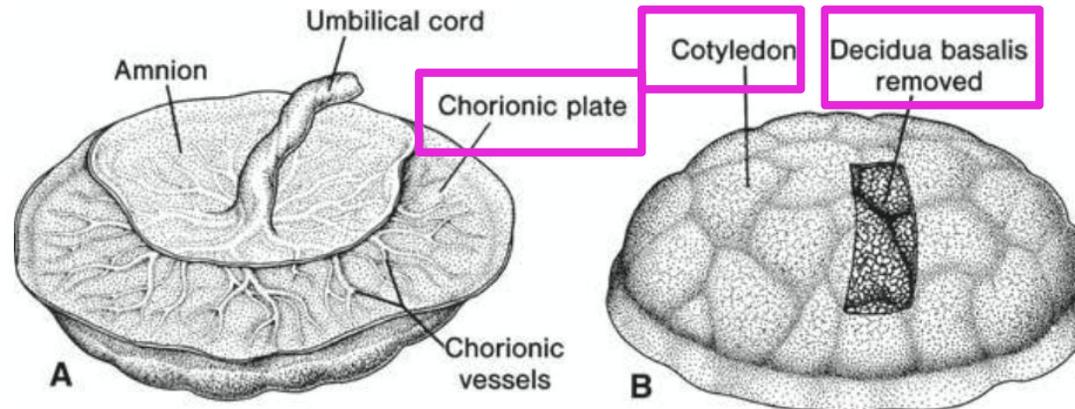
Attachment of umbilical cord to chorionic membrane

## maternal side:

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

## fetal surface:

covered the chorionic plate



**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

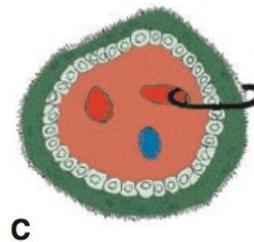
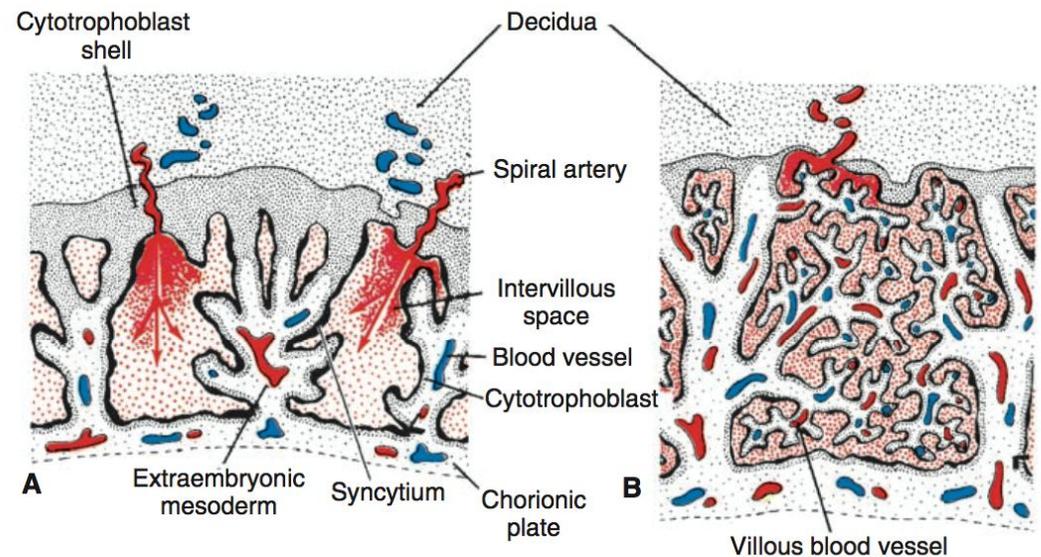
- 80 to 100 spiral arteries pierce the decidual plate
- enter the intervillous spaces
- Placenta blood volume = approximately 150 ml
- Endometrial vein

## Placental membrane

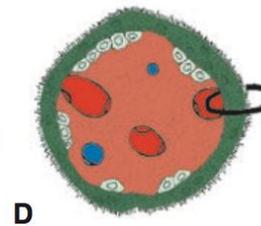
1. Endothelial lining of fetal vessel
2. Connective tissue
3. Cytotrophoblast
4. Syncytiotrophoblast

- Placental barrier

## Placenta is Hemochorial type



- Barrier formed by
1. Syncytium
  2. Cytotrophoblast
  3. Connective tissue
  4. Endothelium



- Barrier formed by
1. Syncytium
  2. Endothelium

# *Function of the placenta*



1. Metabolit exchange (nutrient, IgG on 14<sup>th</sup> week)
2. Gas exchange (20-30 ml O<sub>2</sub>/min)
3. Transition maternal antibody (IgG / 14 weeks / passive immunity)
4. Hormone production (syncytiotrophoblast)
  - Progesteron(end of 4<sup>th</sup> month)
  - Esteriol (uterine growth & mammary glands development)
  - hCG (syncytio trophoblast = first 2 monthes)
  - Somatomammotropin (placental lactogen)

## 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).

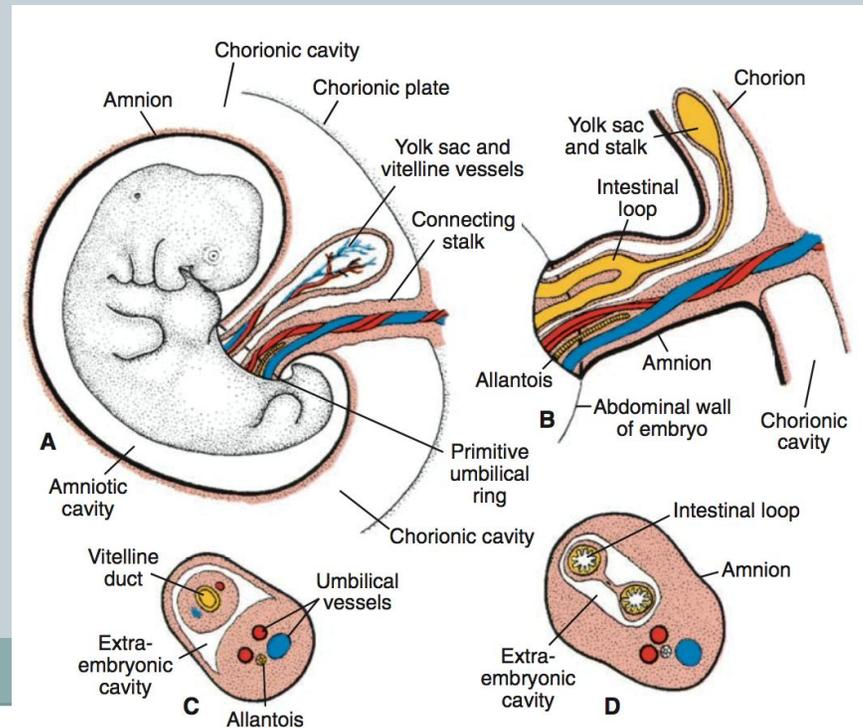
Unfortunately, most drugs and drug metabolites traverse the placenta without difficulty, and many cause serious damage to the embryo (see Chapter 9). In addition, maternal use of heroin and cocaine can cause habituation in the fetus.

# Amnion & umbilical cord

On 5<sup>th</sup> week

Primitive ambilical ring =

- ❖ Connecting stalk (allantois ,two arteries & one vein)
- ❖ yolk stalk (vitelline duct)
- ❖ the connecting canal (Intra & extraembryonic cavities)



## Primitive umbilical cord =

- Connecting stalk (allantois, two arteries & one vein)
- yolk stalk (vitelline duct)

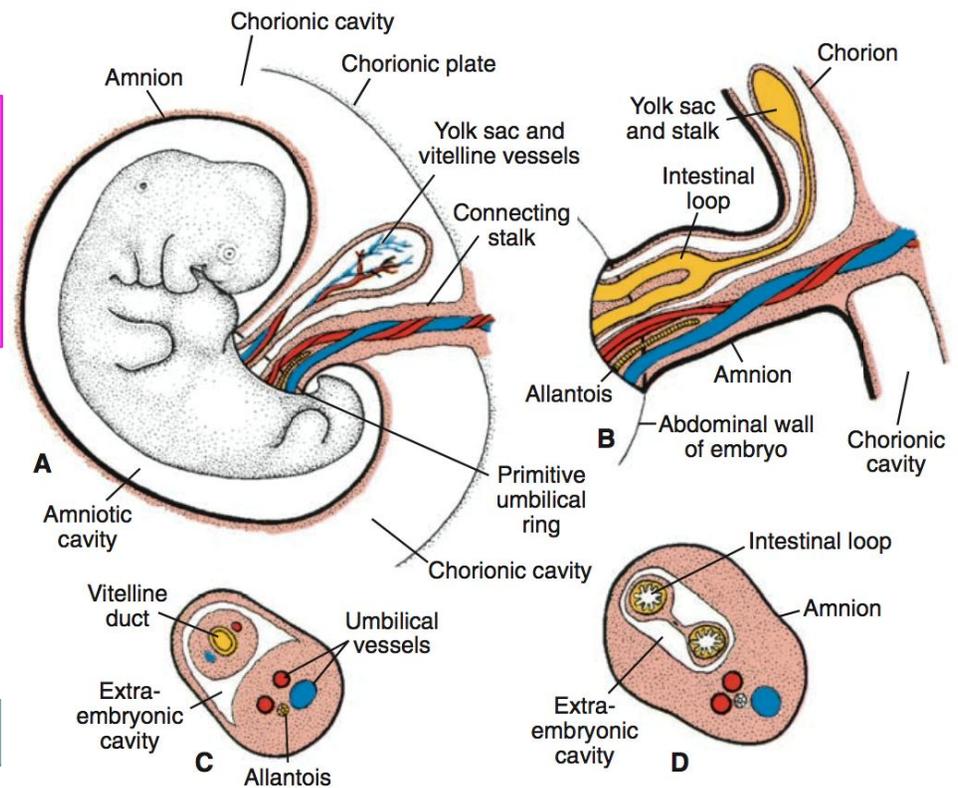
## End of 3th month

**definitive umbilical cord ( closed the connecting canal ) =**

Umbilical vessels & Wharton's jelly

## Physiological umbilical hernia =

Entrance intestinal loop in umbilical cord for short time



## 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.

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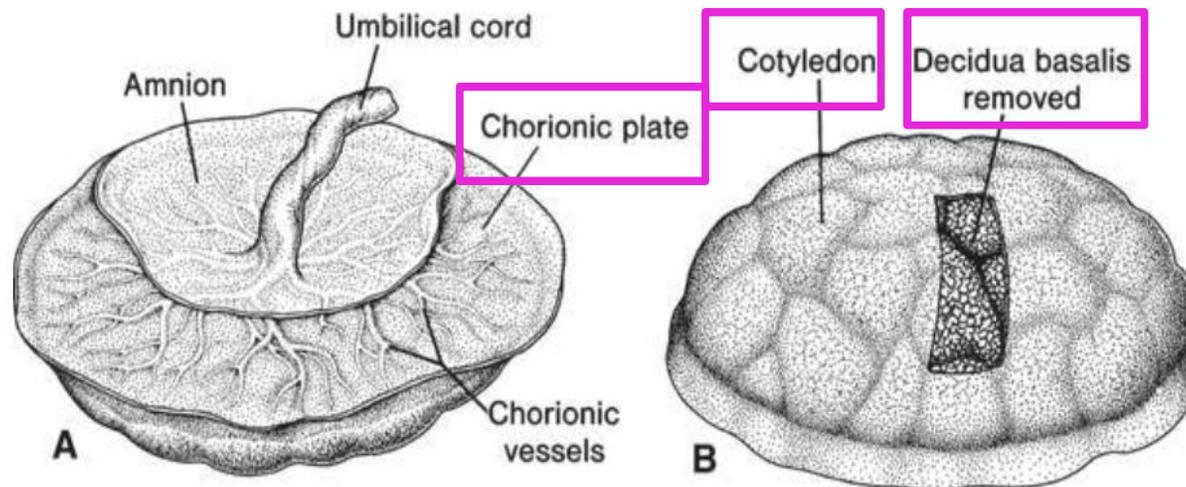
**B**

**Figure 8.17** Limb abnormalities caused by amniotic bands. **A.** Limb constriction ring. **B.** Digit amputation (big toe) and ring constriction (second toe).

# Placental changes at the end 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 surface



**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
  
- 10<sup>th</sup> week: 30 ml
- 20<sup>th</sup> week: 450 ml
- 37<sup>th</sup> 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 5<sup>th</sup> month =**

Fetus swallows amniotic fluid (400ml)

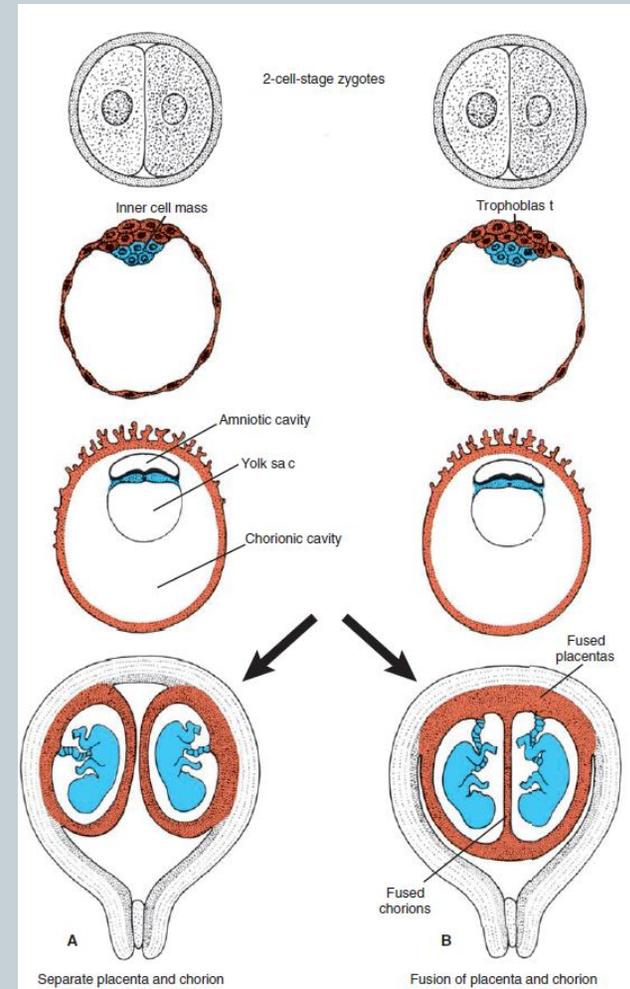
**5<sup>th</sup> month urine added to amniotic fluid**

# Fetal membrane in twins

- 90% of twins are dizygotic (fraternal)

Increases in dizygotic twins:

- Maternal age increase
- ART
- Erythrocyte mosaicism



## Dizygotic Twins

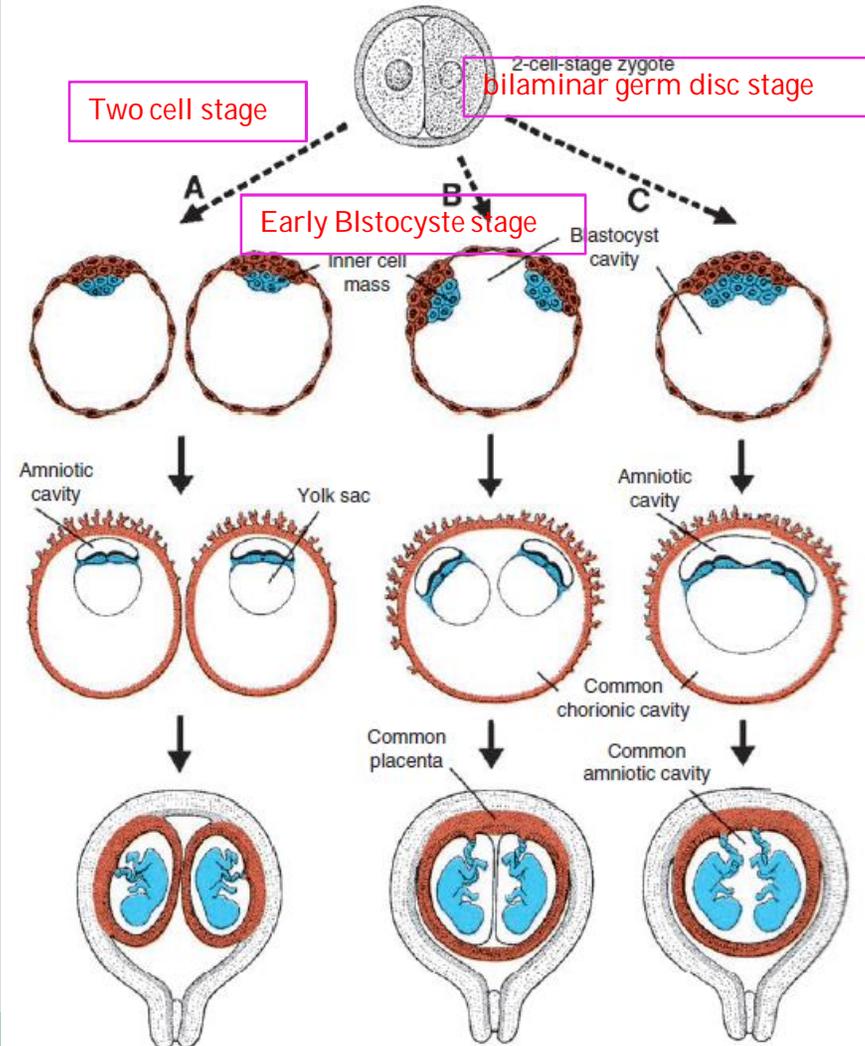
Approximately 90% of twins are **dizygotic**, or **fraternal**, and their incidence increases with maternal age (doubling at age 35) and with fertility procedures, including ART. They result from simultaneous shedding of two oocytes and fertilization by different spermatozoa. Because the two zygotes 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 (Fig. 8.18A). 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 (Fig. 8.18B). 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.

# Fetal membrane in twins

- Monozygotic (identical)
- 3-4 in 1000
- **Is Consequence of zygote cleavage in 3 stages:**
  1. 2 cells embryo stage (A)
  2. Early Blastocyst stage (more common) (B)
  3. Bilaminar disc stage (C)

Triplet  
1 in 7,600



# *Parturition (birth)*



- During last 2 to 4 weeks of pregnancy

## **Labor:**

1. Effacement (cervix thinning, shortening & dilatation) / uterus contraction + force of amnion membrane or head of fetus
2. Fetus delivery / uterus contraction + abdominal muscle contraction
3. Placenta & fetal membrane delivery / uterus contraction + abdominal muscle contraction

## 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.



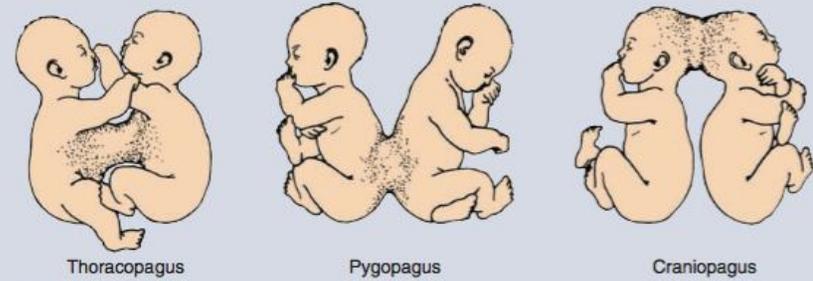
**Figure 8.20** Fetus papyraceus. One twin is larger, and the other has been compressed and mummified, hence the term *papyraceus*.



**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.

## 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.