

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

**CHANGES IN THE 4<sup>TH</sup> WEEK,  
FETAL MEMBRANES,  
CONGENITAL ANOMALIES**

## 4<sup>TH</sup> WEEK OF PREGNANCY

- **Critical period of embryological development**

- ⇒ All external & internal structures are developed.
- ⇒ All the main organ & system have begun to develop.
- ⇒ Folding of the embryo.
- ⇒ The Embryo has human appearance.

- **Folding of the embryo**

- **Definition:** folding of flat trilaminar embryo upon itself Ventrally to form cylindrical embryo

- **Time:** at the beginning of **4th week**.

- **Types of folding:**

- A. **Cephalo-caudal folding:** leads to formation of head and tail folds.

- B. **Two lateral folds.**

## 4<sup>TH</sup> WEEK OF PREGNANCY

### - Causes of folding:

- ◆ Progressive **expansion** of **amniotic cavity**.
- ◆ Rapid **growth** of the **axial area of the disc (somites)** more than its **periphery**.
- ◆ **Notochord** and **primitive streak** are **firm** structures [**not undergo folding**] so they limits of head and tail folding.

### - Process:

#### 1) Folding of the ends:-

- a) Head fold at cranial end.
- b) Tail fold at caudal end.

#### 2) Folding of sides:-

- a) Right lateral fold.
- b) Left lateral fold.

### - Results:

#### A) Lateral folding

1) **Shape:** embryo becomes cylindrical.

#### 2) Amniotic Cavity:

- a) **Expands** on expense of yolk sac. B) **Enlarges and Completely** surround the embryo.

### 3) Yolk Sac Cavity: (FORMATION OF THE GUT)

- **The yolk sac is divided into three parts:**
  - ➡ Incorporation of major part of yolk sac inside embryo to form **primitive gut**.
  - ➡ Remaining minor part of yolk sac outside embryo to form **definitive yolk sac**.
  - ➡ communication between primitive gut & definitive yolk sac is called **vitello-intestinal duct** [vitellus=yolk sac]
- **The primitive gut is differentiated into:**
  1. **Foregut:** part within head fold.
  2. **Midgut:** the middle part continuous with definitive yolk sac by vitello-intestinal duct.
  3. **Hindgut:** part within tail fold.

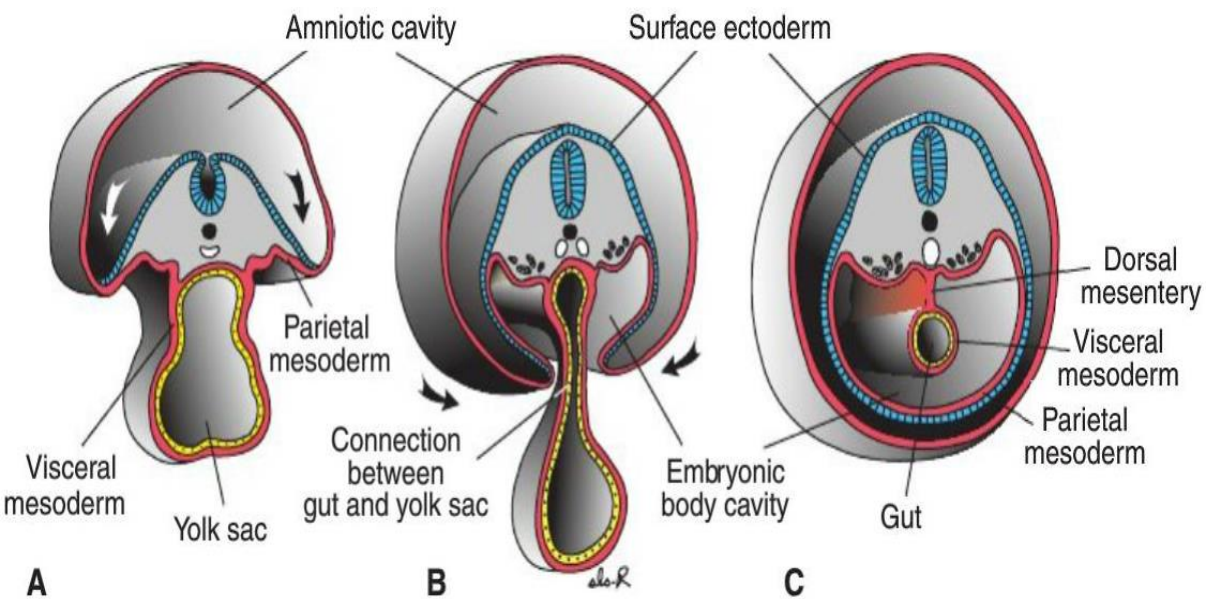
## A. Cephalocaudal folding

### 1) Results of head fold:

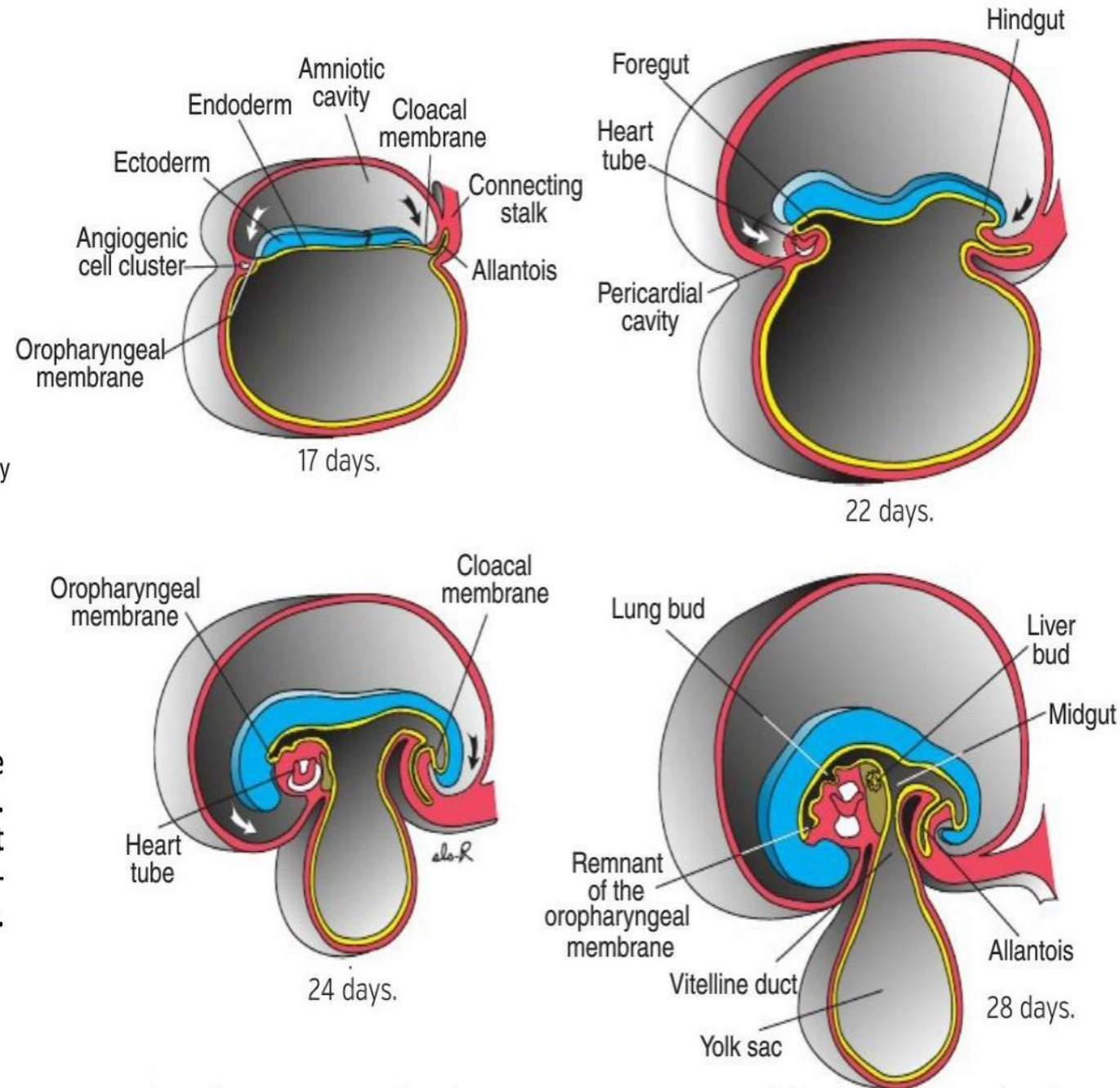
- ▶ **Bucco pharyngeal membrane, cardiogenic area, septum transversum** are carried to the **ventral** aspect of the embryo.
- ▶ **Forebrain** lies at cranial (**cephalic**) end of embryo.
- ▶ Part of yolk sac lies inside the head fold— — — —> **foregut**.

### 2) Results of tail fold:

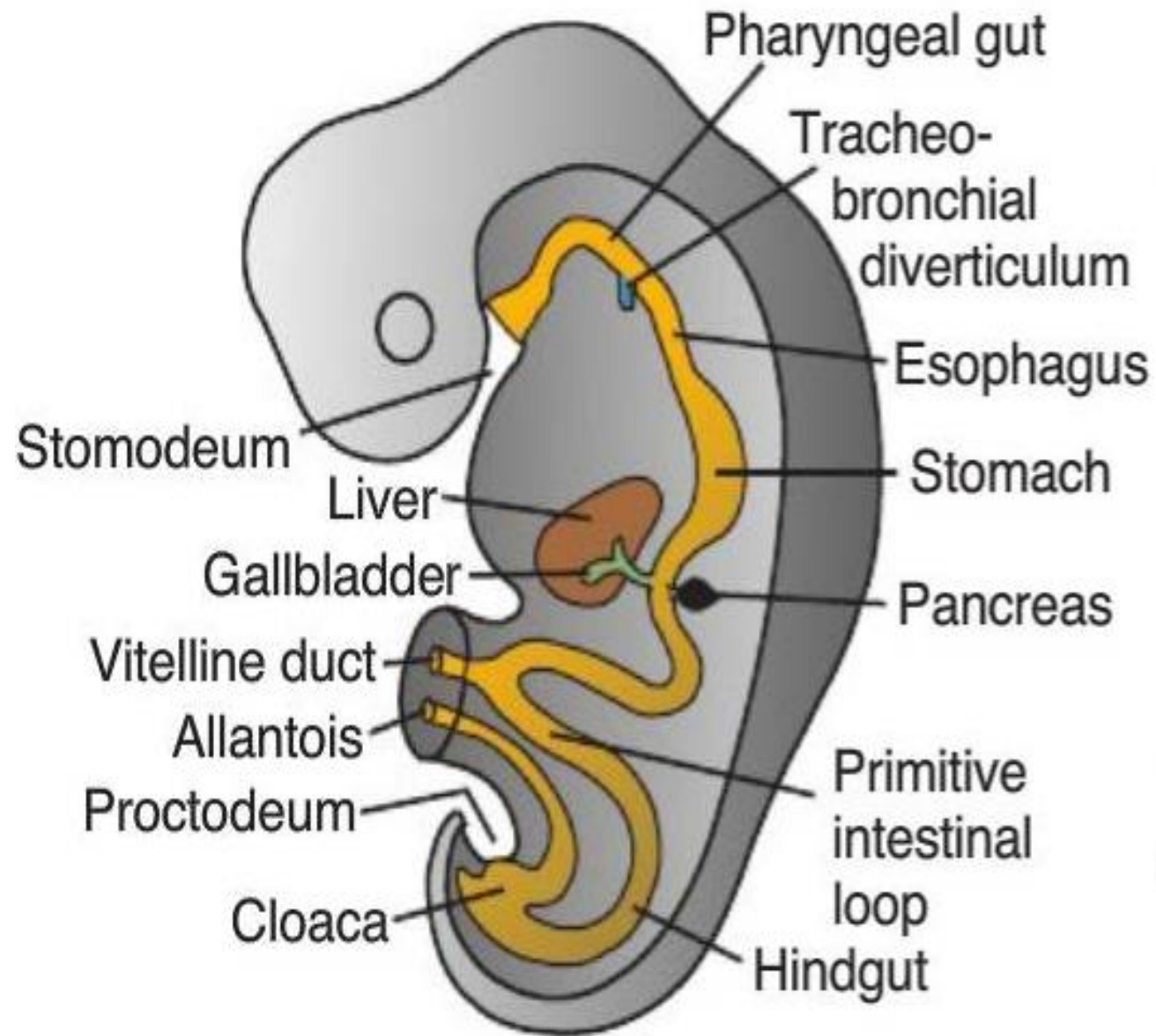
- ▶ **Cloacal membrane and connecting stalk** are carried to the **ventral** aspect of the embryo.
- ▶ **Connecting stalk** takes the permanent position **of the umbilical cord**.
- ▶ Part of yolk sac lies inside the tail fold— — — —> **hind gut and terminal dilated part**.



Cross sections through embryos at various stages of development to show the effect of lateral folding on the endoderm-lined cavity. A. Folding is Initiated. B. Transverse section through the midgut to show the connection between the gut and yolk sac. C. Section just below the midgut to show the closed ventral abdominal wall and gut suspended from the dorsal abdominal wall by its mesentery.



Sagittal midline sections of embryos at various stages of development to demonstrate cephalocaudal folding and its effect on position of the endoderm lined cavity.



Sagittal sections through embryos showing derivatives of the endodermal germ layer.



# Fetal Membranes

**Definition:** Structures derived from fertilized ovum and not share in formation of embryo.

Fetal membranes include:

- 1) Amnion.
- 2) Yolk sac.
- 3) Allantois.
- 4) Chorion.
- 5) Placenta.
- 6) Connecting stalk and umbilical cord.

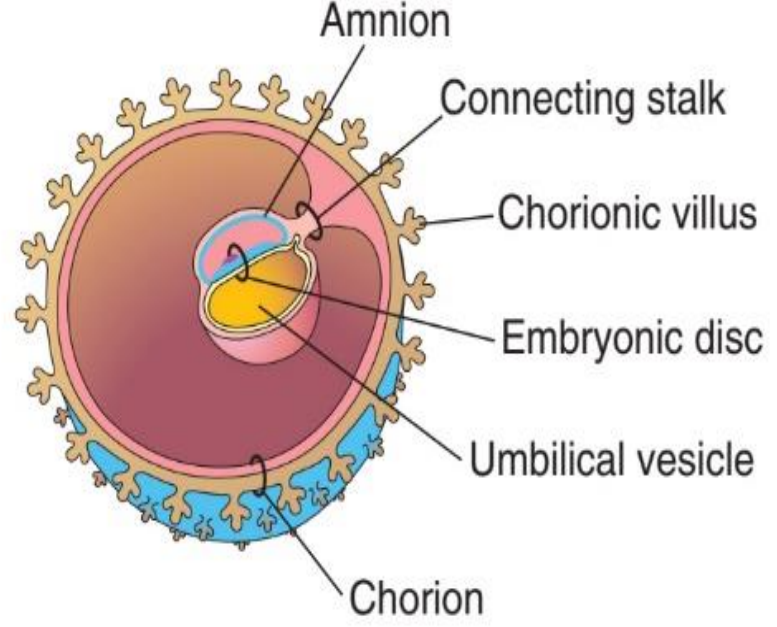
# The Amnion

**Definition:** sac filled with fluid that surrounds the embryo and fetus.

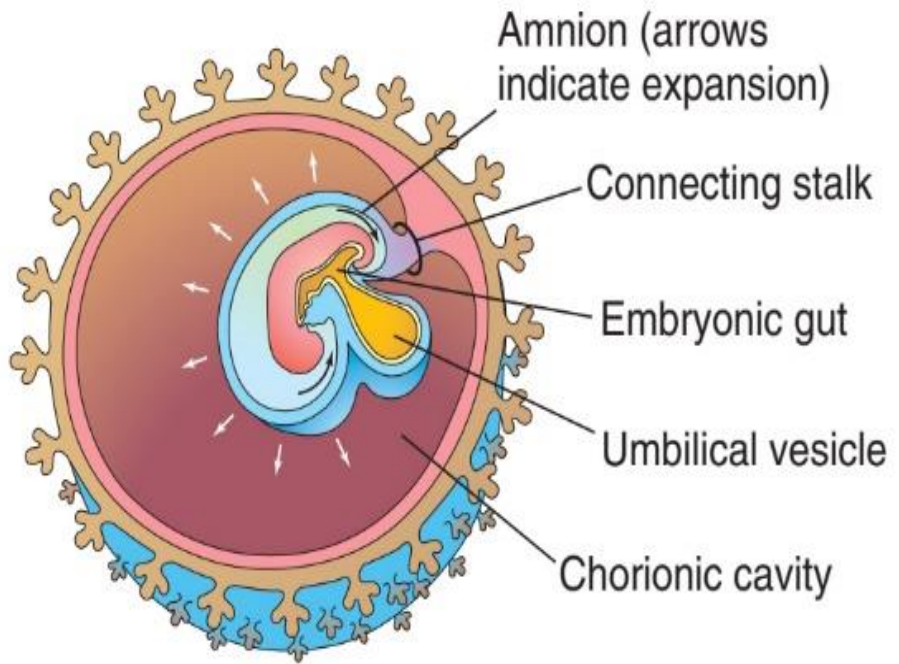
**Time of appearance:** 7th or 8th day after fertilization.

**Development:**

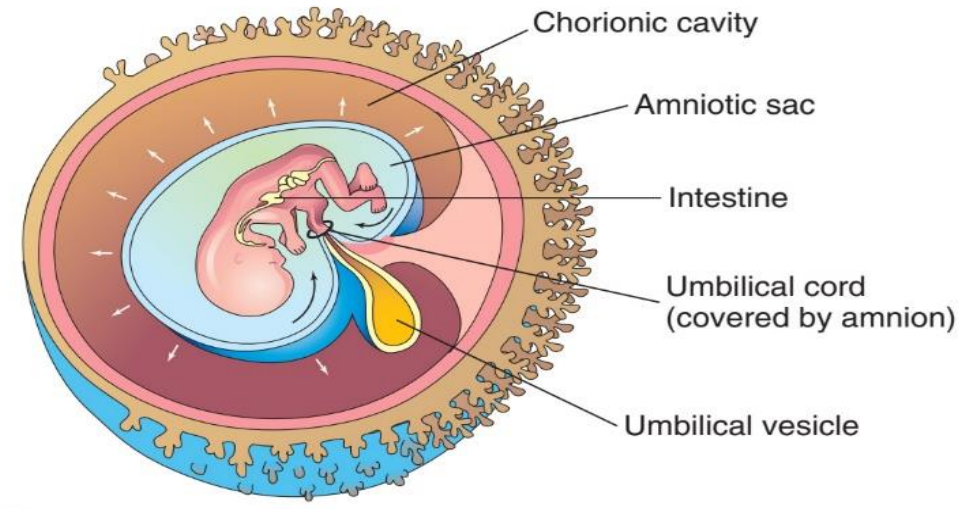
- Small cavity appears in inner cell mass.
- Before folding: amnion attached to margin of embryonic disc.
- After folding: amnion expanded and enlarges at the expense of yolk sac to surround embryo completely.
- At birth: amnion ruptures by uterine contraction and fluid pass through cervical canal.



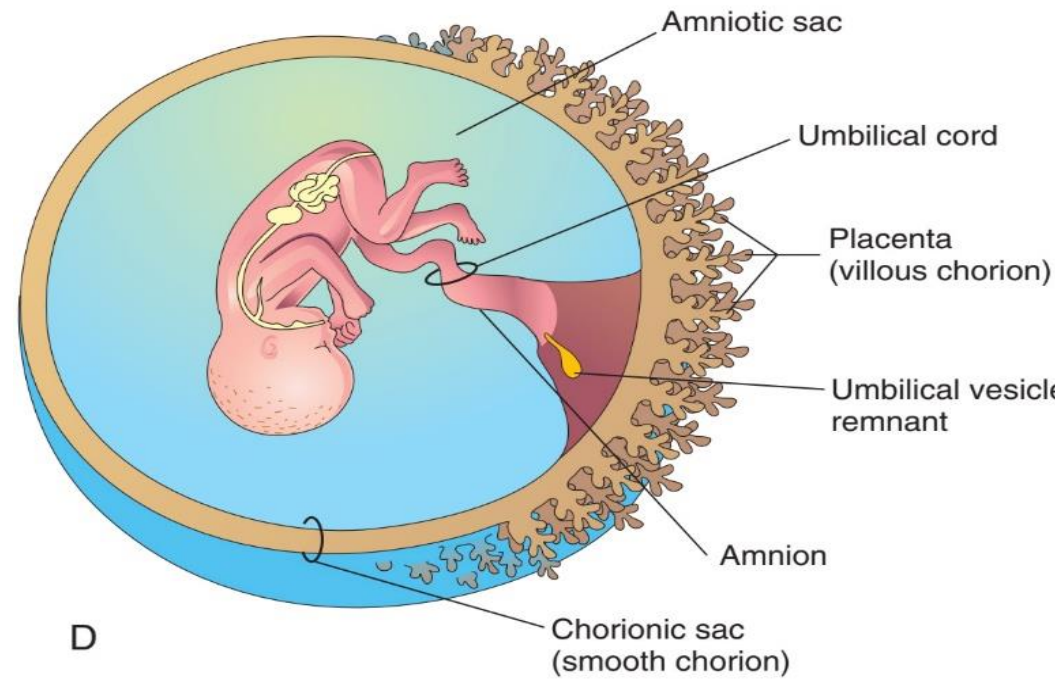
A



B

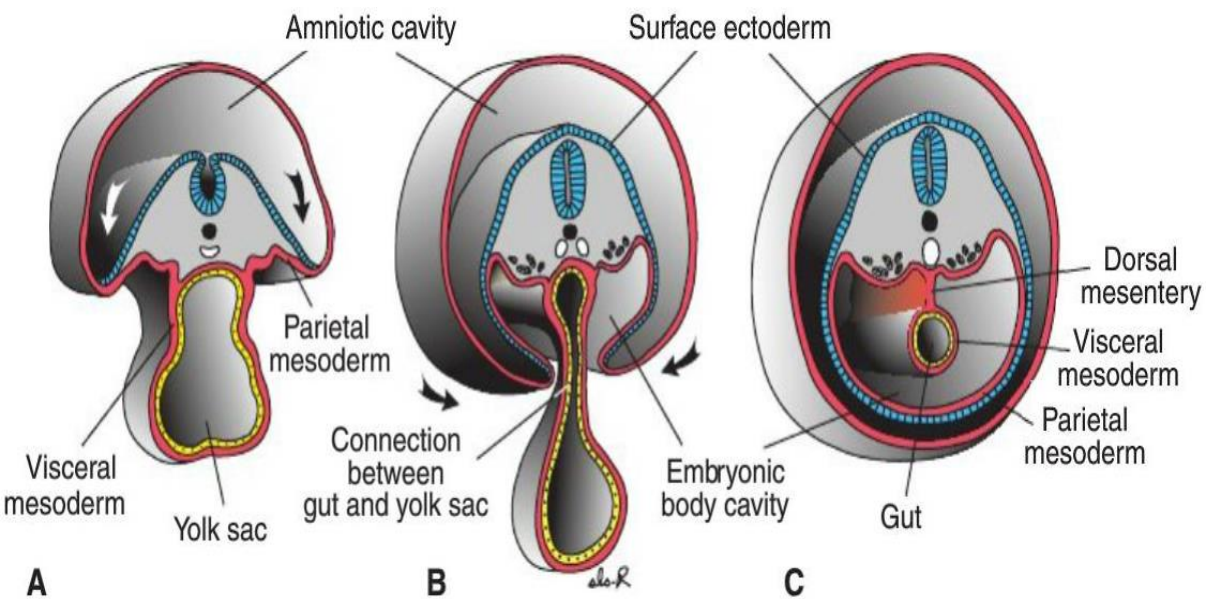


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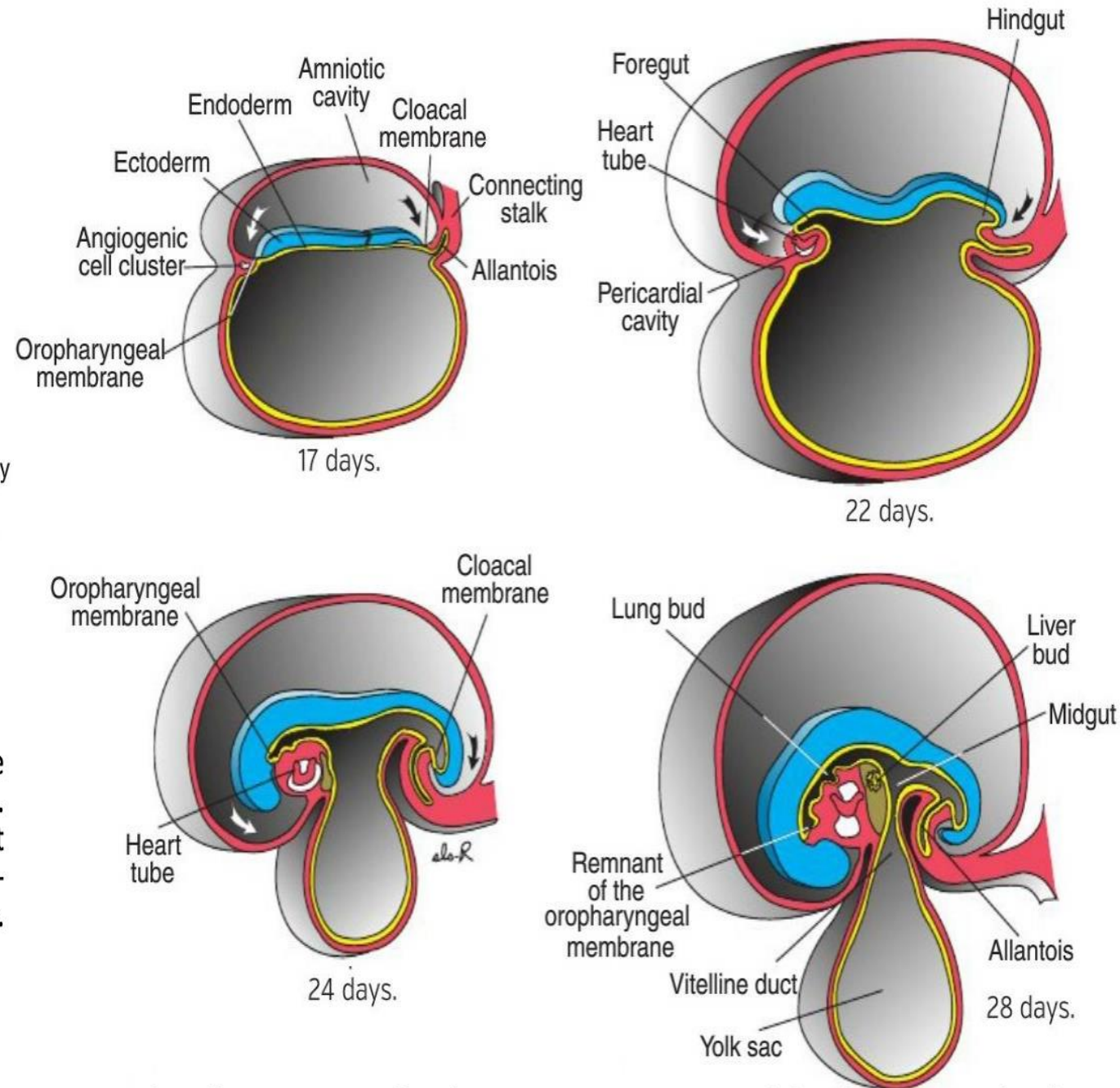


D

Developmental changes of the Amnion



Cross sections through embryos at various stages of development to show the effect of lateral folding on the endoderm-lined cavity. A. Folding is Initiated. B. Transverse section through the midgut to show the connection between the gut and yolk sac. C. Section just below the midgut to show the closed ventral abdominal wall and gut suspended from the dorsal abdominal wall by its mesentery.



Sagittal midline sections of embryos at various stages of development to demonstrate cephalocaudal folding and its effect on position of the endoderm lined cavity.

## Amniotic fluid

**Definition:** fluid fills amniotic cavity .

**Amount:** one liter at birth.

**Source:**

- Amnio-blast.
- Placenta.
- Kidneys of fetus.

## Composition

1- 99 % :- water

2- 1 % :- □ Epithelial cells.

□ Organic constituents:- CHO , FATS , PIGMENTS.

□ In-organic constituents.

3- Fetal excreta [urine & stool] are added in advanced pregnancy.

### Function:

1. **Growth:** permits symmetrical growth of embryo.
2. **Movements:** allows movements of fetus.
3. **Temperature:** control embryo's temperature.
4. **Infection:** act as barrier to infection.
5. **Trauma:** protects fetus from effect of trauma.
6. **Adhesion:** prevent adhesion between different parts of body.
7. **Balance:** maintaining electrolytes balance.
8. **Cervix:** dilatation of cervix
9. **Vagina:** anti-septic [washing the vagina]

# Yolk sac

**Definition:** Cavity that develops in relation to ventral surface of embryonic disc.

**Time of appearance:** 2nd & 3th week after fertilization

**Stages of development:**

a) 1ry Yolk sac is formed at 2nd week

B) 2ry Yolk sac is formed at 3rd week

allantois arises as a caudal diverticulum from yolk sac at day 16

**During 4 week:**

Yolk sac constricted into two parts after folding:

Part enclosed within embryo form primitive gut (most of G.I.T derived)

Part outside embryo becomes definitive yolk sac or yolk sac proper.

## FETAL MEMBRANES

### Primitive gut differentiated into

- 1) Part enclosed in head fold forms foregut.
- 2) Part enclosed in tail fold forms hind gut.
- 3) Part enclosed in two lateral folds forms midgut.
- 4) Midgut remains temporally opens with yolk sac by broad duct (vitellointestinal duct) then it become narrow and long.

### During 5th week:

- Vitellointestinal duct elongates, atrophy and detach (by 5-9th week).
- Definitive yolk sac gets smaller and starts to degenerate (at 10th month).



### Function of yolk sac

- 1. Transfer nutrients to embryo (in 2nd and 3rd weeks) before function of placenta.**
- 2. Development of blood cells and blood vessels first occur in extraembryonic mesoderm covering wall of yolk sac.**
- 3. Endoderm of yolk sac is incorporated into embryo as primitive gut.**
- 4. Its endoderm gives epithelium of trachea, bronchi, lungs and digestive tract (in 4th week).**
- 5. Primordial germ cell appears in endoderm of wall of yolk sac and migrates to developing sex organ at 3week.**

# Allantois

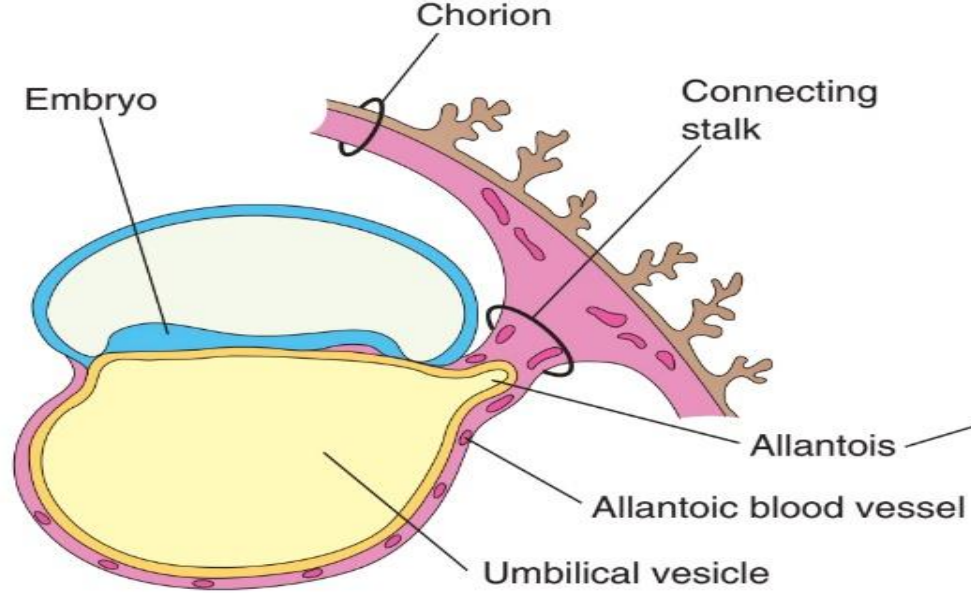
**Definition:** Diverticulum from caudal wall of secondary yolk sac extends into connecting stalk

**Fate:** runs from umbilicus to urinary bladder that will differentiate into:

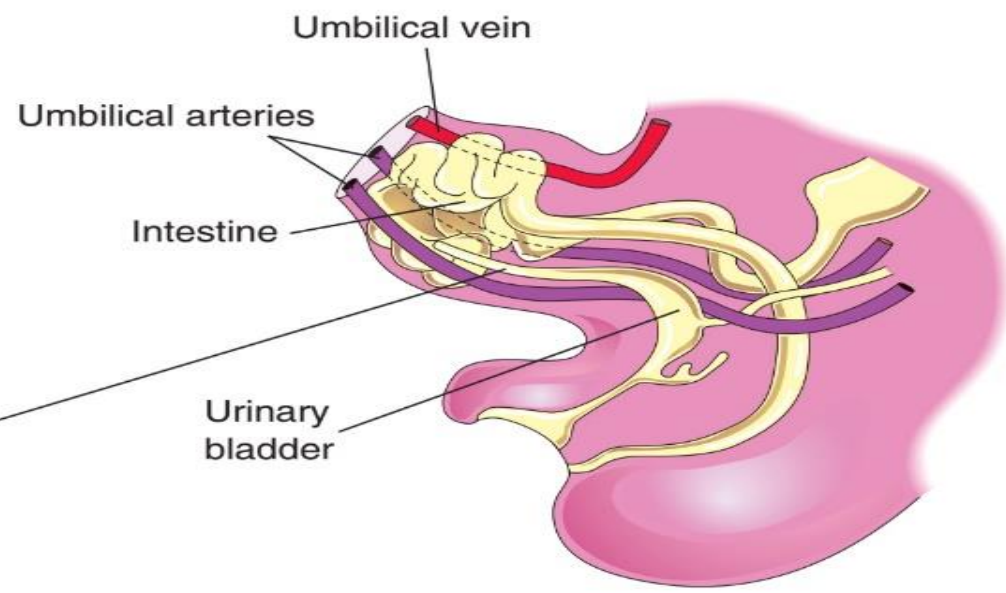
- 1) Proximal part of allantois:** that will enlarge to form the apex of urinary bladder
- 2) Distal part of allantois:** that will form the urachus; which is a thick tube. After birth, the urachus becomes fibrous band and form median umbilical ligament which extend from apex of urinary to umbilicus.

**Function:**

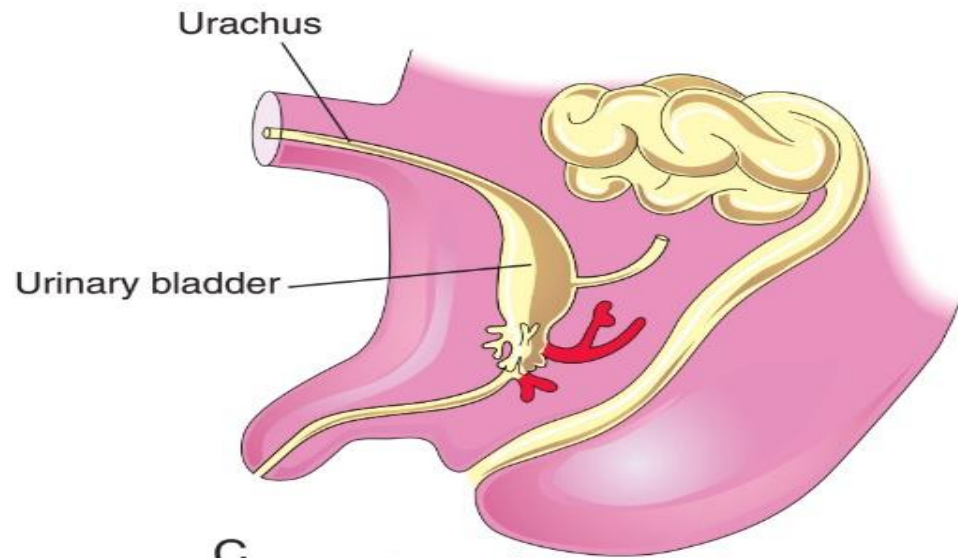
- 1) Blood formation in its wall (in 3rd to 5th weeks).**
- 2) Blood vessels persist as umbilical veins and arteries.**
- 3) Proximal part of allantois shares in formation of urinary bladder.**



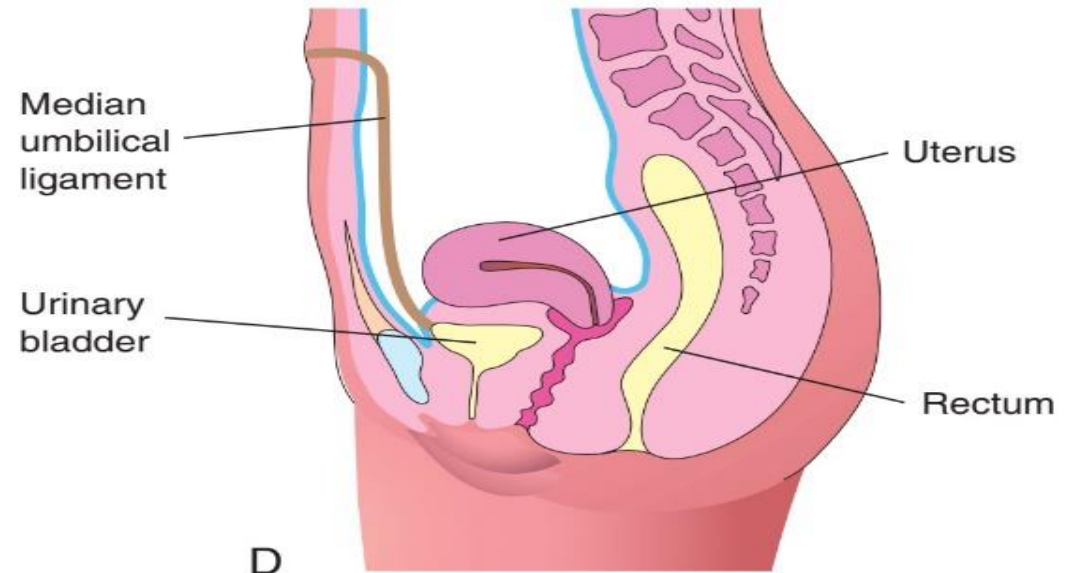
A A 3-week embryo.



B A 9-week fetus.



C A 3-month



D Adult female.

Illustrations of development and usual fate of the allantois.

## FETAL MEMBRANES

### Chorion

- Chorion is the wall of chorionic sac [gestational sac] it is formed of:
  - ❖ E.E.M. [somatic layer]
  - ❖ Trophoblast [two layers]
- Chorionic cavity: It is the E.E.C. Cavity that contains:
  - =Embryo.                      =Amniotic sac.
  - =Yolk sac.                      =Suspended by connecting stalk.

### Chorionic Villi

Definition: finger like processes from trophoblast into decidua basalis and capsularis that covers chorionic sac.

### Types of chorionic villi

[1] According to its relation to decidua:-

- Chorion laeve.                      □ Chorion frondosum

# FETAL MEMBRANES

## Development:

- Chorionic villi cover the entire chorionic sac till beginning of 8th week.
- As the chorionic sac grows , has the following changes:-
  - Villi associated with decidua capsularis degenerates producing avascular bare area called Chorion laeve
  - Villi associated with decidua basalis rapidly increase in number , branched & enlarged and called Chorion frondosum.

## [2] Types according to structure:

### 1) Primary chorionic villi: formed of:

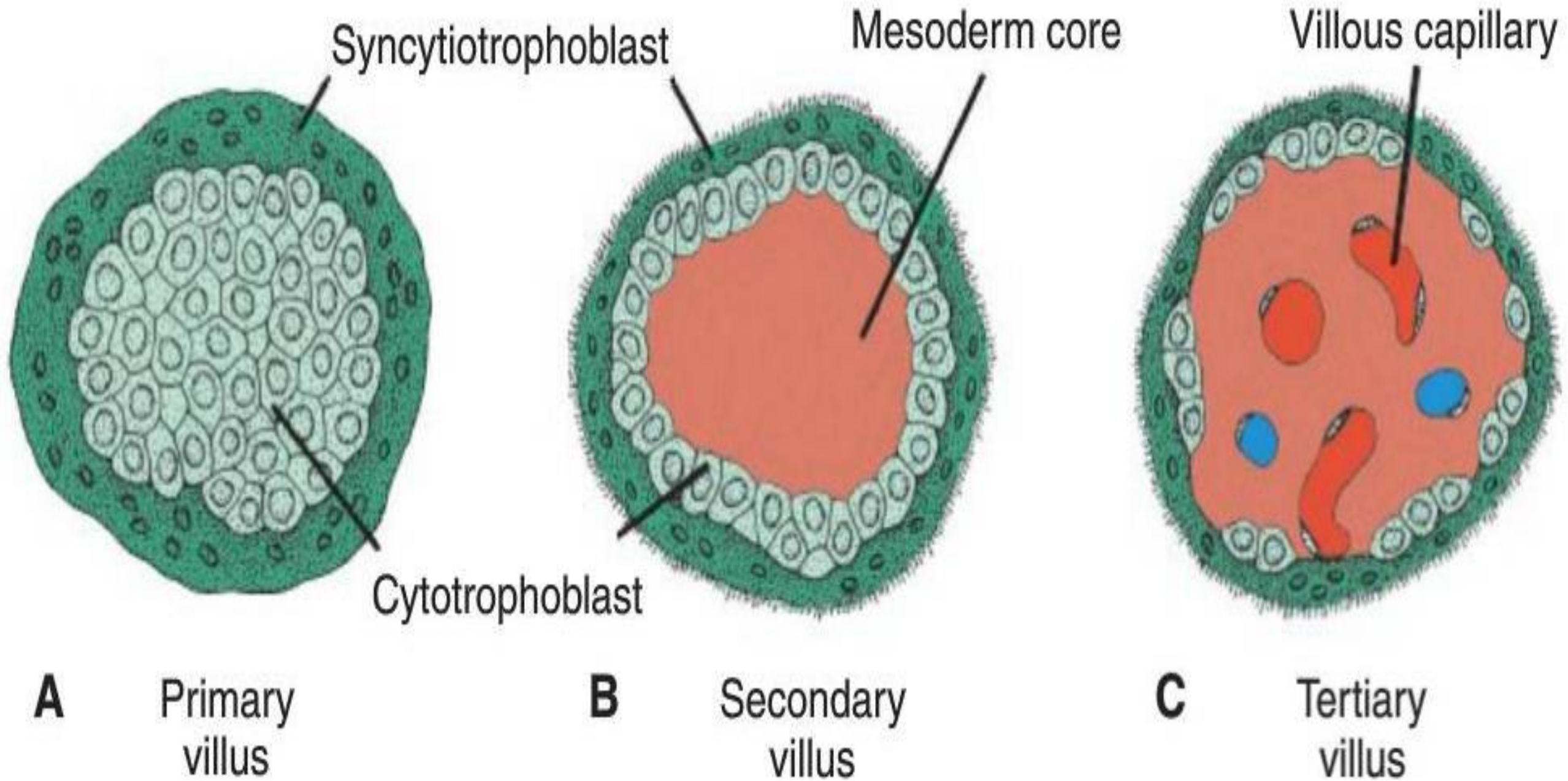
- Outer syncytiotrophoblast. □ Inner cytotrophoblast

### 2) Secondary chorionic: villi formed of:

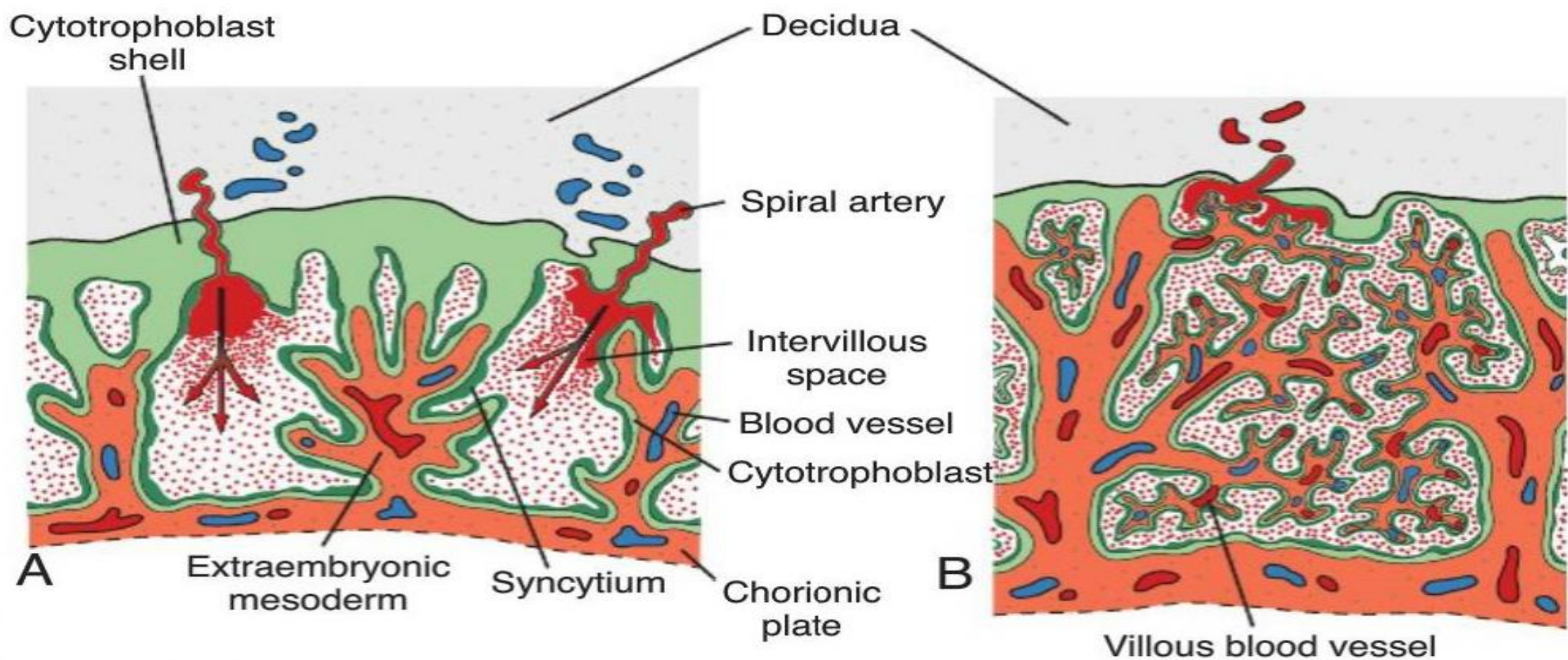
- Outer syncytiotrophoblast. □ Inner cytotrophoblast.
- Core of extraembryonic mesoderm.

### 3) Tertiary chorionic villi: formed of:

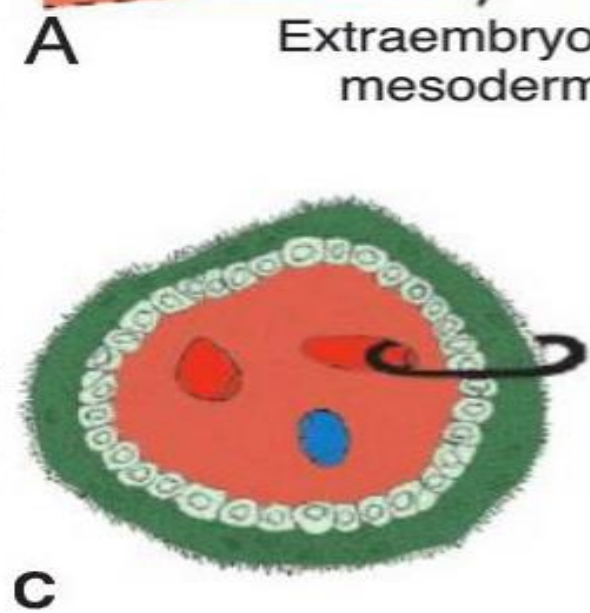
- Outer syncytiotrophoblast. □ Inner cytotrophoblast.
- Core of extraembryonic mesoderm. □ Blood vessels develop in the core of villi.



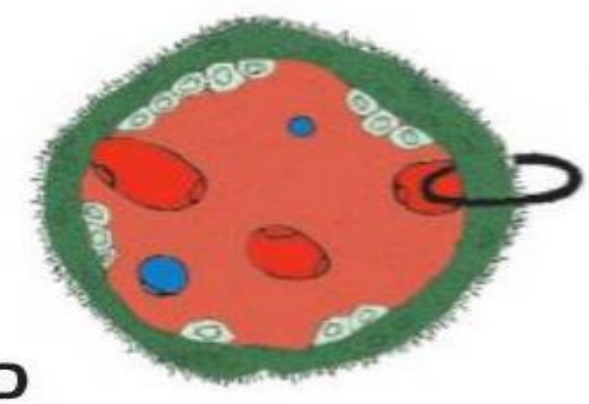
Development of a villus.



During the fourth week.



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



Barrier formed by  
 1. Syncytium  
 2. Endothelium

During the fourth month.

# FETAL MEMBRANES

## Placenta

**Definition:** Primary site of gases exchange & transmission of nutrient materials & metabolites between mother & fetus.

### Structure:-

- Fetal Part: develops from chorionic sac & chorion frondosum
- Maternal part: derived from :-
  - a) Endometrium of Decidua basalis. B) Maternal blood in inter-villous space.

### Function of Placenta:-

- 1) Respiratory function. [by simple diffusion]
- 2) Nutritive function. [by simple diffusion & selective]
- 3) Excretory function. [by simple diffusion & selective]
- 4) Protective function:-
  - (a) Transfer of maternal antibodies. (b) Barrier. (c) Metabolic function. (d) Transfer drugs.
- 5) Endocrine function:-
  - (a) C.H.G. (b) Progesterone (c) Estrogen

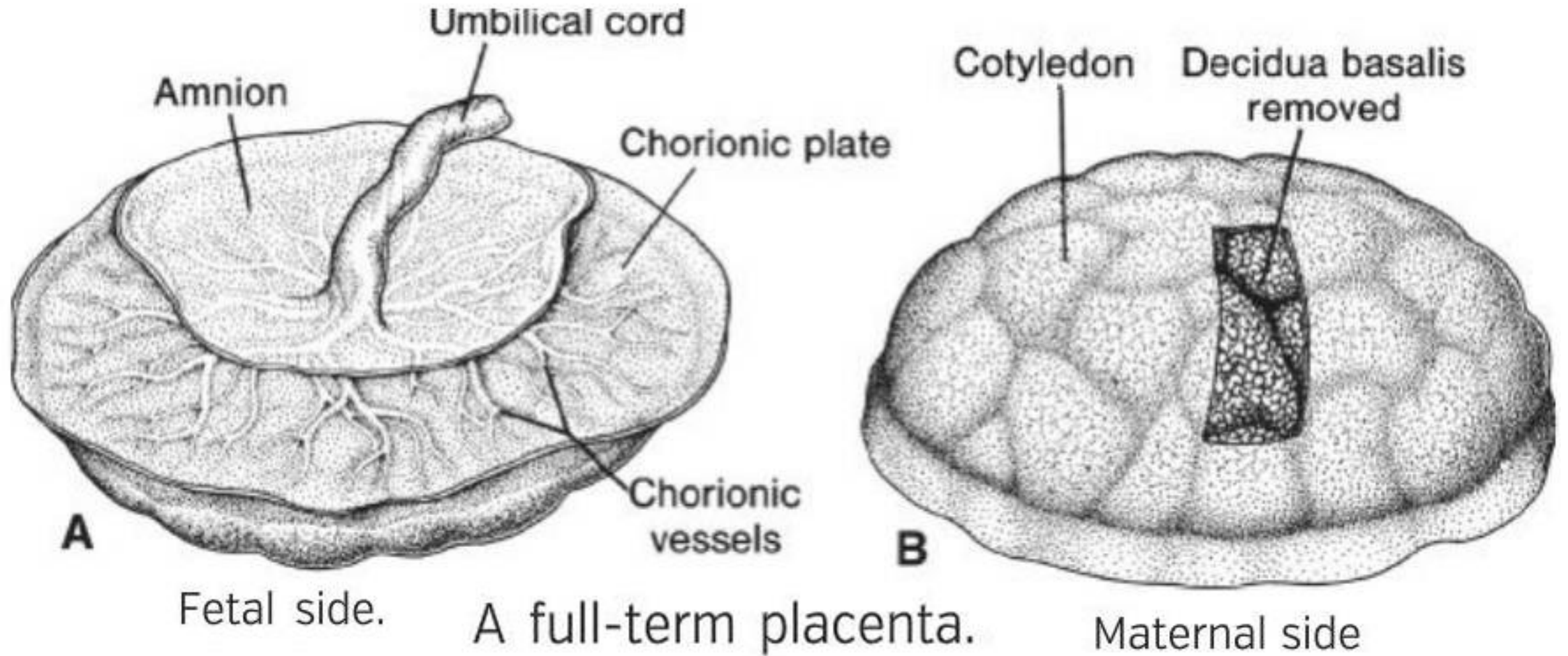


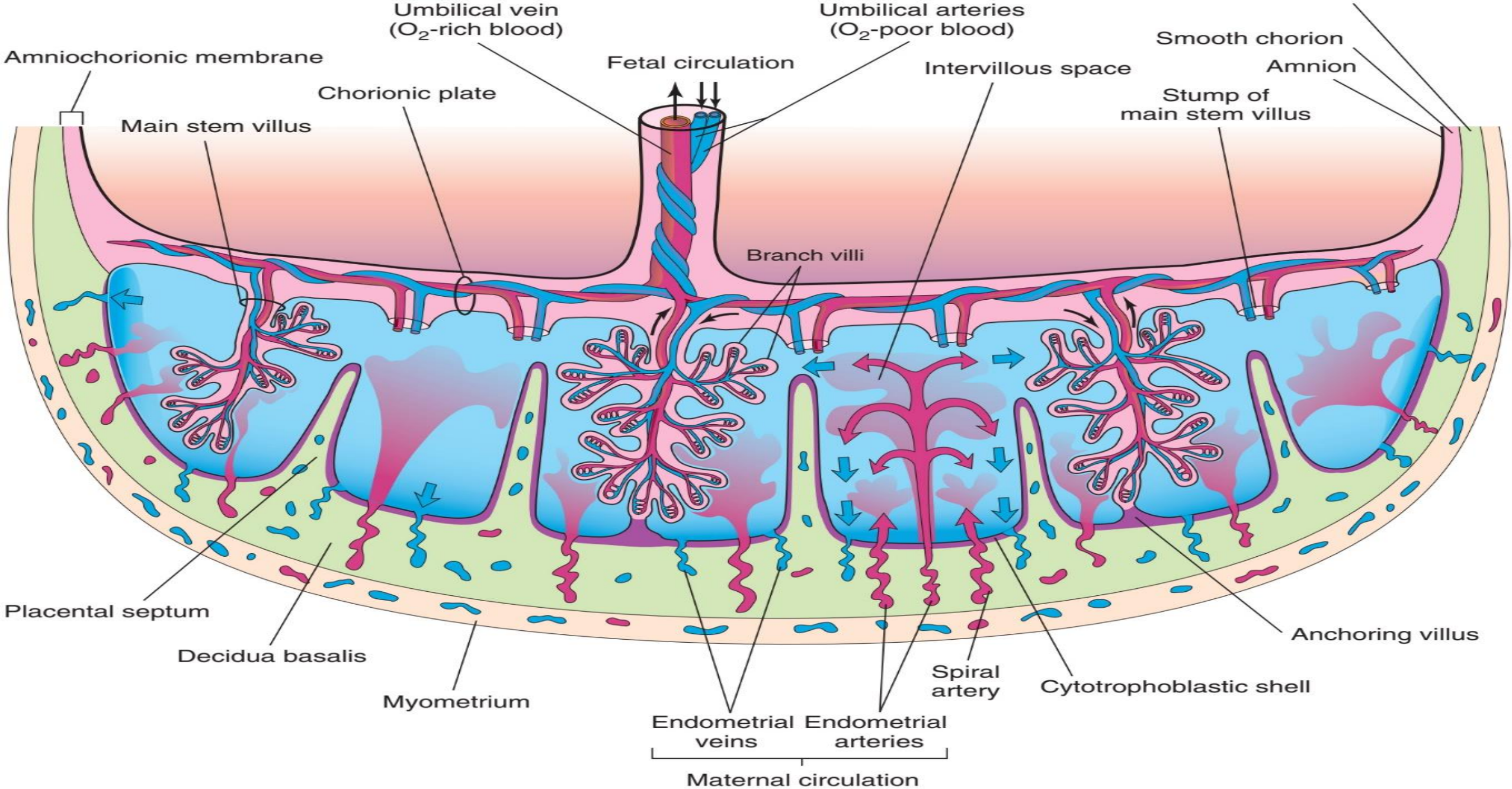
# FETAL MEMBRANES

## Gross appearance:

1. Shape: discoid.
2. Diameter: 15-20cm.
3. Thickness: 2-3cm.
4. Weight: 500-600gm (about  $\frac{1}{6}$  weight of fetus).
5. Surfaces:
  - i. Fetal surface of placenta:
    - (a) Smooth-shiny and covered by amnion.
    - (b) Umbilical cord attached near its center.
    - (c) Umbilical vessels branch on its surface to form chorionic vessels which enter chorionic villi.
  - ii. Maternal surface of placenta:
    - Shows cotyledons with Cobblestone appearance produced by bulging villi.

# FETAL MEMBRANES





Schematic drawing of a transverse section through a full-term placenta.

### Connecting stalk and Umbilical cord

**Definition:** cord connects mother with fetus containing umbilical vessels for gases exchange and transmission of nutrient and metabolites.

**Length:** 50-60 cm.

**Diameter:** one cm.

**Shape:**

- Twisted because vein shorter than artery.
- False knots along its length.
- Amniotic membrane covers both surfaces.

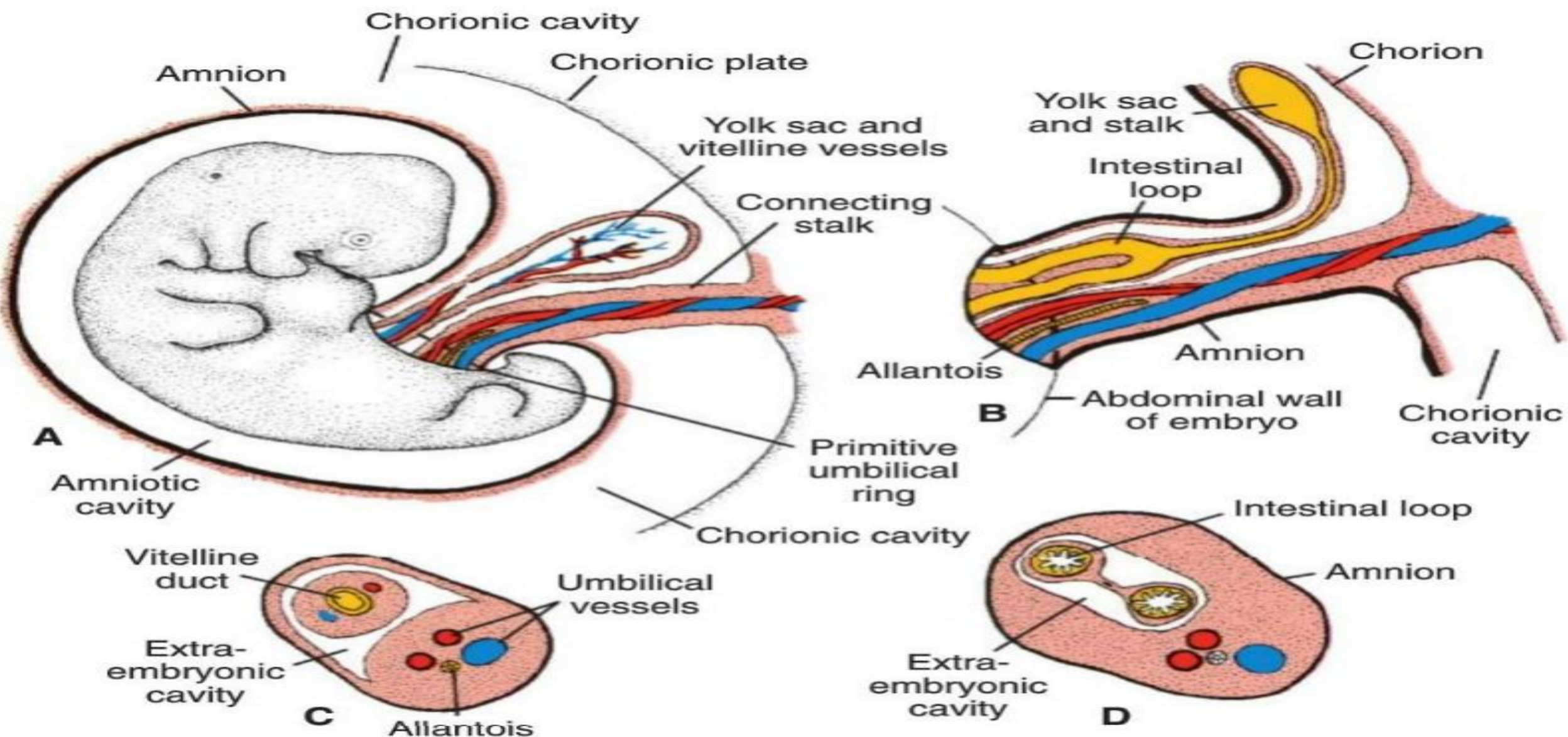
**Attachment to placenta:** near center of fetal surface of placenta.

**Function of umbilical cord:**

1. Allows blood flow between fetus and mother.
2. Allows free fetal movement.

### Structure of umbilical cord

1. Amniotic sheath.
2. Extra embryonic mesoderm of connecting stalk become loose and gelatinous (Wharton's jelly).
3. Umbilical vessels:
  - a) Two umbilical arteries: carry non oxygenated blood.
  - b) Left umbilical vein: carry oxygenated blood.
4. Remnant of extra embryonic coelom: disappear at 10 week.
5. Remnant of vitello intestinal duct: disappear at by (5th – 9th week).
6. Definitive yolk sac: starts to disappear at 10th week.
7. Allanois which connected with urachus of urinary bladder.
8. Intestinal loop of midgut (6-10week).



**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.

# CONGENITAL ANOMALIES

**Definition:** It is a structural, functional, behavioral or metabolic disorders that is present at birth.

## **Types of Abnormalities:**

### **Malformations:**

Occur during formation of structures.

Most malformations have their origin during the third to eighth weeks of gestation.

### **Disruptions:**

Result in morphological alterations of already formed structures and are caused by destructive processes.

### **Deformations:**

Result from mechanical forces that mold a part of the fetus over a prolonged period.

### **A syndrome:**

Is a group of anomalies occurring together that have a specific common cause.

### **Association:**

Is the nonrandom appearance of two or more anomalies that occur together more frequently than by chance alone, but the cause has not been determined.

## The causes of birth defects:

1. **Environmental factors**
2. **Genetic factors**
3. **Multifactorial:** an interaction of the environment with a person's genetic susceptibility. Most birth defects fall into this last category.



## Genetic factors:

### 1. Abnormality in number :

#### A. sex chromosome:

- I. 44+xxy: Klinefelter syndrome
- II. 44+xxx: triple x (super female) syndrome
- III. 44+x: Turner syndrome

#### B. Somatic chromosomes:

- I. Trisomy 21: down syndrome
- II. Trisomy 18
- III. Trisomy 13

### 2. Structural Abnormalities

Structural chromosome abnormalities, which involve one or more chromosomes, usually result from chromosome breakage. It has been suggested that breaks are caused by environmental factors, such as viruses, radiation and drugs,

## CONGENITAL ANOMALIES

### **Environmental Factors (Teratogenic agents):**

#### **1. Infectious agents**

**virus as:** Rubella virus Herpes simplex virus

**Bacteria as:** Syphilis

**Parasite as:** Toxoplasmosis

#### **2. Physical agents**

X-rays and Hypertension

#### **3. Chemical agents as:**

Alcohol, Lead, Thalidomide, Diphenylhydantoin [phenytoin], Lithium, Opioids [codeine, hydrocodone, oxycodone] and Organic mercury

#### **4. Hormones as:**

Androgenic agents, diethylstilbestrol (DES) and Maternal diabetes

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