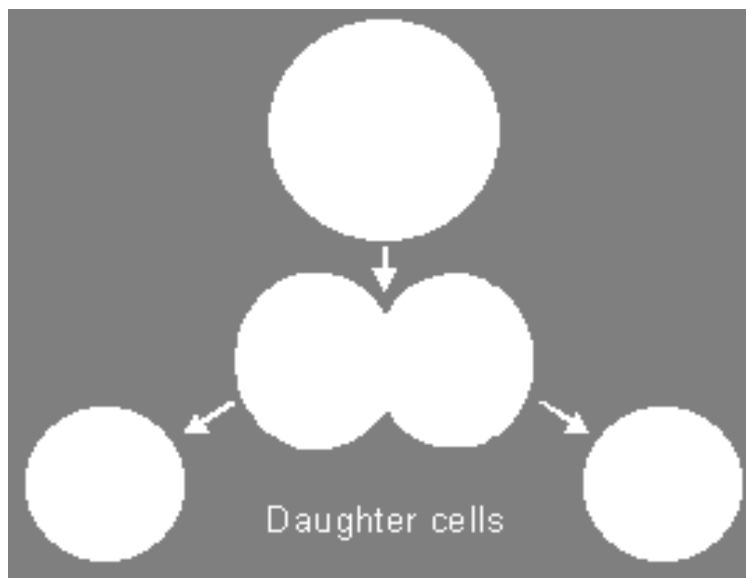


Gen. Embryology

lecture I, cell division, part I

CELL DIVISION

A cell divides by pinching into two. Each of two daughter cells produced contains genetic material inherited from the original (parent) cell.



Why Divide ?

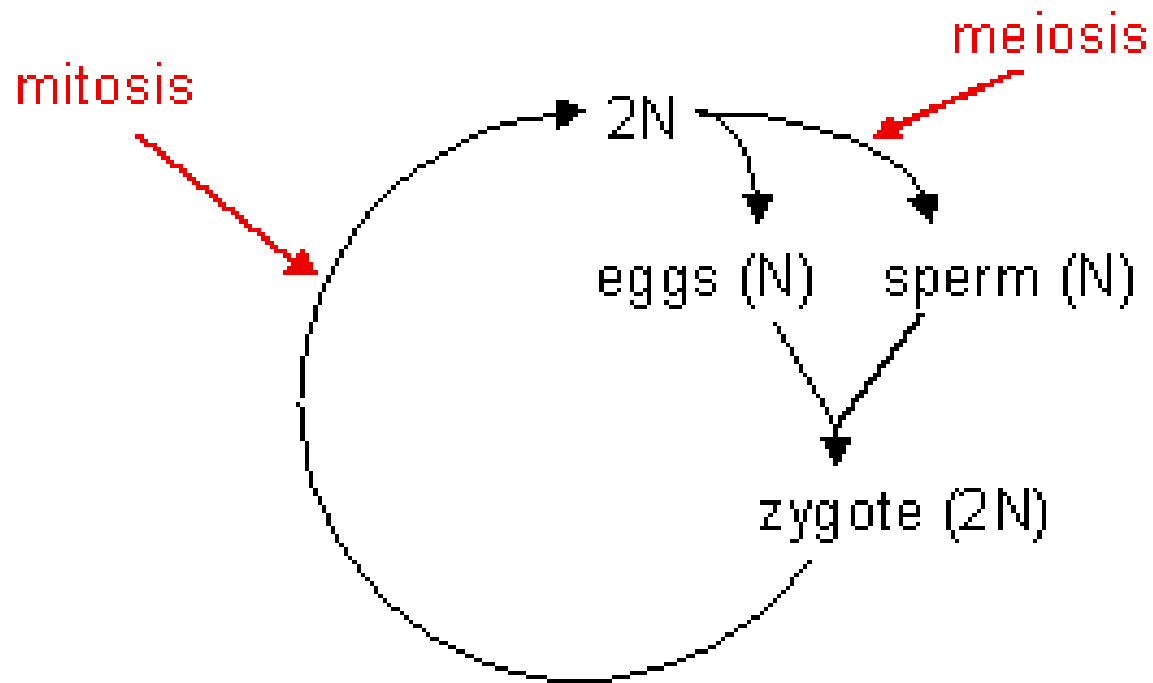
- Single-celled organisms divide to reproduce.
 - Cell division in multicellular organisms enables the organism to grow larger while the cells remain small.
 - Organisms with many cells can have cells which are specialized for different functions and tasks. For example, red blood cells are specialized for carrying oxygen but neurons (nervous tissue) are specialized for conducting signals from one cell to another.
-
- Some cells of multicellular organisms must divide to produce sex cells (gametes).
 - **Mammalian** cells typically divide only about 50 times.
 - **This limit is set by the presence of repeated sequences of DNA at the tips of the chromosomes called *telomeres*.**

Types of Cell Division

- **Mitosis** produces identical daughter cells.
- **Meiosis** produces cells with $1/2$ the number of chromosomes as the parent cell.

Life Cycles

- Meiosis functions to reduce the number of chromosomes to one half. Each daughter cell that is produced will have one half as many chromosomes as the parent cell.
- Meiosis is part of the sexual process because gametes (sperm, eggs) have one half the chromosomes as diploid ($2N$) individuals.



Mitosis

- Mitosis produces two daughter cells that are identical to the parent cell. If the parent cell is haploid (N), then the daughter cells will be haploid. If the parent cell is diploid, the daughter cells will also be diploid.

$$N \longrightarrow N$$

$$2N \longrightarrow 2N$$

- This type of cell division allows multicellular organisms to grow and repair damaged tissue.

Chromatin, Chromosomes

- **Chromatin** is a mass of uncoiled DNA and associated proteins called **histones**.
- When cell division begins, DNA coils around the proteins forming visible structures called **chromosomes**.

Haploid, Diploid

- Diploid cells (2N) have two complete sets of chromosomes. The body cells of animals are **diploid**.
- Haploid cells have one complete set of chromosomes. In human, gametes (sperm and eggs) are **haploid**.

Homologous Chromosomes

- Diploid organisms have two copies of each chromosome (except the sex chromosomes). Each pair of chromosomes is **homologous**. For example, the two #7 chromosomes are homologous. The homologue to the #3 chromosome would be the other #3 chromosome.

Genes

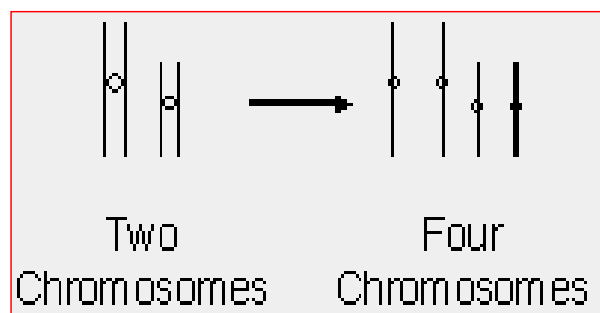
- A small segment of DNA that contains the information necessary to construct a protein or part of a protein (polypeptide) is called a gene. Genes are the unit of inheritance

Chromosome Structure and Replication

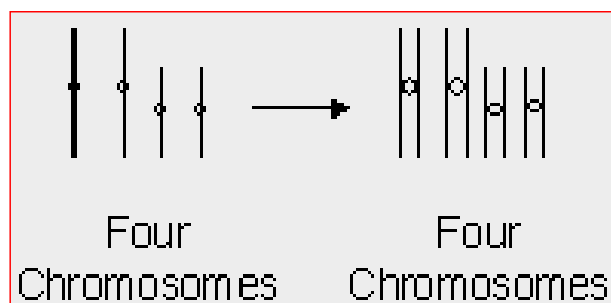
- A **chromatid** is a single DNA molecule.
- Double-stranded chromosomes have two chromatids; normally, each one is identical to the other. The point where the two chromatids are attached is called the **centromere**

Chromosome Doubling vs DNA Synthesis

Splitting chromosomes into two will double their number because each chromatid is identical.



DNA replication occurs when a single-stranded chromosome produces a second chromatid.



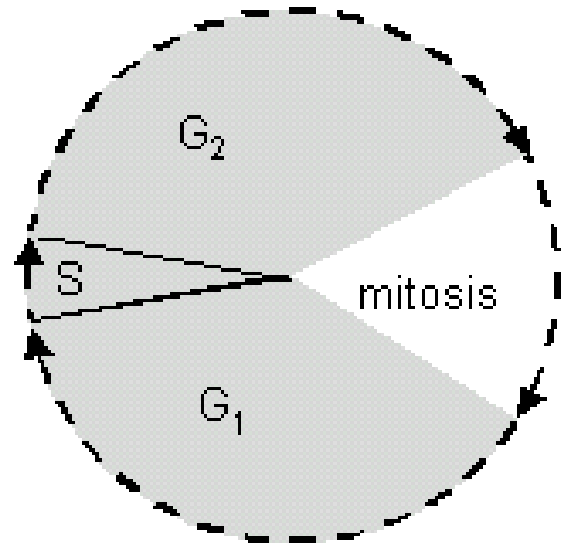
Summary of Mitosis

prophase - coil

metaphase - align

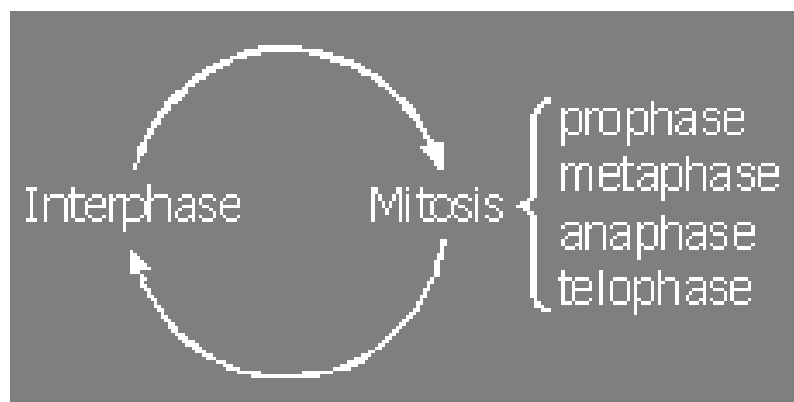
anaphase - separate

telophase - uncoil



The Cell Cycle

The cell cycle alternates between *interphase* and *mitosis* as diagrammed below.



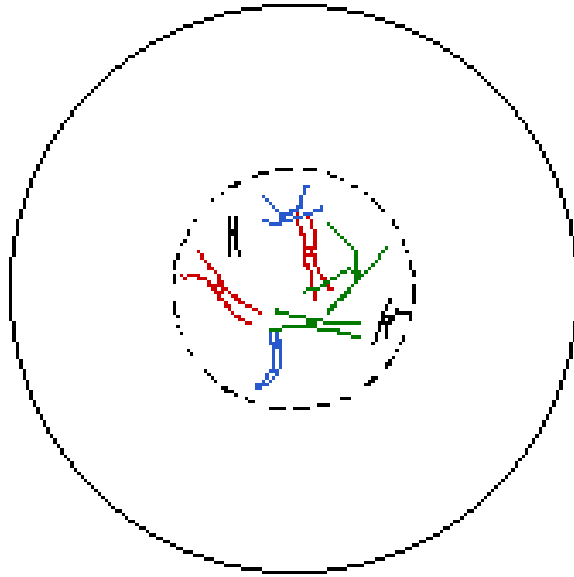
Mitosis has these four phases: prophase, metaphase, anaphase, and telophase.

1- Prophase

The chromosomes coil.

The nuclear membrane disintegrates.

The spindle apparatus forms

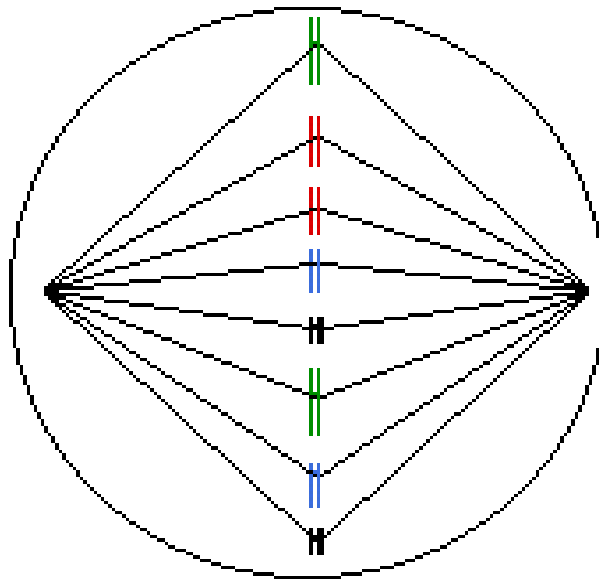


Prophase

- During prophase, chromosomes begin condensing (forming) as DNA becomes coiled. The genes cannot function (produce mRNA and therefore protein) when the DNA is coiled. Coiling facilitates movement.
- The nucleolus disappears.
- The nuclear membrane becomes fragmented and disappears by the end of prophase.

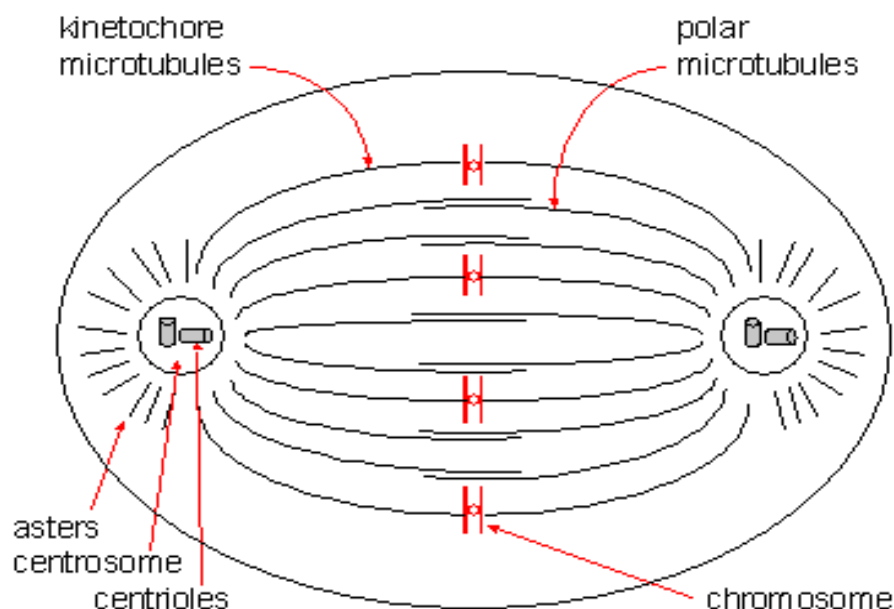
2- Metaphase

The chromosomes become aligned.



Metaphase

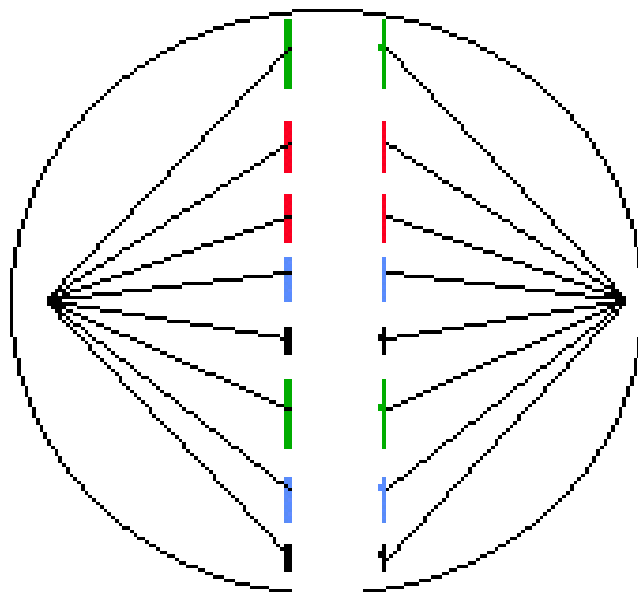
During metaphase, the chromosomes have moved to the center of the cell (diagram below, photograph above). This line of chromosomes is referred to as the metaphase plate.



- **Metaphase ends when chromosomes split, thus doubling the number of chromosomes.**

3- Anaphase

The chromatids separate (The number of chromosomes doubles).

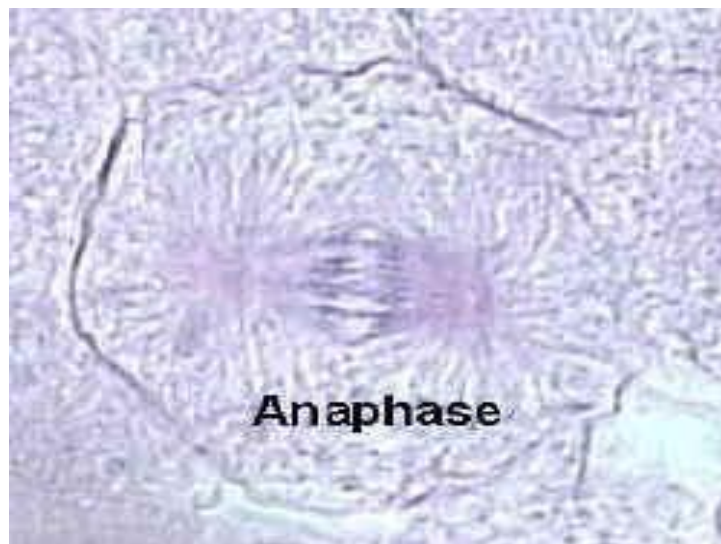


Anaphase

- When the chromosomes split at the end of metaphase, the chromosome number is doubled. For example, the number of chromosomes and chromatids during each phase in a human cell is:

Phase	# Chromosomes	# Chromatids
Prophase	46	92
Metaphase	46	92
Anaphase	92	92
Telophase	92	92

- The chromosomes move toward poles of cell.
- **Cytokinesis** (division of the cytoplasm) begins in anaphase. A cleavage furrow forms as actin filaments underneath the plasma membrane constrict in a band called the contractile ring. Two cells will be produced as this process continues.



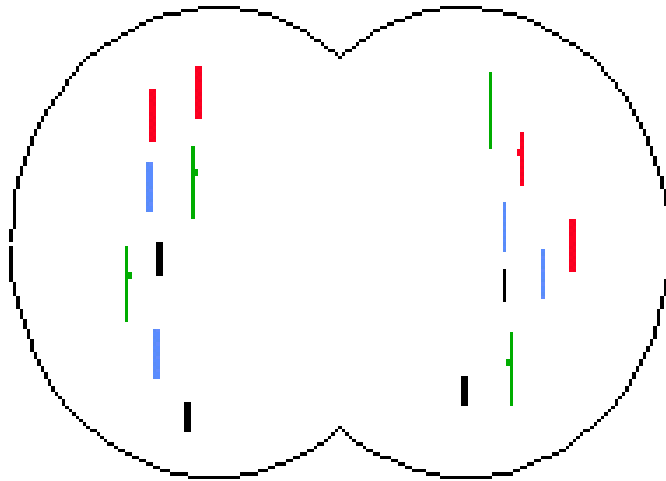
4- Telophase

The nuclear membrane reappears.

The chromosomes uncoil.

The spindle apparatus breaks down.

The cell divides into two



Telophase

- Telophase begins when chromosomes reach the poles of the daughter cells.
- Many of the events in telophase are the reverse of prophase. The chromosomes uncoil, the nuclear membranes around daughter nuclei appear, the spindle apparatus breaks down, and the nucleolus reappears.
- Cytokinesis is completed as telophase ends.

Interphase

- This is the non-dividing phase.
- During interphase, the nucleus is visible and the chromosomes are uncoiled and invisible.
- Interphase includes **G1, S and G2**.

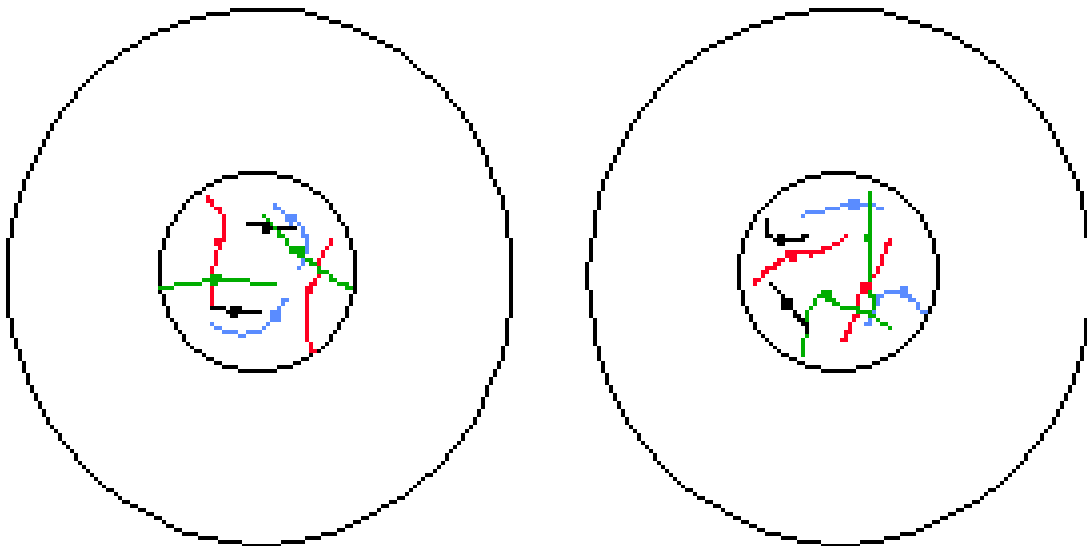


G1 Interphase

The chromosomes have only one chromatid

The cell grows in size.

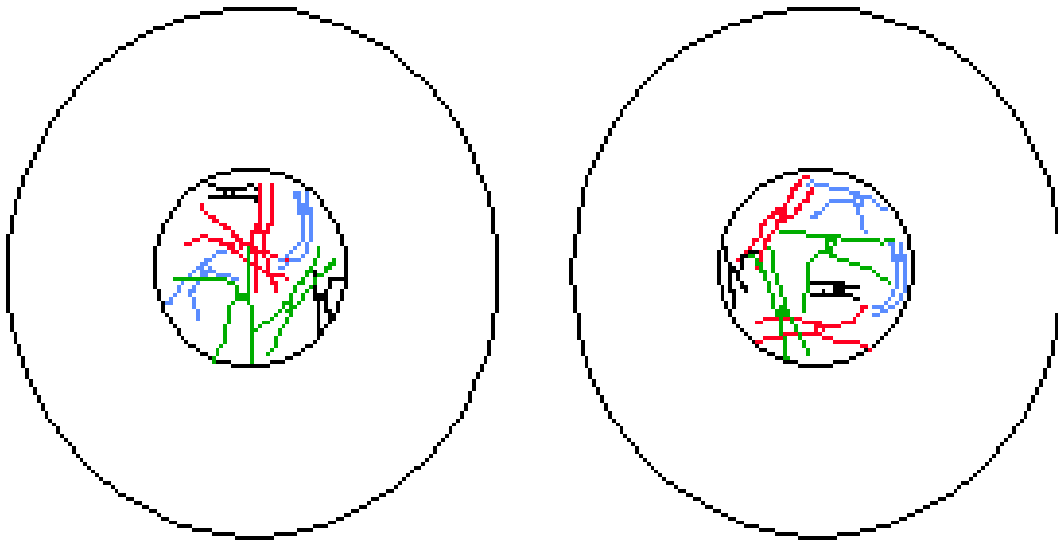
Synthesis of organelles occurs.



G2 Interphase

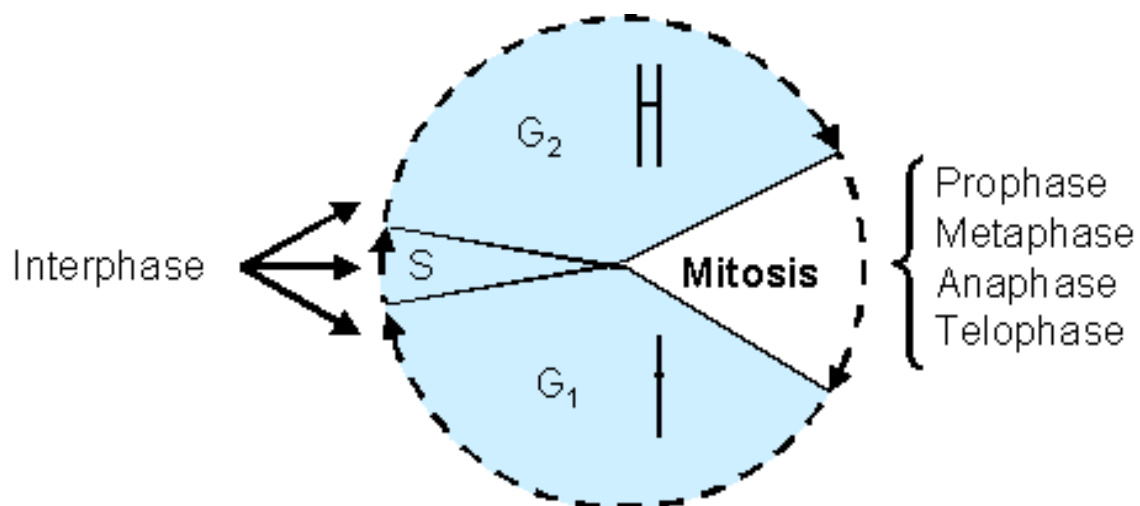
The chromosomes have two chromatids.

The synthesis of enzymes and other proteins in preparation for mitosis occurs during this period.



S Interphase

This is when DNA synthesis occurs.



Control of the cell cycle

1- Telomeres

- Mammalian cells typically divide only about 50 times.
- This limit is set by the presence of repeated sequences of DNA at the tips of the chromosomes called *telomeres*.
- When the telomere is reduced to a certain size, the cell will no longer divide.
- Telomeres are restored to their original length by an enzyme called *telomerase*. This enzyme contains a single strand of RNA that is used to synthesize the telomeres.
- Telomerase is usually found in cells involved in the production of gametes. It is not normally found in somatic cells.

2- Cyclin-Dependent Kinases

- Some cells stop dividing in G1; others stop in G2.
- *Kinases* are enzymes that activate proteins by transferring a phosphate group from ATP to the protein being activated. An activated protein is needed for the cell cycle to proceed from G1 to S. Similarly, another activated protein is needed to move the cycle from G2 to mitosis.
- Kinases activate these proteins and thus stimulate the cell cycle to continue.
- Kinases are normally inactive and must be activated before they can activate other proteins. Cyclin-dependent kinases become activated by combining with a protein called *cyclin*.

- The level of cyclin fluctuates (cycles). At low levels, kinases are not activated and the cell cycle is halted. At high levels, activation occurs and the cycle resumes.

3- Growth Factors

- Growth factors are molecules that stimulate nearby cells to divide by promoting the binding of cyclin to kinase.
- Under normal conditions, cyclin combines with kinase only when growth factors are present. For example, damaged tissue releases growth factors to stimulate cell division needed to repair the tissue.
- S-Cyclin
- S-Kinase combines with S-cyclin and the resulting active complex stimulates DNA replication.

Thank you

Gen. Embryology

lecture II, cell division, part II

Meiosis

- Meiosis produces daughter cells that have one half the no. of **chromosomes** as the parent cell.
 $2N \longrightarrow N$
- Meiosis enables organisms to reproduce sexually. Gametes (sperm and eggs) are haploid.
- Meiosis is necessary in sexually-reproducing organisms because the fusion of two gametes (fertilization) doubles the No. of chromosomes.
- Meiosis involves two divisions producing a total of four daughter cells

- [Sexually](#) ; **sexual reproduction** is reproduction that involves the fusion of gametes from two different parents.

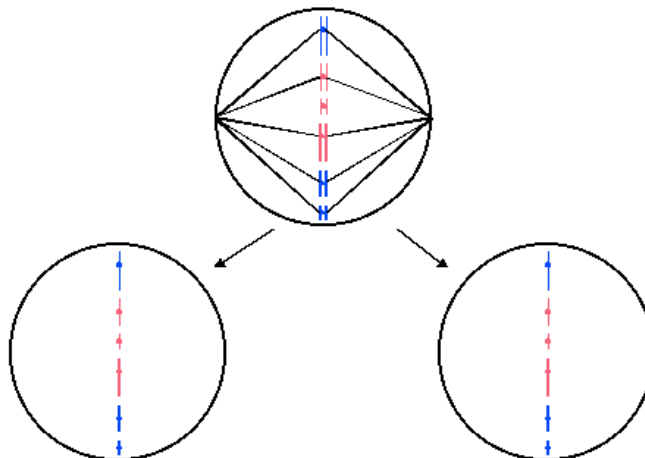
As a consequence of combining genes from two different parents, sexual reproduction promotes genetic variation in populations.

Phases of Meiosis

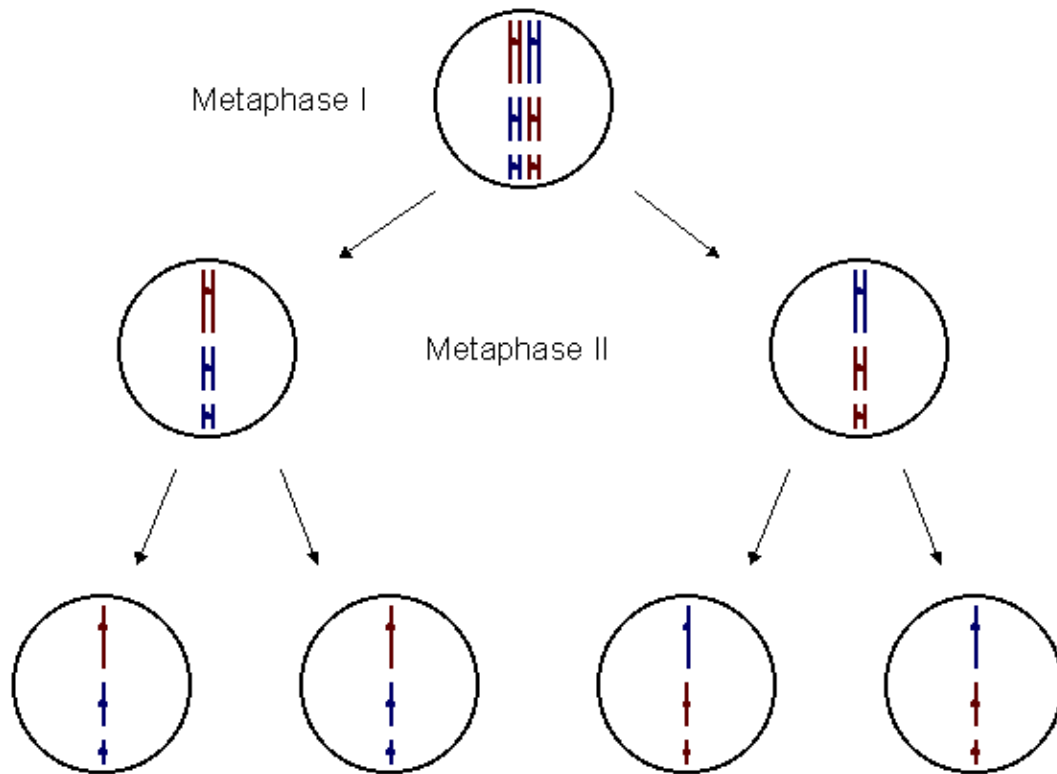
- There are two divisions in meiosis; the first division is meiosis 1 and the second is meiosis 2.
- The phases have the same names as those of mitosis:
Meiosis 1: prophase 1, metaphase 1, anaphase 1, and telophase 1
Meiosis 2: prophase 2, metaphase 2, anaphase 2, and telophase 2

- In **the first meiotic division**, the number of cells is doubled but the number of chromosomes is not. This results in 1/2 as many chromosomes per cell.
- **The second meiotic division** is like mitosis; the number of chromosomes does not get reduced.

The diagram below shows that the chromosome alignment pattern during **metaphase** of *mitosis* results in the chromosomes splitting (doubling). Prophase, anaphase and telophase are not shown. The alignment pattern during **metaphase I** of *meiosis* results in pairs separating; there is no doubling.



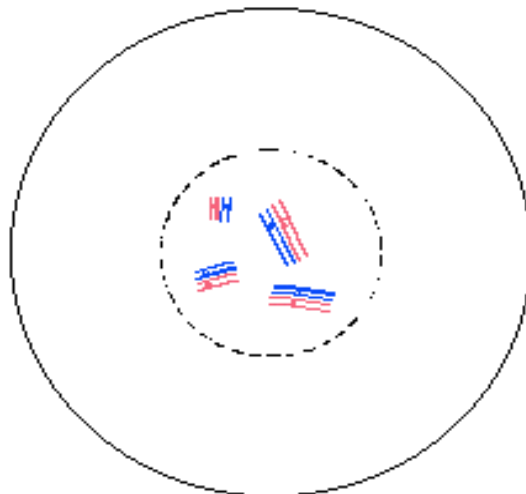
Metaphase 1 & metaphase 2 of meiosis



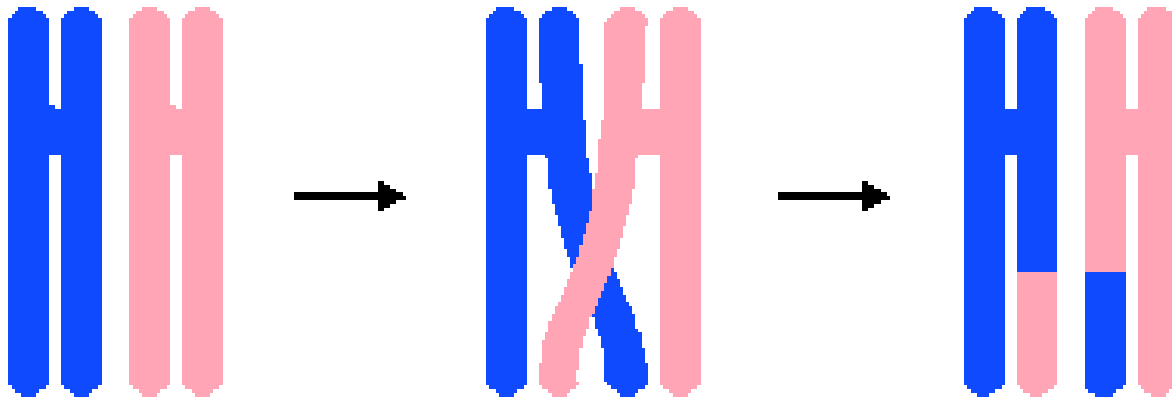
Prophase I

The events that occur during prophase of mitosis also occur during prophase I of meiosis. The chromosomes coil up, the nuclear membrane begins to disintegrate, and the centrosomes begin moving apart.

Synapsis (joining) of homologous chromosomes produces tetrads (also called bivalents).



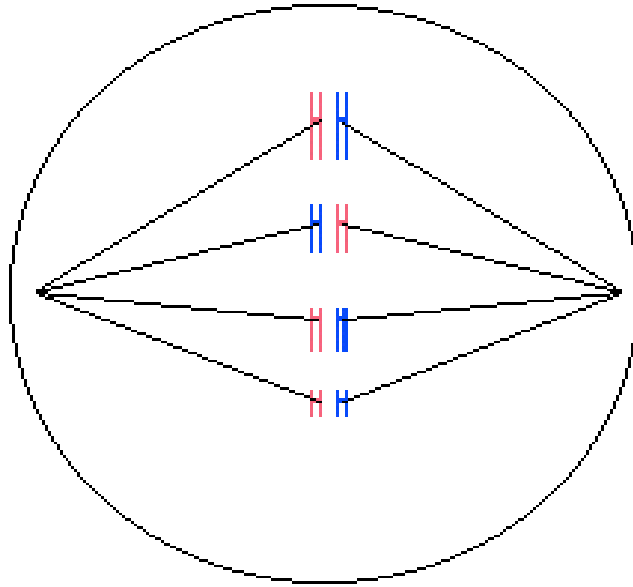
The two chromosomes may exchange fragments by a process called [crossing over](#).



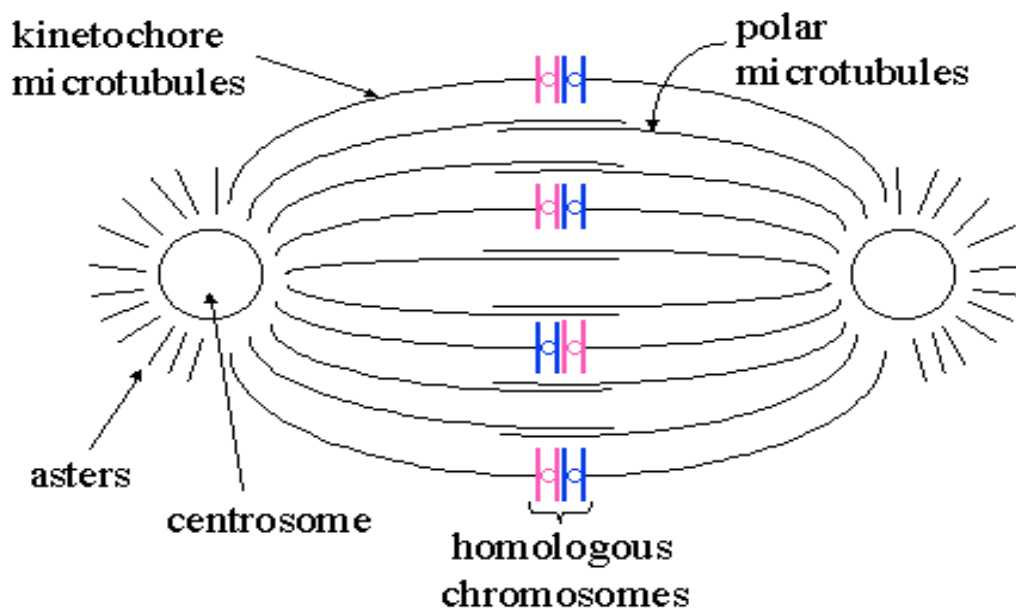
- When the chromosomes partially separate in late prophase, the areas where crossing over occurred remain attached and are referred to as ***Chiasmata*** . They hold the chromosomes together until they separate during anaphase.
- Crossing over between [homologous chromosomes](#) is likely to occur at several different points, resulting in chromosomes that are mixtures of the original two chromosomes.

Metaphase I

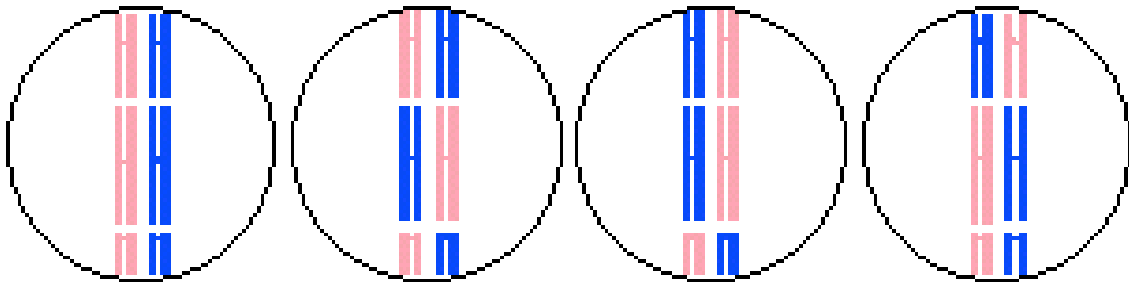
Bivalents (tetrads) become aligned in the center of the cell and are attached to spindle fibers.



The chromosome alignment illustrated below is from a cell with a diploid chromosome number of 8.

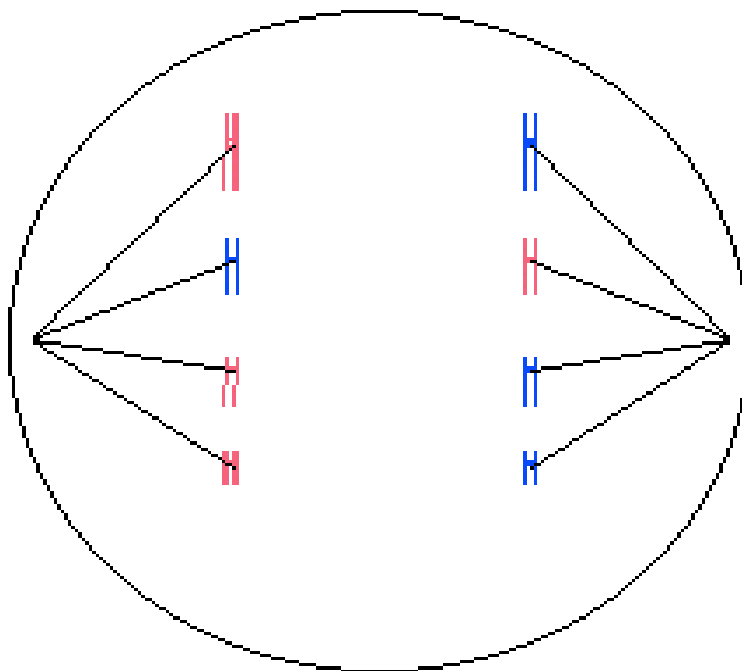


Independent assortment refers to the random arrangement of pairs of chromosomes. The diagram below shows four possible arrangements of chromosomes during metaphase 1 from an individual that has 6 total chromosomes. Suppose that the pink chromosomes are those that the individual inherited from its mother and the blue colored ones were inherited from its father. For each chromosome pair, the chromosome that is on the left (maternal or paternal) is determined randomly. As can be seen, there are several alignment possibilities.



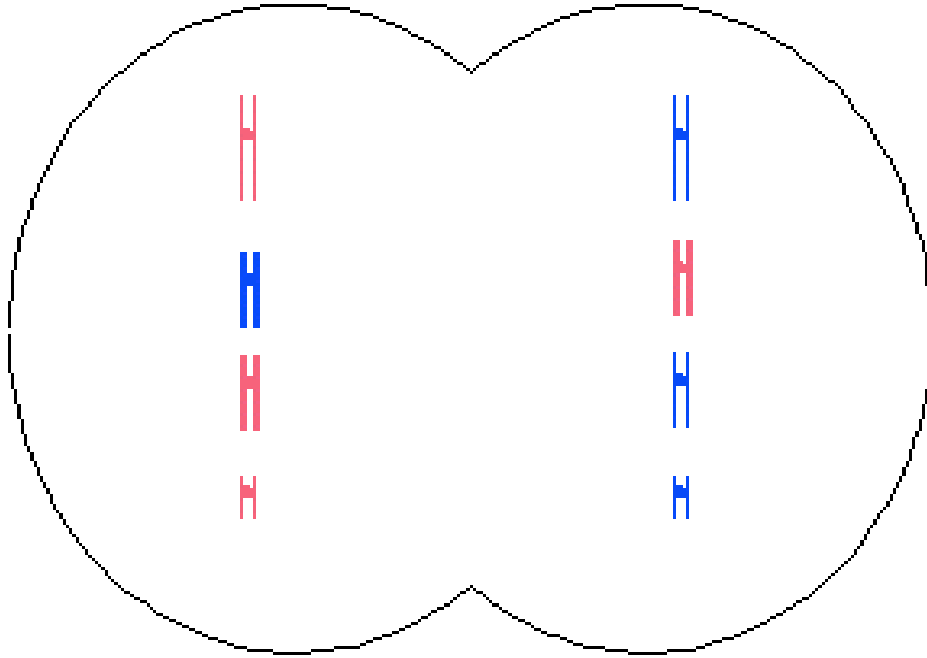
Anaphase I

Anaphase I begins when homologous chromosomes separate.



Telophase I

*The nuclear envelope reforms and nucleoli reappear.
This stage is absent in some species.*

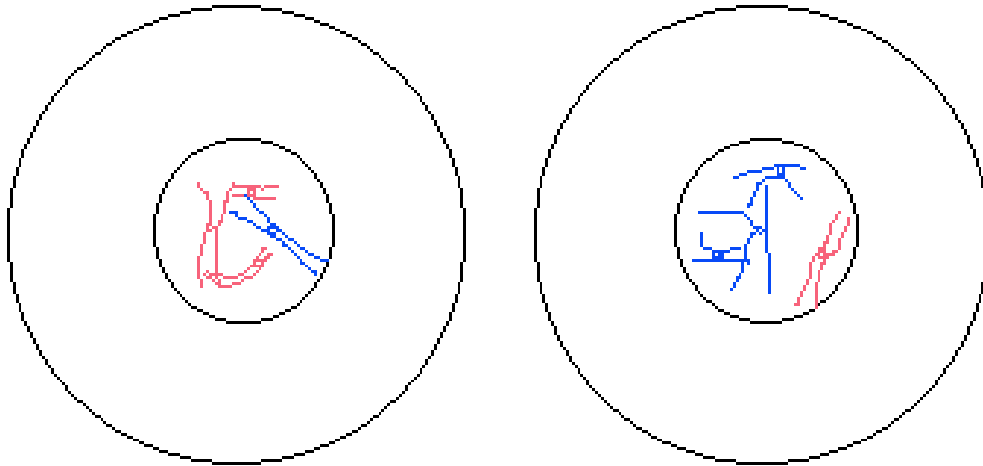


Interkinesis

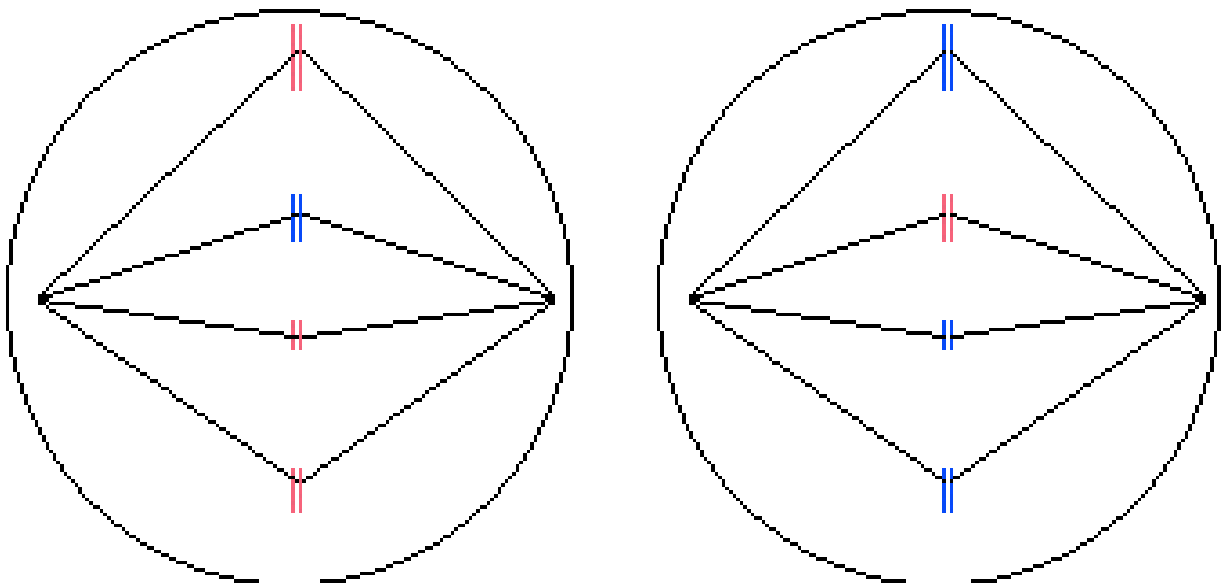
- Interkinesis is similar to interphase except DNA synthesis does not occur.
- The events that occur during meiosis II are similar to **mitosis**.

The events that occur during meiosis II are similar to mitosis.

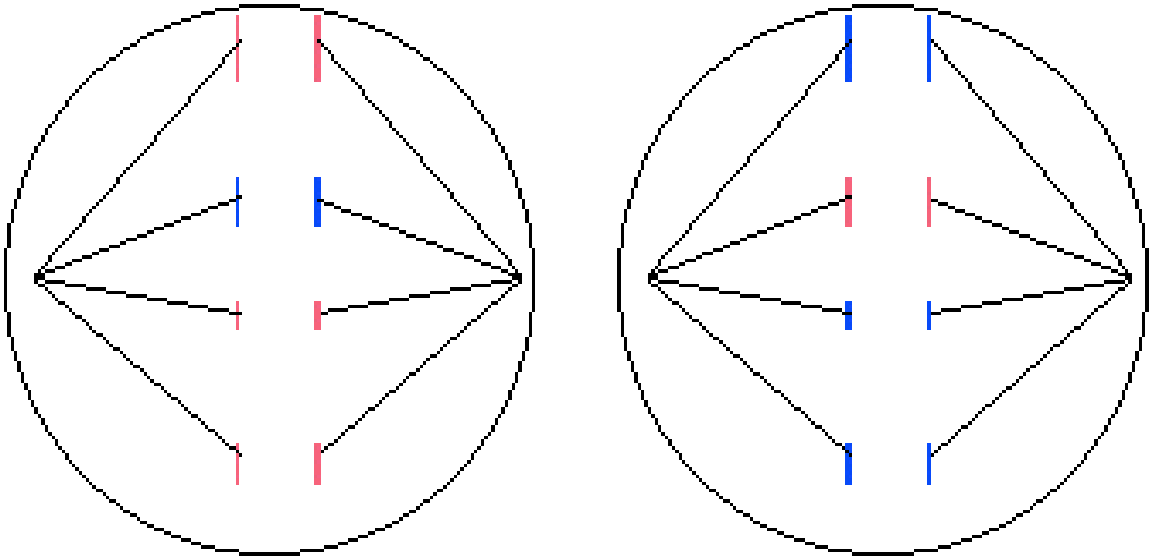
1- Prophase II



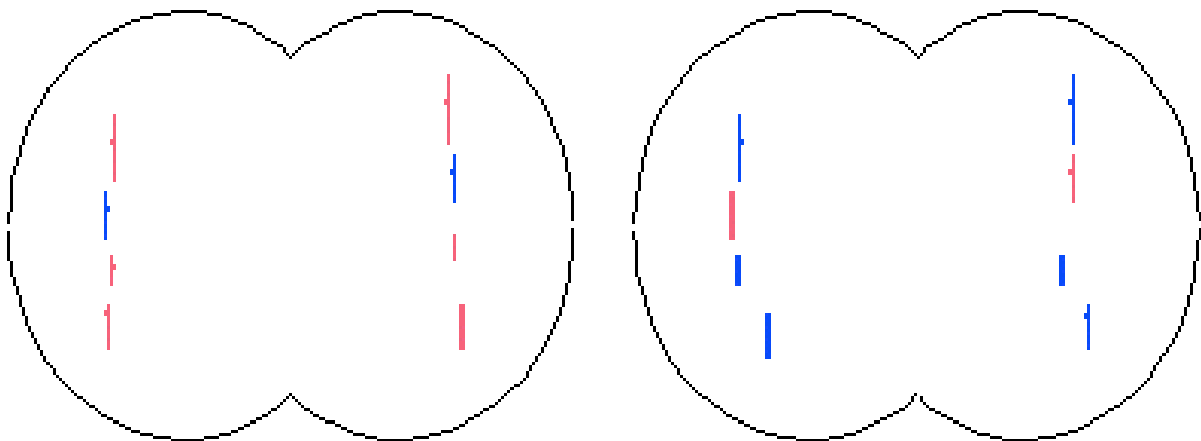
2- Metaphase II



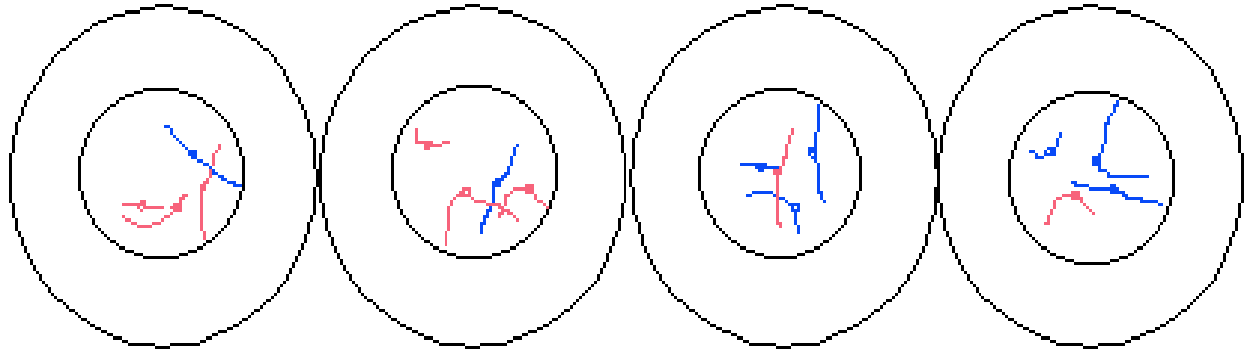
3- Anaphase II



4- Telophase II



Daughter Cells



Variation

- Sexual reproduction promotes variation because each gamete (sperm or egg) contains a mixture of genes from two different parents.
- **Crossing-over** and **Independent assortment** promote variation. During prophase of meiosis, crossing-over results in chromosomes that have some genes from one parent and some genes from the other parent.

- Individuals contain two sets of each chromosome but gametes contain only one set. For each homologous pair of chromosomes, one chromosome will be randomly selected for each gamete formed (*independent assortment*).
- Variation is necessary for natural selection. Recall that natural selection favors individuals with characteristics that are best adapted to their environments. Variation is therefore necessary for species to become adapted to their environment and it enables them to change when the environment changes.

THANK YOU

Gen. Embryology, lecture III, Gametogenesis

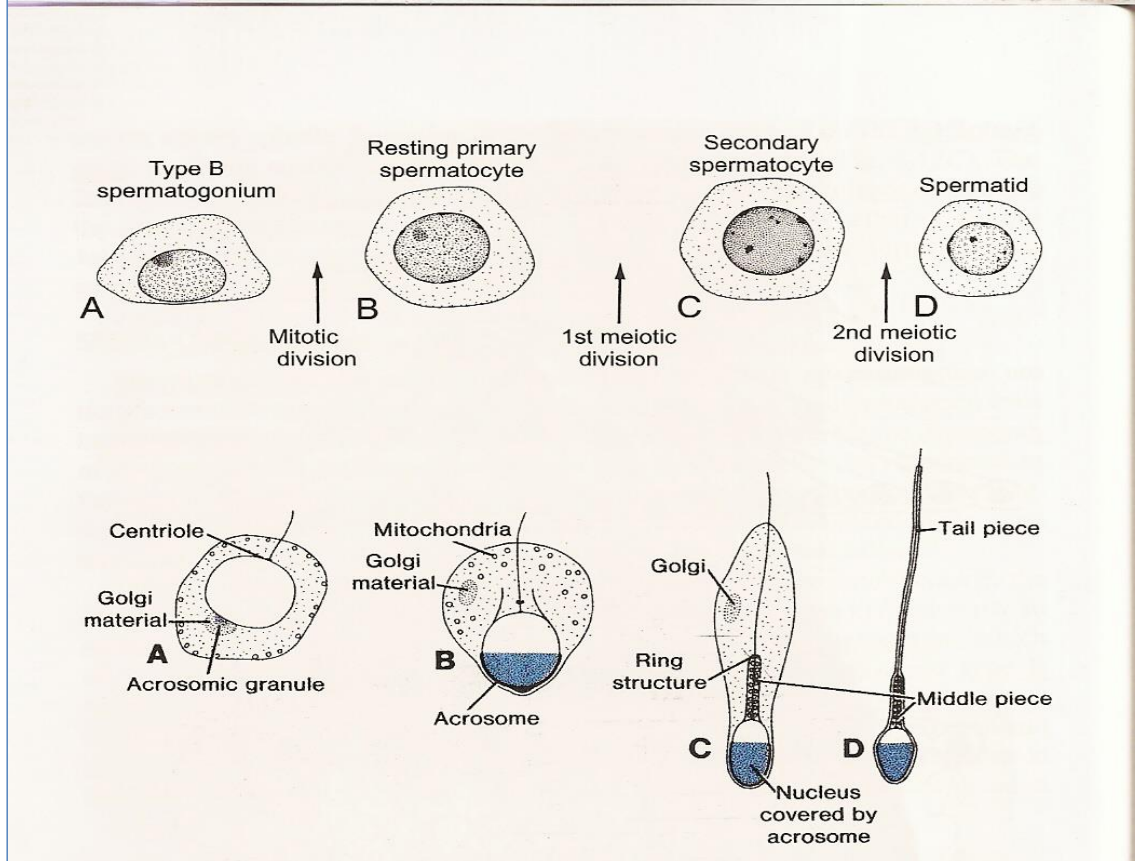
Gametogenesis

- Gametogenesis is the formation of gametes. The formation of eggs is *oogenesis* and the formation of sperm is *spermatogenesis*.
- Gametes are formed by meiosis.

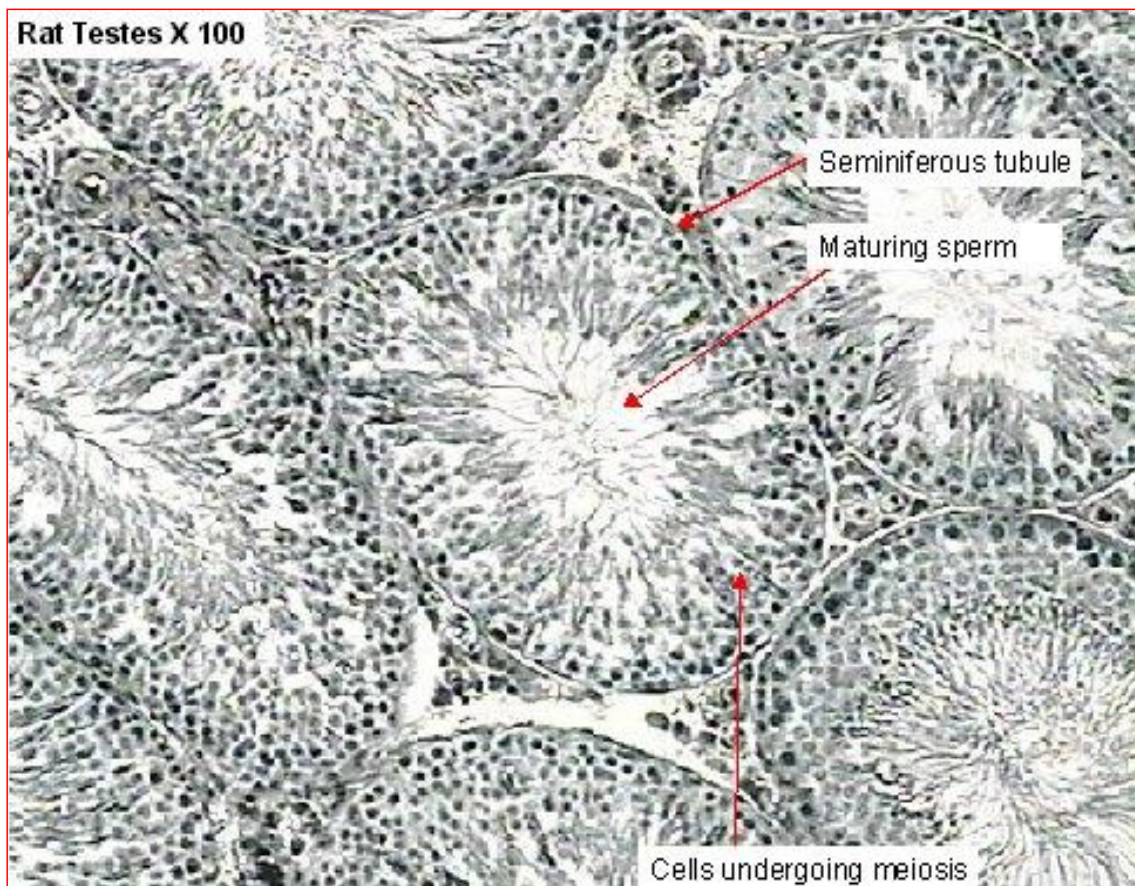
Spermatogenesis

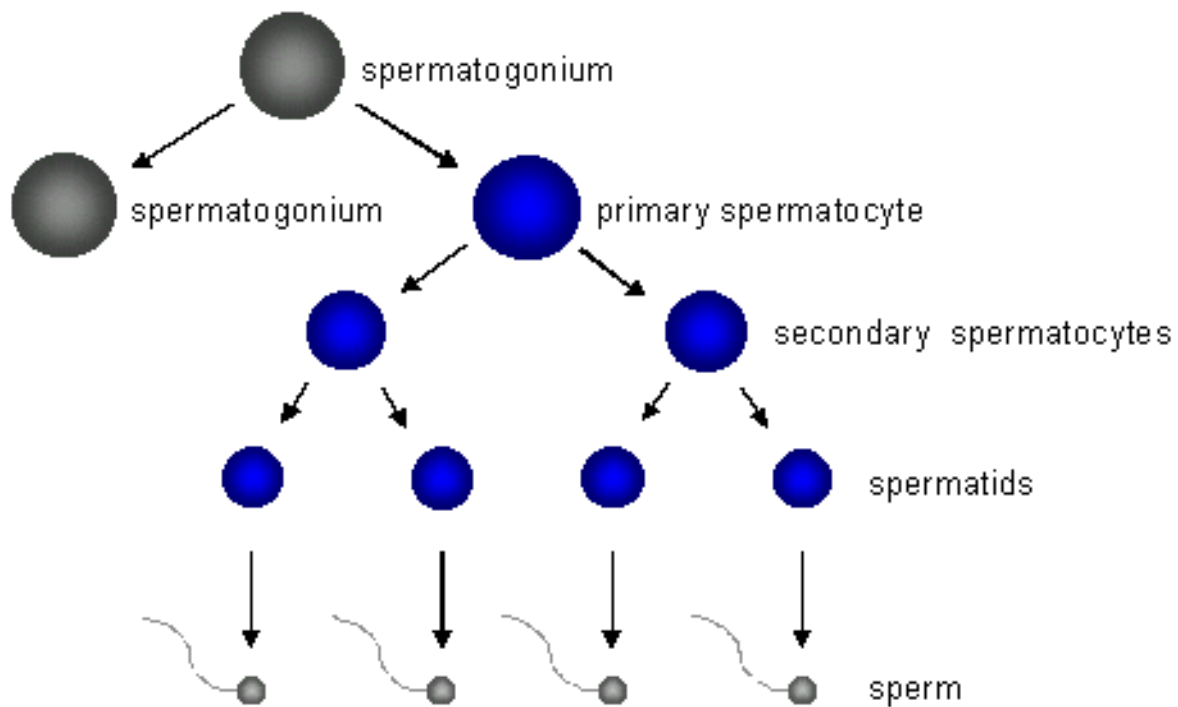
- Spermatogenesis occurs in **seminiferous tubules** in testes.
- In males; differentiation of primordial germ cells begins at puberty (produce spermatogonia).
- **Spermiogenesis** series of changes resulting in the transformation of spermatids into spermatozoa.
- Human males produce approximately 1000 sperm per second (30 billion/year).
- Each ejaculation should contain 200 - 300 million sperm

The cell that undergoes meiosis is a **primary spermatocyte**. The first meiotic division produces two **secondary spermatocytes** and the second division produces **spermatids**, which mature to form sperm. Meiosis I, Meiosis II, and the maturation process each take approximately 16 days (48 days total).

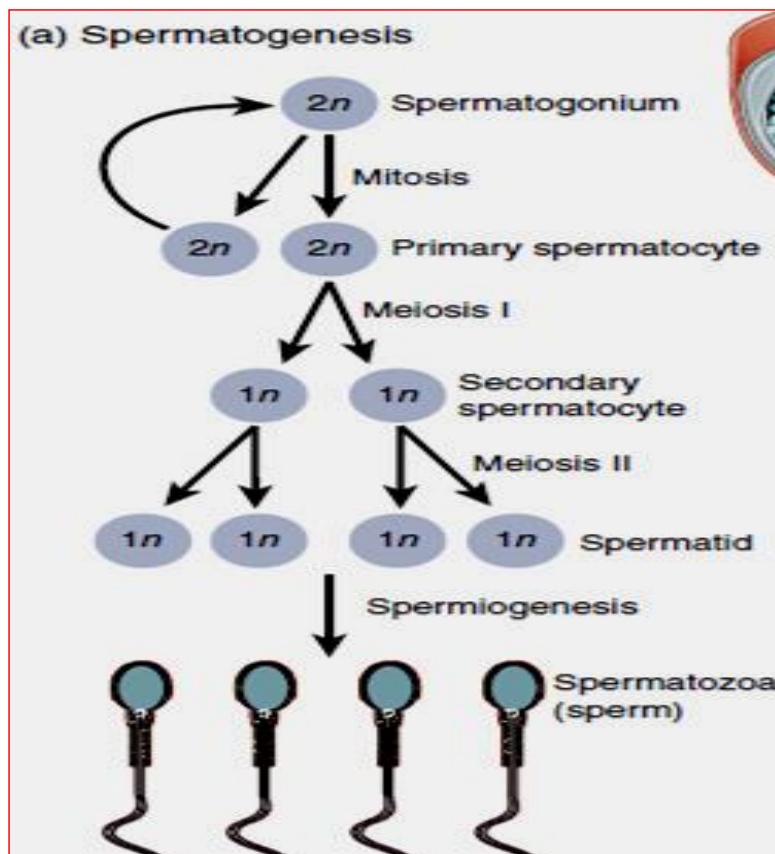


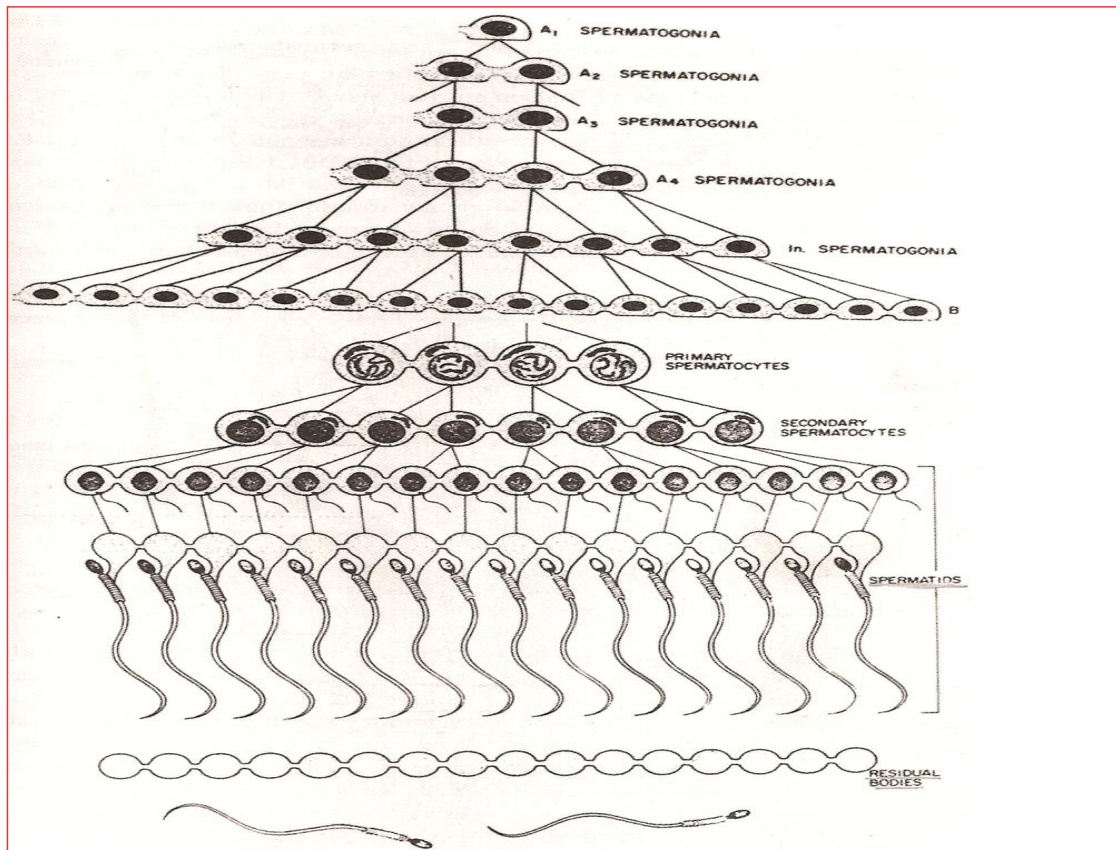
Spermiogenesis series of changes resulting in transformation of spermatids into spermatozoa.





Males do not run out of sperm because mitosis precedes each meiosis. The diagram above shows that a spermatogonium divides by mitosis to produce a primary spermatocyte and a spermatogonium.

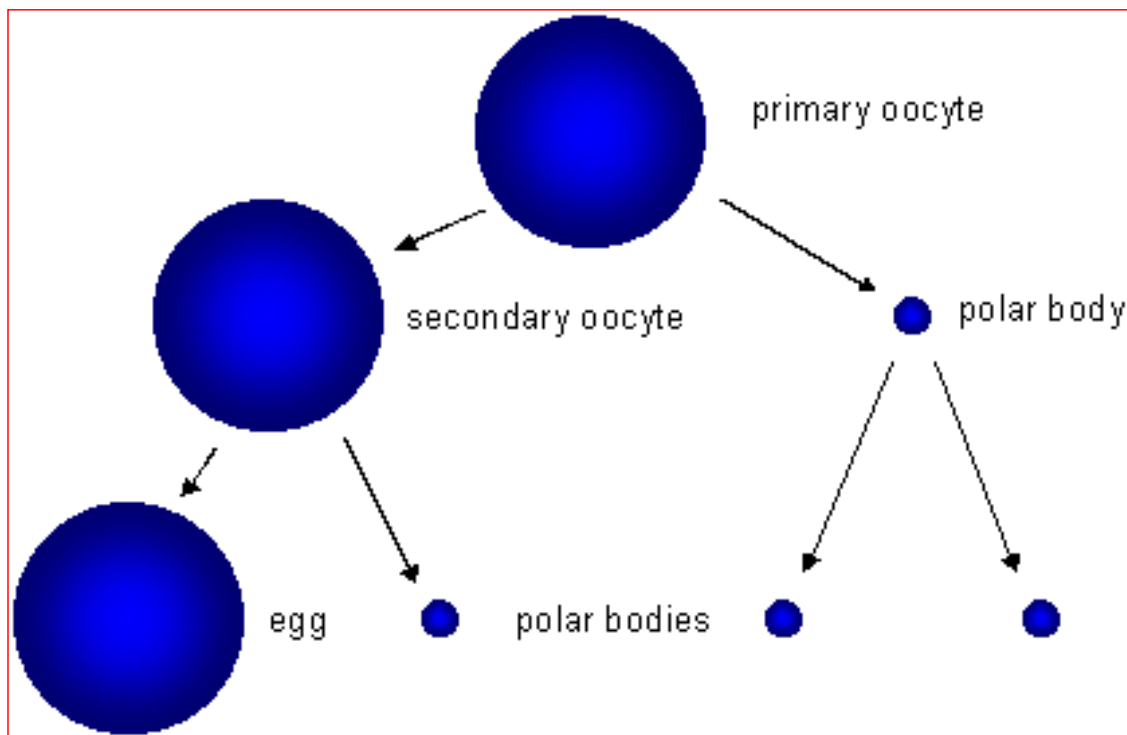
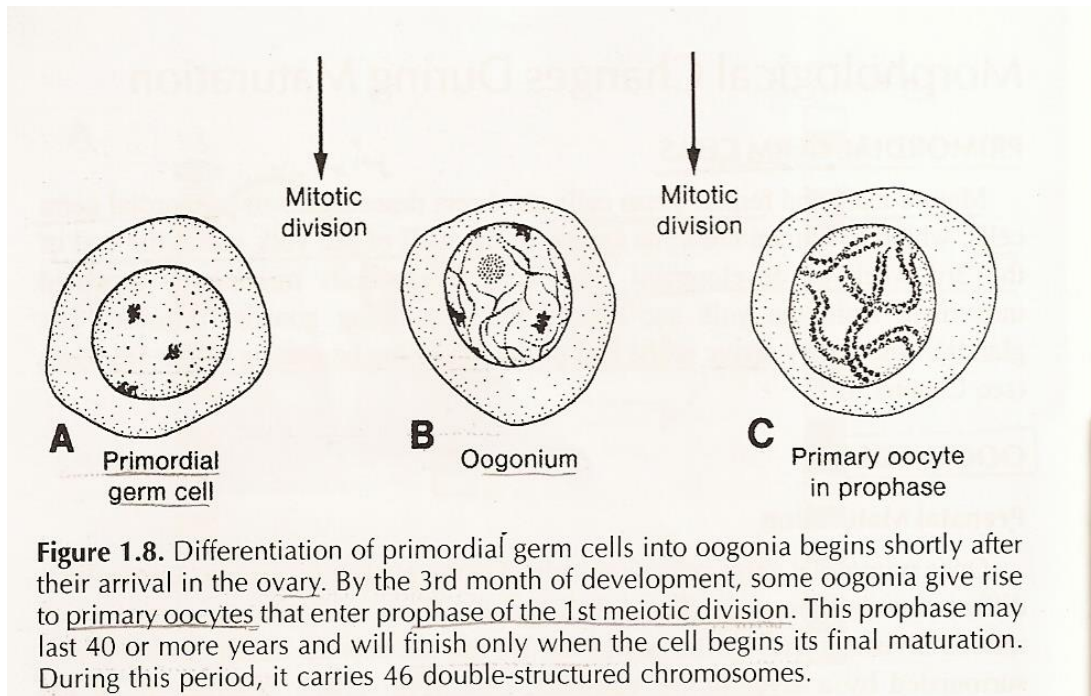




Oogenesis

- Oogenesis occurs in the ovary.
- Each of the divisions in humans is unequal. During the first meiotic division, a large secondary oocyte and a small polar body are produced. The secondary oocyte will divide to produce an egg and a polar body. The first polar body may divide to produce two more polar bodies.
- Although the polar bodies are very small and nonfunctional, they contain a full set of chromosomes.

primordial germ cells have arrived to the gonads of genetic female, they differentiate to oogonia



Prenatal maturation

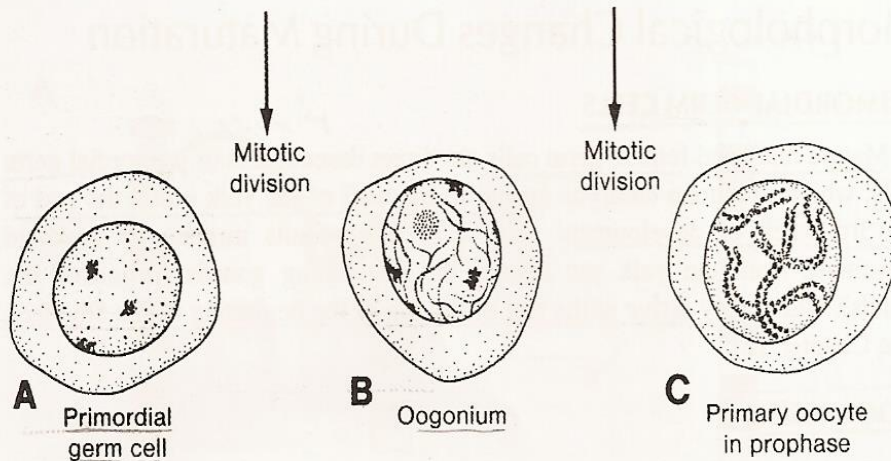


Figure 1.8. Differentiation of primordial germ cells into oogonia begins shortly after their arrival in the ovary. By the 3rd month of development, some oogonia give rise to primary oocytes that enter prophase of the 1st meiotic division. This prophase may last 40 or more years and will finish only when the cell begins its final maturation. During this period, it carries 46 double-structured chromosomes.

Postnatal maturation

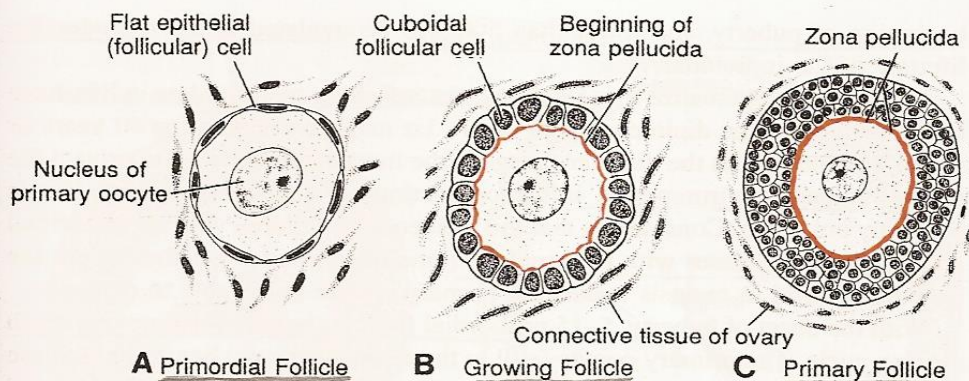
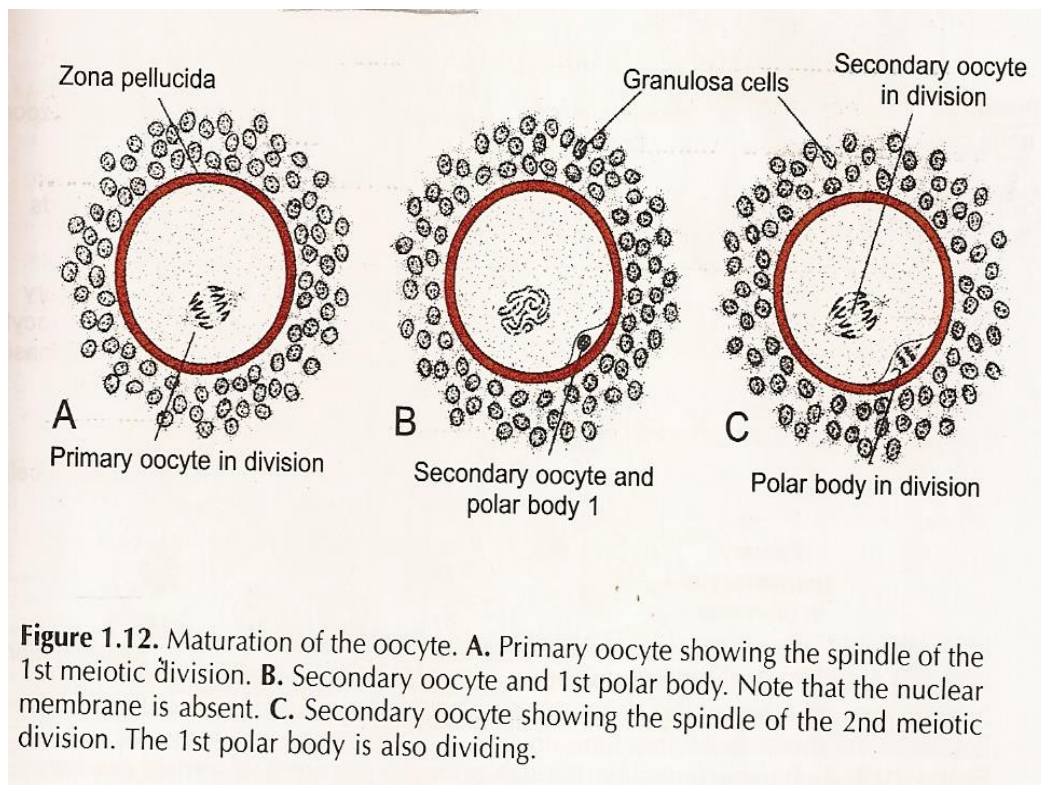
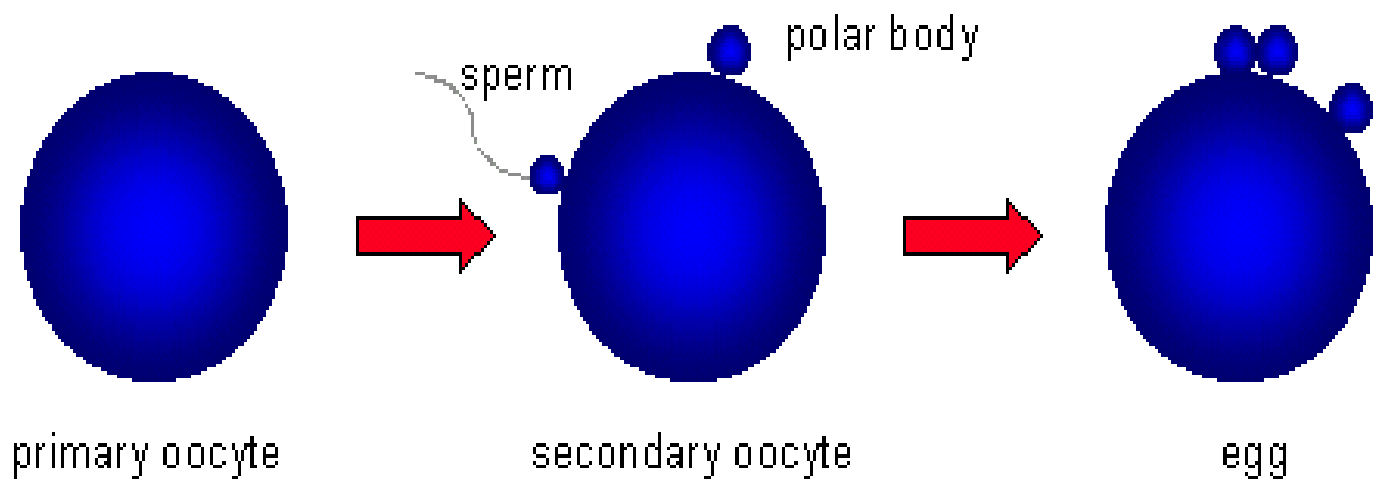


Figure 1.10. A. Schematic drawing of a primordial follicle consisting of a primary oocyte surrounded by a layer of flattened epithelial cells. B. As maturation of the follicle proceeds, the follicular cells become cuboidal. They now begin to secrete the zona pellucida, which is visible in irregular patches on the surface of the oocyte. C. With further maturation, the follicular cells form a stratified layer of granulosa cells around the oocyte, thus transforming the primordial follicle into a primary follicle, and the zona pellucida is well defined.



- Meiosis in human females begins before person is born but stops in prophase I and does not resume until after puberty.
- Each month, approximately 1000 primary oocytes will mature but most will die.
- Ovulation occurs approximately once every 28 days. Females ovulate approximately 400 times during their lifetime.
- Secondary oocytes are released at ovulation. The second meiotic division resumes after penetration by sperm.
- In humans, secondary oocytes are fertilized. Eggs are produced only after fertilization of a secondary oocyte.



In the diagram above, the first polar body produced after the first meiotic division did not divide again. Women are born with all of the primary oocytes that they will ever have (2 million). At puberty, there are approximately 400,000 left.

THANK YOU

Normal Development

- During the first month of development, the germ layers of the embryo and the extraembryonic structures form concurrently.
- An overview of each week has been included to describe the sequence of events, including those occurring at the same time. Critical events are then presented in tutorial form.

Gen. embryology,

lecture IV,

First week of development

1. Ovulation & fertilization

Ovarian cycle

At puberty, the female begins to undergo regular monthly cycle(sexual cycles), which controlled by hypothalamus.

Gonadotropin-releasing hormones (GnRH) affect anterior Pituitary which secrete gonadotropins (FSH,LH), stimulate & control cycle changes in the ovary.

At the beginning of each cycle, 5-15 primordial follicles begin to grow (under FSH). Normally only one of these follicles reaches full maturity, & only one oocyte is discharged.

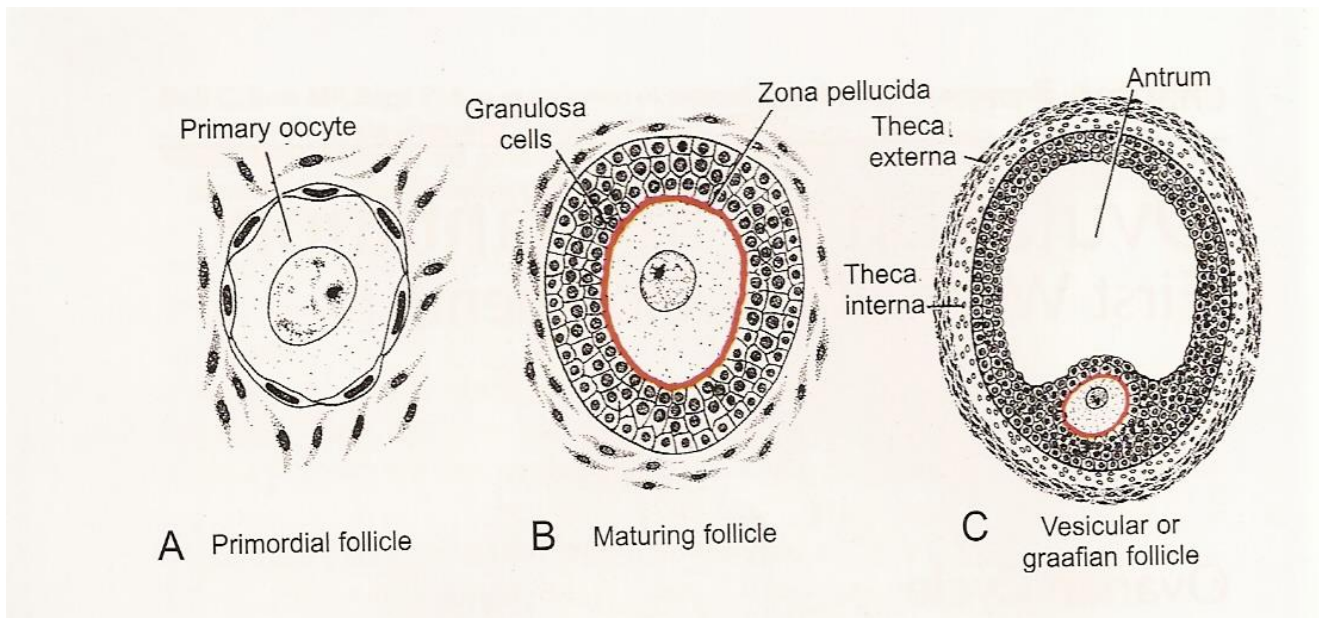
Majority of follicles degenerate & atretic without maturity.

During growth of the follicle, large no. of follicular and thecal cells are formed. These cells produce **estrogens** which:

(a) Cause the uterine endometrium to enter the follicular or proliferative phase.

(b) Stimulate the pituitary gland to secrete LH.

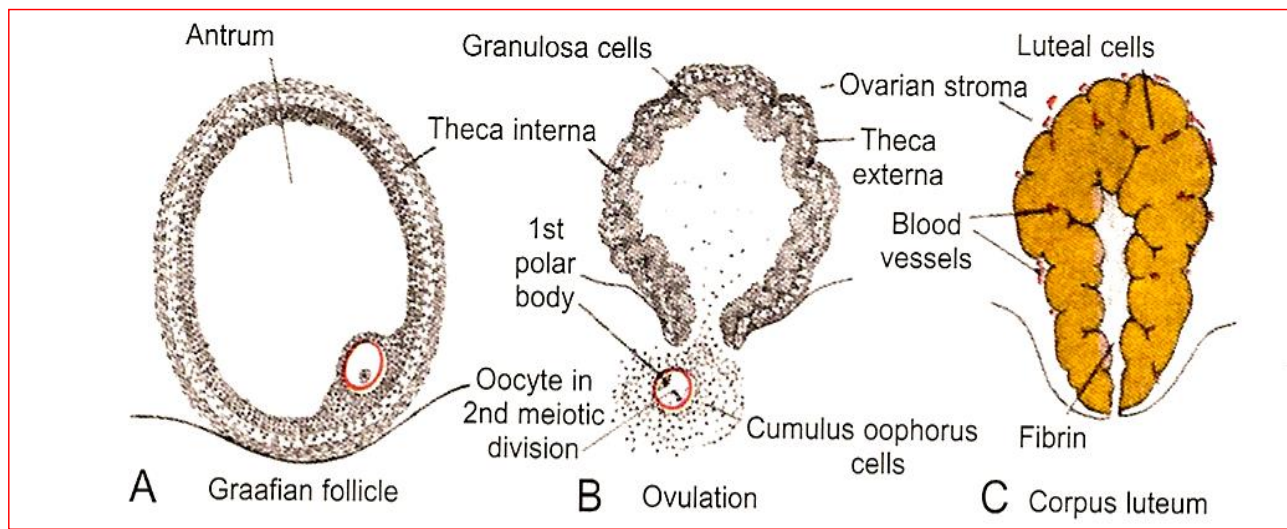
This hormone is needed for final stages of follicle maturation & for ovulation.



Changes occurring in the primordial follicle during the first half of the ovarian cycle. Under FSH the primordial follicle (A) matures into the graafian follicle (C). The oocyte remains a primary oocyte until shortly before ovulation.

Ovulation

- Immediately before ovulation, the graafian follicle increases rapidly in size under the influence of FSH & LH.
- Coincident with final development of the graafian follicle, the primary oocyte, finishes its 1st meiotic division.
- In the; meantime, the surface of the ovary begins to bulge locally, and at the apex an a vascular spot, **the stigma**, appears.
- Because of local weakening and degeneration of the ovarian surface, increasing intrafollicular pressure, and muscular contraction in the ovarian wall, the oocyte is extruded.
- Thus, the oocyte, together with surrounding granulosa cells from the region of the cumulus oophorus, breaks free and floats out of the ovary.



A. Graafian follicle just before rupture

B. Ovulation. The oocyte, beginning its 2nd meiotic division, is discharged from the ovary, Follicular cells remaining inside the collapsed follicle differentiate into luteal cells.

C. Corpus luteum. hypertrophy & accumulation of lipid in the cells.

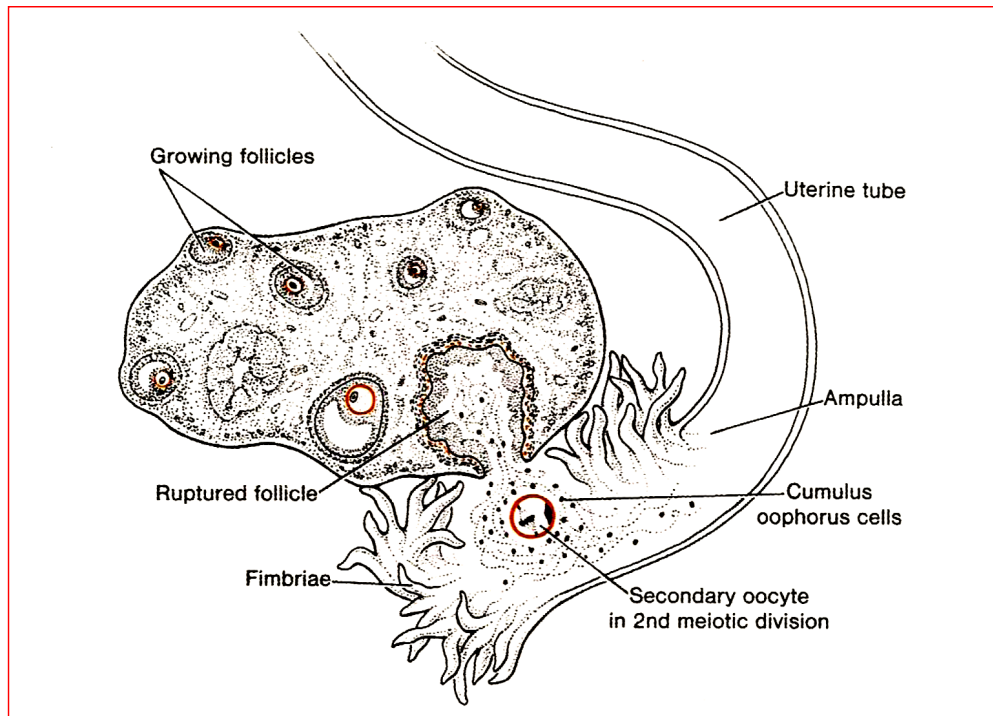
- Some of the cumulus oophorus cells then rearrange themselves around the zona pellucida to form the corona radiata.
- (ovulation), the 1st meiotic division is completed, and the secondary oocyte has started its 2nd meiotic division (see below).

CLINICAL CORRELATES

In some women, ovulation is accompanied by slight pain, and rise in basal temperature,

Some women fail to ovulate due to a diminished concentration of gonadotropins.

Relationship of fimbriae and ovary.



Corpus Luteum

- Following ovulation, granulosa cells remaining in the wall of the ruptured follicle, together with cells from the theca interna, are vascularized by surrounding vessels and become polyhedral.
- Under influence of LH, these cells develop a yellowish pigment and change into luteal cells, which form the corpus luteum and secrete progesterone (see fig. before).

Oocyte Transport

Shortly before ovulation.

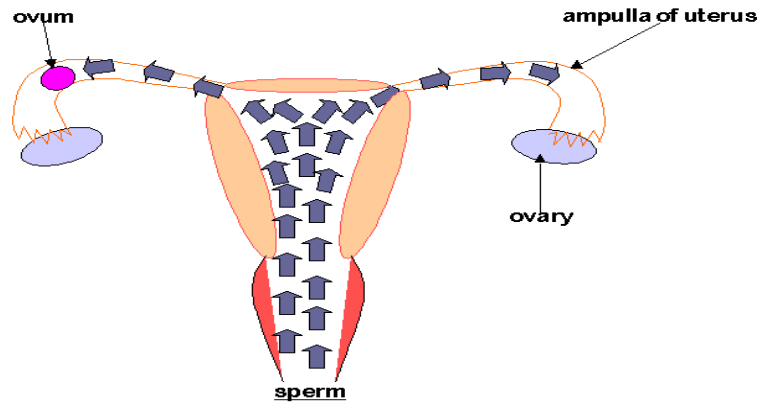
- Fimbriae, of the oviduct begin to cover the surface of the ovary. The tube begins to contract rhythmically.
- The oocyte is carried into the tube by sweeping movements of the fimbriae and by motion of cilia on the epithelial lining.
- Once the oocyte is in the uterine tube, it is pushed toward the uterine lumen by contractions of the muscular wall.
- The rate of transport is affected by the endocrine status during and after ovulation,
- In humans the fertilized oocyte reaches the uterine lumen in approximately 3-4 days.

Corpus Albicans

- If fertilization fails to occur. the corpus luteum reaches maximum development about 9 days after ovulation.
- Subsequently. the corpus luteum decreases in size through degeneration of luteal cells and forms a mass of fibrotic scar tissue, known as corpus albicans.
- Simultaneously, progesterone production decreases, precipitating menstrual bleeding.
- If the oocyte is fertilized. degeneration of the corpus luteum is prevented by chorionic gonadotropin (hCG), which is secreted by the trophoblast of embryo which is continuous to grow.
- Luteal cells continue to secrete progesterone until the end of the 4th month; thereafter, they regress slowly as secretion of progesterone by the trophoblastic component of the placenta becomes adequate for maintenance of pregnancy.

Fertilization

The ovum is surrounded by sperm in the ampulla of the uterine tube



- Sperm produces hyaluronidase to penetrate the follicular cell layer of the corona radiata (see diagram below). It will then interact with only **one** of many receptors.
- At a ZP3 receptor, and the **acrosomal reaction**.
- Once a receptor has been activated, a series of reactions to prevent **polyspermy** (the entrance of more than one sperm).will be initiated. Cortical granules (lysosomes) released into the perivitelline space will hydrolyze the other receptors.

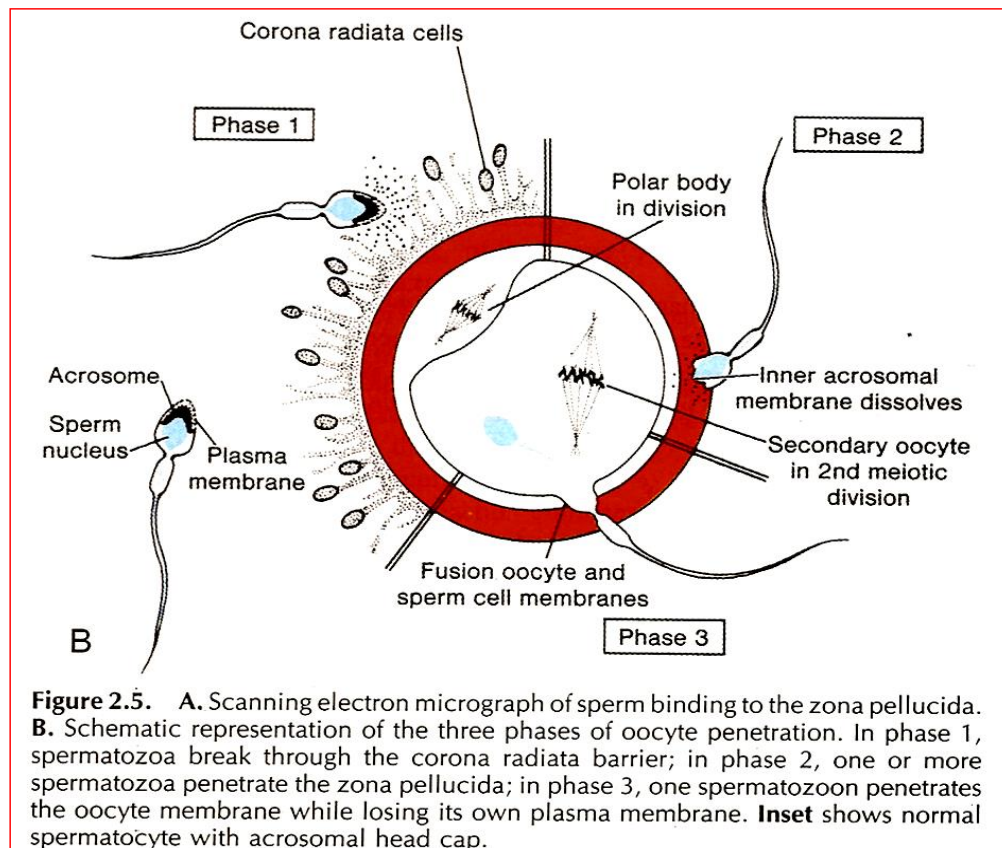
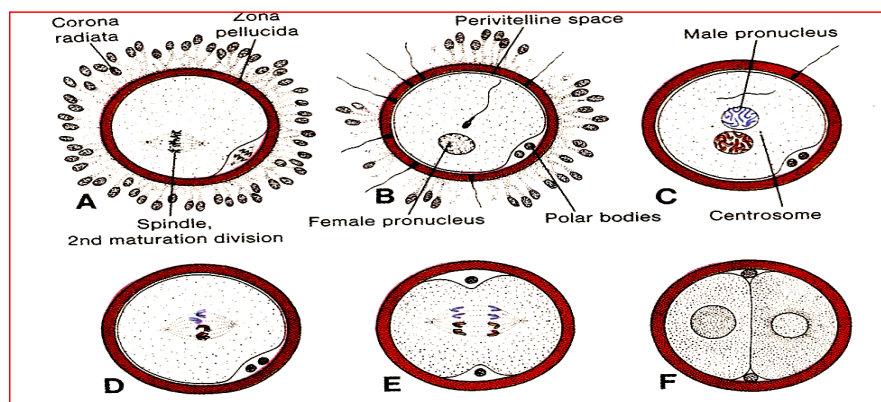
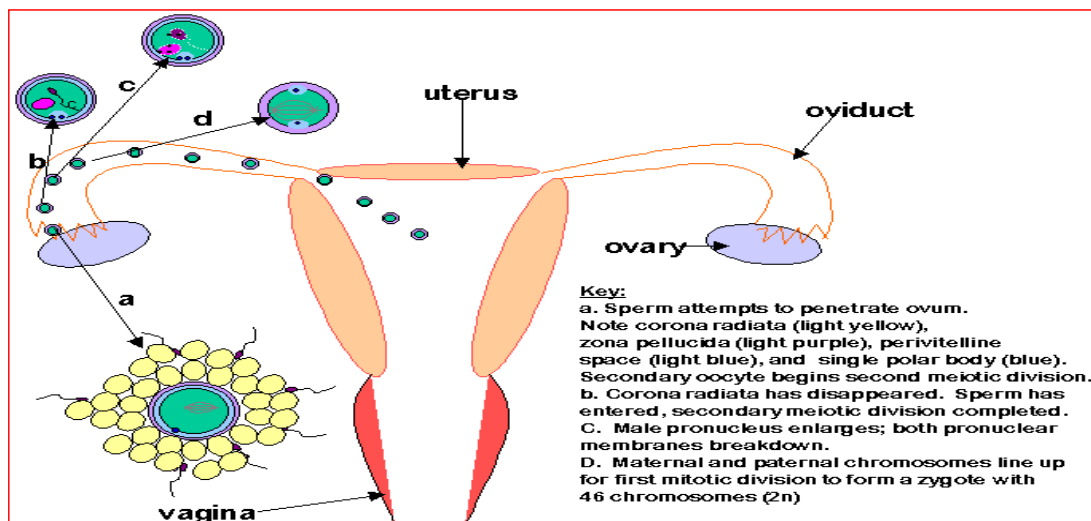


Figure 2.5. A. Scanning electron micrograph of sperm binding to the zona pellucida. B. Schematic representation of the three phases of oocyte penetration. In phase 1, spermatozoa break through the corona radiata barrier; in phase 2, one or more spermatozoa penetrate the zona pellucida; in phase 3, one spermatozoon penetrates the oocyte membrane while losing its own plasma membrane. **Inset** shows normal spermatocyte with acrosomal head cap.

- Fusion of the plasma membranes of the oocyte & sperm occurs; the sperm nucleus is released into the cytoplasm of the oocyte; the rest of the sperm degenerates
- Entrance of sperm into the oocyte causes the secondary oocyte to complete its second meiotic division (2 polar bodies at this point)
- Male pronucleus forms and swells; pronuclei membranes become porous
- Membranes breakdown, chromosomes condense and 46 chromatids line up on metaphase plate in preparation for mitosis



The main result of fertilization are:

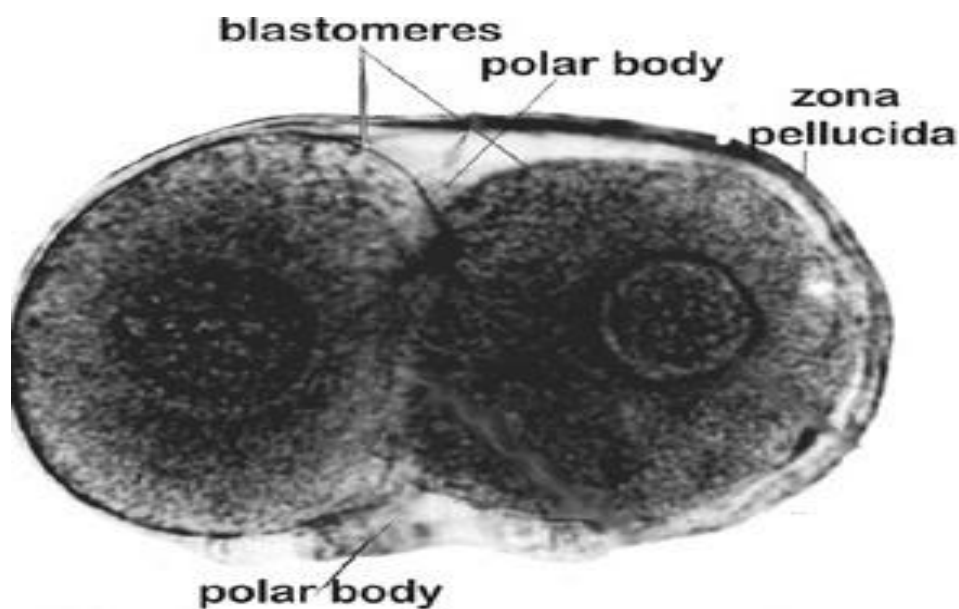
- 1- Restoration of the diploid number of chromosomes.
- 2- Determination of the sex of the new individual female (XX) embryo, male (XY) embryo.
- 3- Initiation of cleavage; without fertilization the oocyte usually degenerates 24 hours after ovulation.

THANK YOU

General embryology, Lecture V, Cleavage & Implantation

Cleavage

Following mitosis, two blastomeres form, each one totipotent (capable of forming its own organism)



- Continuing along the uterine tube, the zygote divides to four, then eight cells
- Size of individual blastomeres decreases with progressive divisions as zygote maintains size
- A ball of 12 or more cells, the **morula**, enters the uterus around day 3

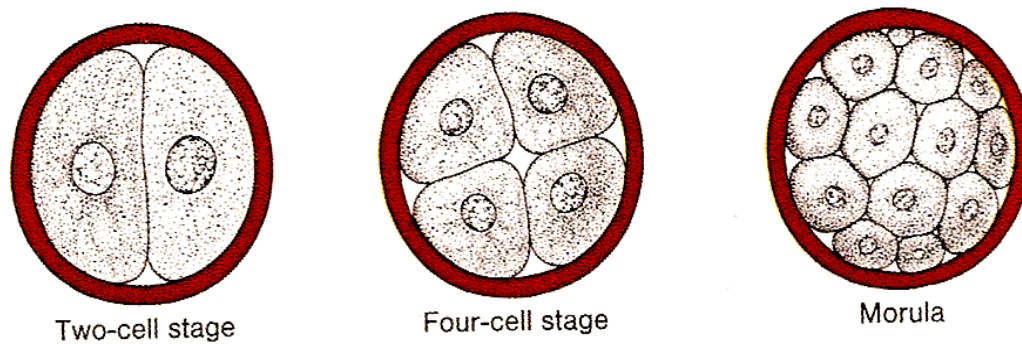
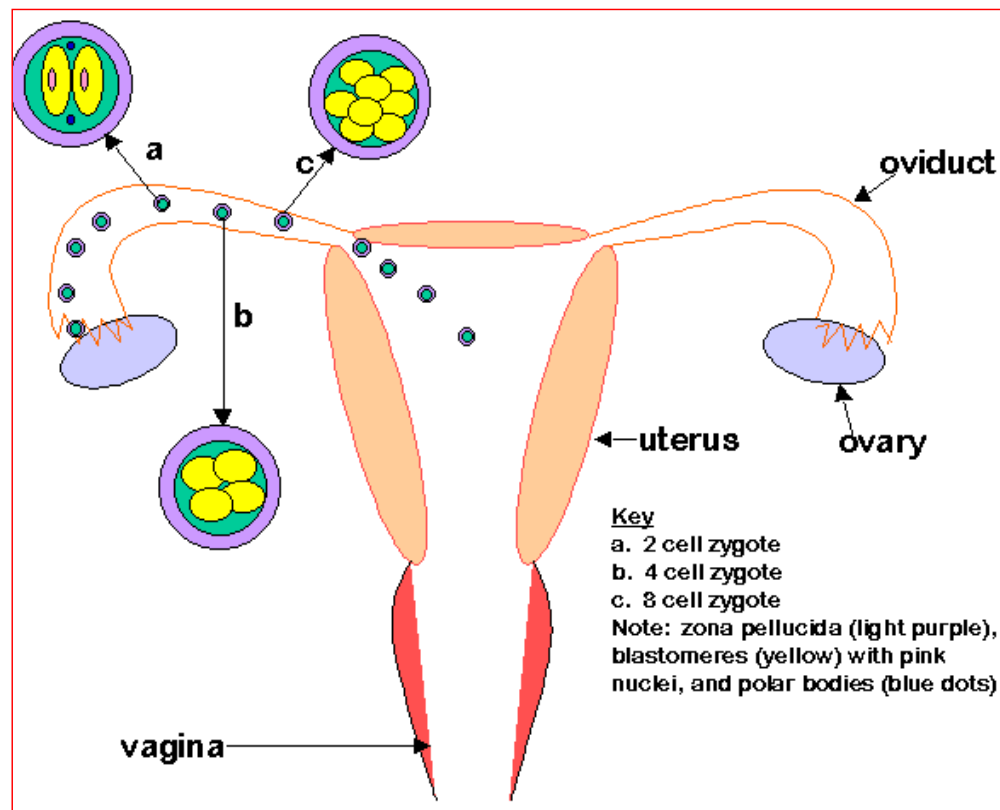
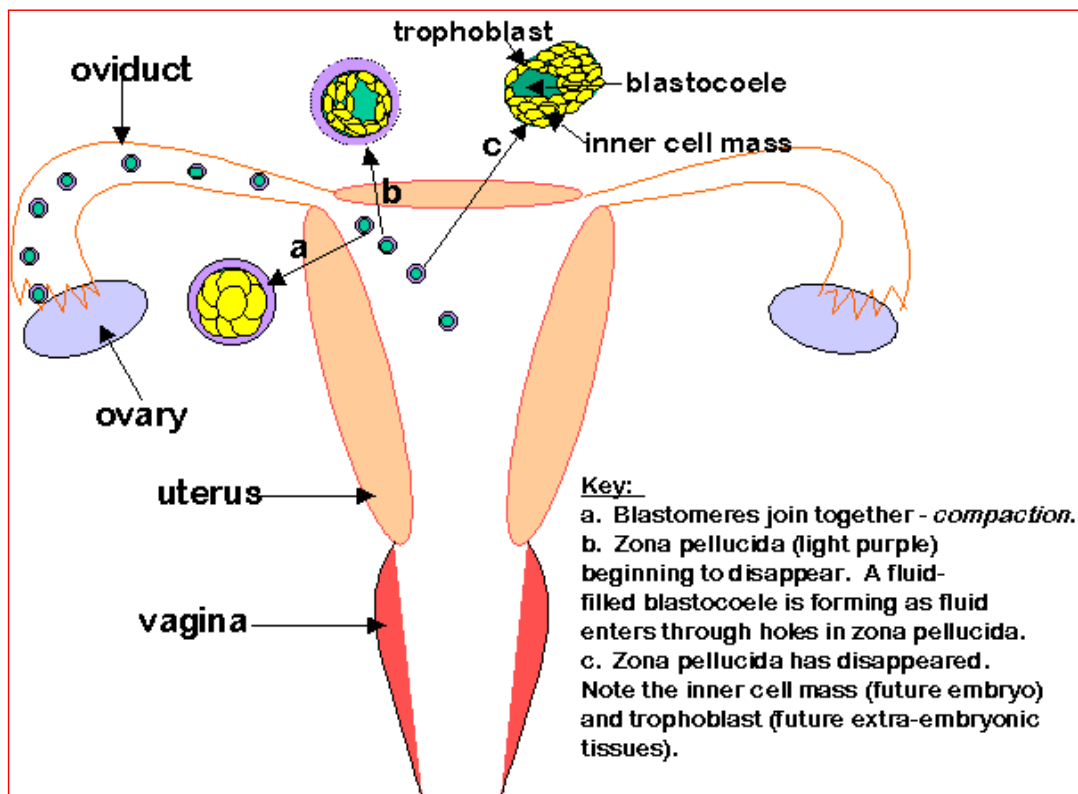


Figure 2.8. Schematic representation of the development of the zygote from the two-cell stage to the late morula stage. The two-cell stage is reached approximately 30 hours after fertilization; the four-cell stage, at approximately 40 hours; the 12- and 16-cell stage, at approximately 3 days; and the late morula stage, at approximately 4 days. During this period, blastomeres are surrounded by the zona pellucida, which disappears at the end of the 4th day.

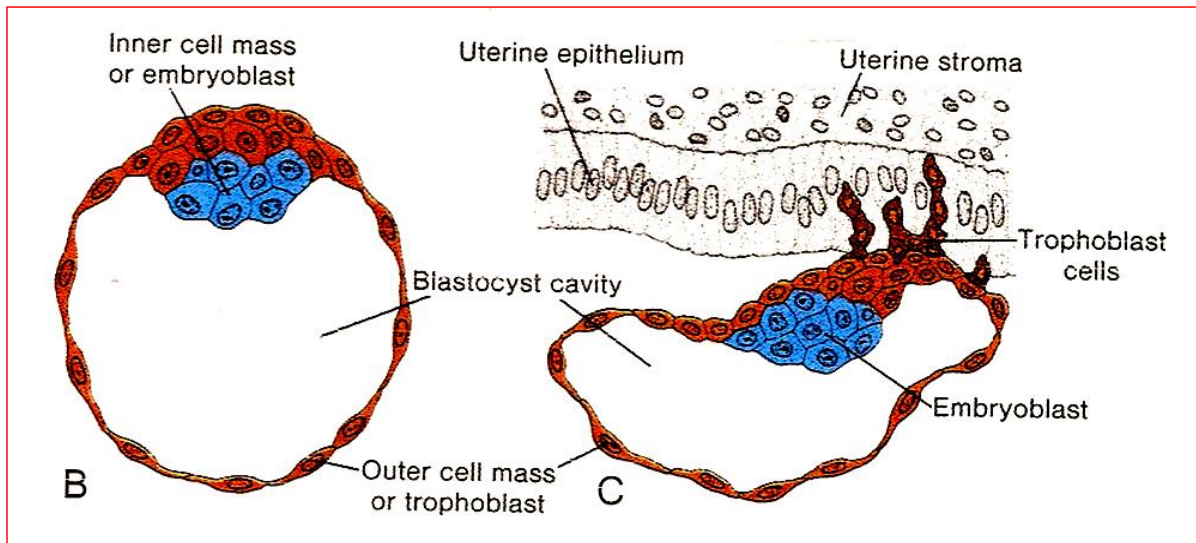


Formation of the Blastocyst

- Compaction: Blastomeres clump together; the amount of cytoplasm is reduced
- Adhesion: E-cadherin gene is expressed; these proteins facilitate intercellular adhesion and communication
- Zona pellucida is shed, allowing for cell growth and for uterine fluid to infiltrate
- A fluid-filled cavity (blastocoele) forms in the center, pushing cells to the periphery
- The outer cell layer, the trophoblast ("tropho" - to nourish), may have a nutritive role as the future embryonic part of the placenta
- The inner cell mass, the future embryo, forms as a ball of cells on one side of the spherical

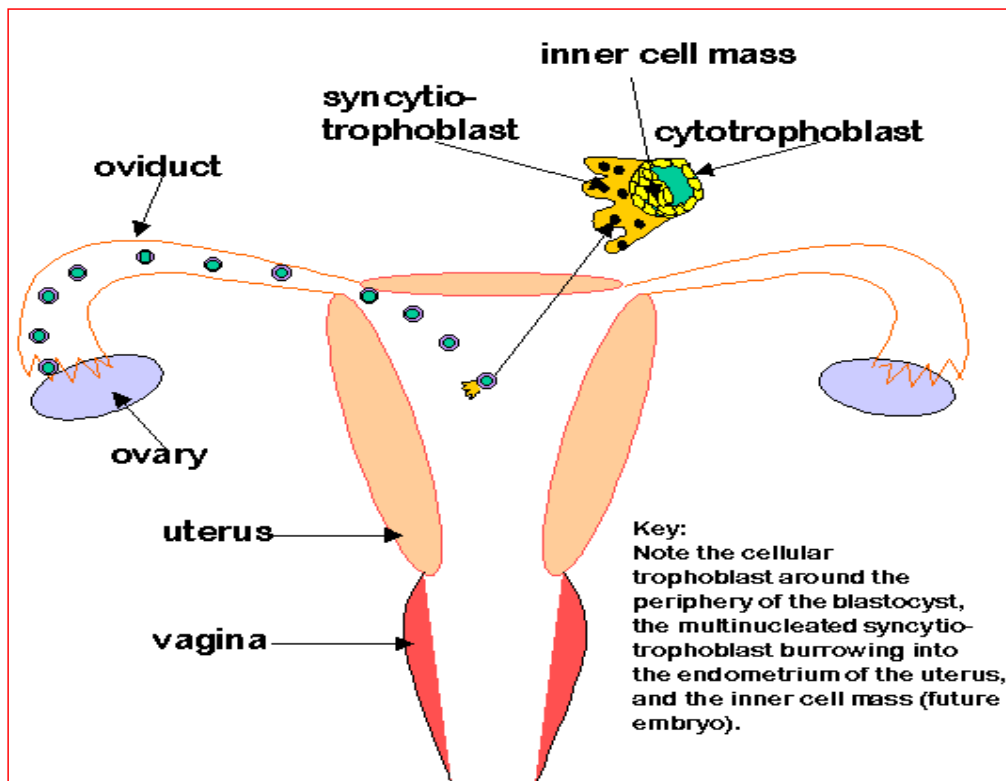


- After floating in the uterine cavity for about two days, the blastocyst completely loses its zona pellucida, and begins to grow rapidly. At day 6, it latches onto the endometrial epithelium, with the side of the inner cell mass (embryonic pole), attached to the uterine wall. Eventually the embryo will be attached by its dorsal side.



implantation

- **Differentiation into the Cytotrophoblast/Syncytiotrophoblast**
- Near the end of the first week, the blastocyst implants in the posterior wall of the uterus in the presence of high hormone levels; the blastocyst attaches at the embryonic pole (inner cell mass) so the embryo will eventually be attached dorsally. Occasionally, the blastocyst will implant on another spot in the uterus, potentially causing problems ([placenta previa](#)).
- The trophoblast layer undergoes mitosis upon contact with the uterine wall and differentiates into the cytotrophoblast ("cellular" layer) and the syncytiotrophoblast ("multinucleated" layer).

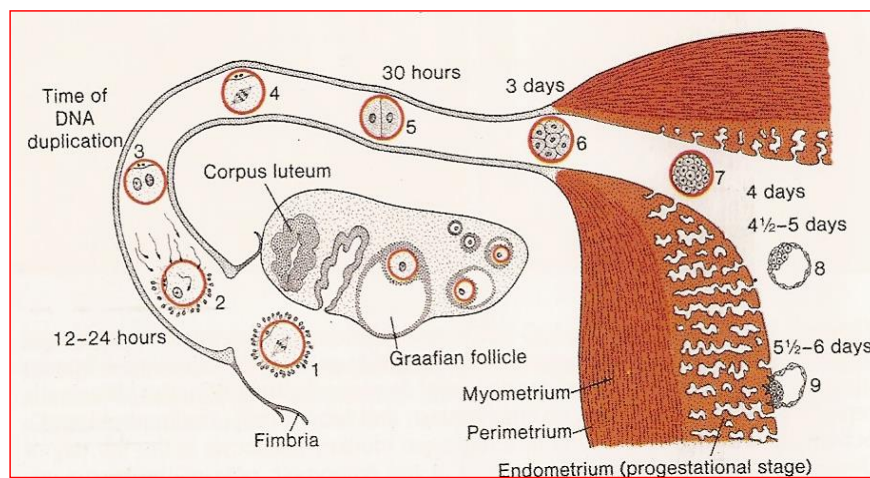


Uterus at Time of Implantation

- The wall of the uterus consists of three layers: [see below](#)
 - endometrium or mucosa lining the inside wall;
 - myometrium, a thick layer of smooth muscle;
 - perimetrium, the peritoneal covering the outside wall.

From puberty (11-13 years) until menopause (45-50), the endometrium undergoes cyclical changes that occur approximately every 28 days & are under hormonal control by the ovary.

During this menstrual cycle. the uterine endometrium passes through three stages. which consist of the [follicular or proliferative](#) phase, the [secretory or progestational](#) phase, and the [menstrual](#) phase.

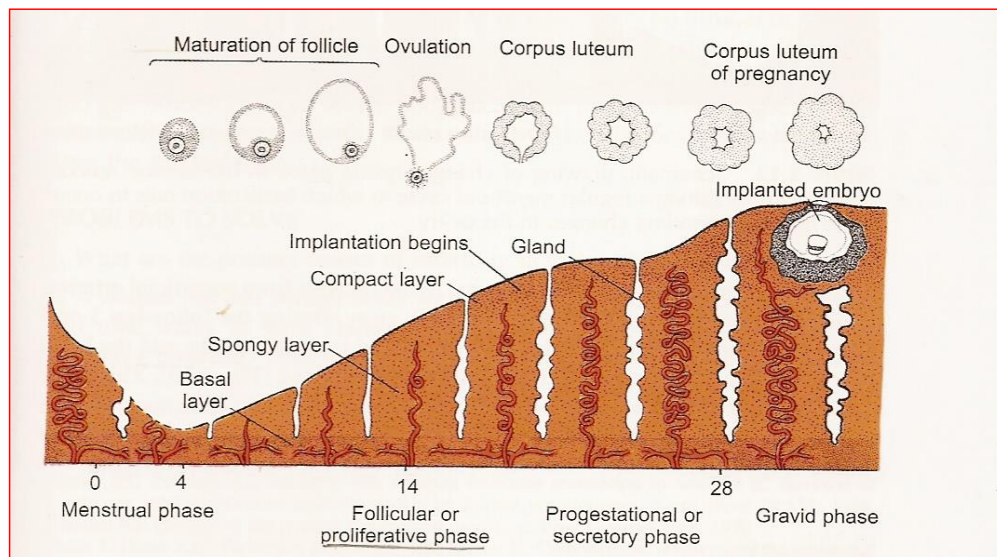


Events taking place during the 1st week of human development

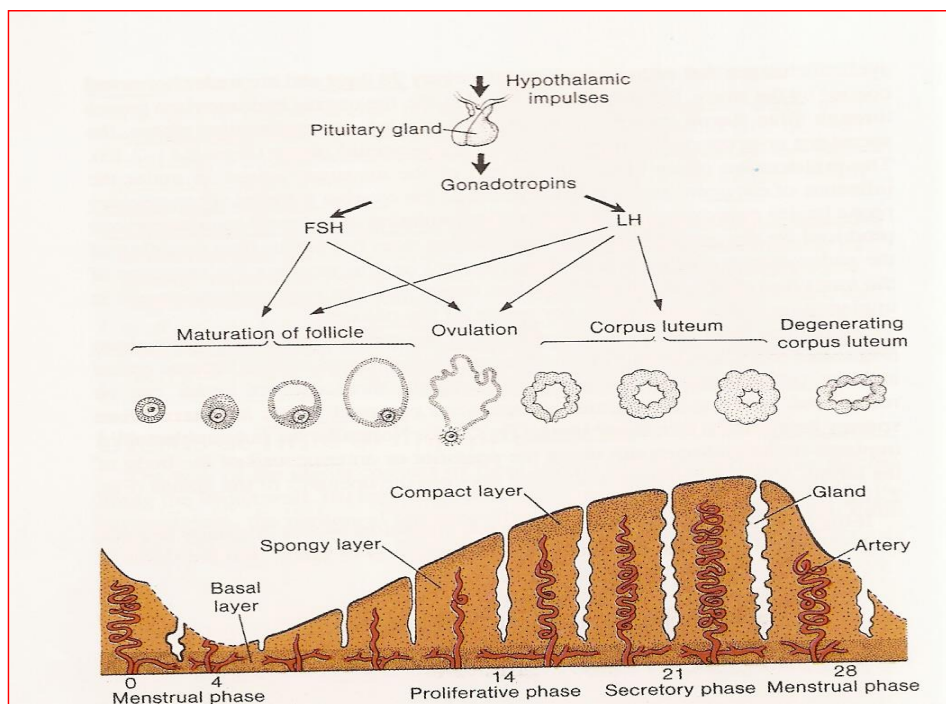
- 1, Oocyte immediately after ovulation. 2, Fertilization approximately 12-24 hours after ovulation.
 - 3, Stage of the male and female pronuclei.
 - 4, Spindle of the 1st mitotic division.
 - 5, Two-cell stage (approximately 30 hours of age).
 - 6, Morula containing 12-16 blastomeres (approxim. 3 days of age). 7, Advanced morula stage reaching the uterine lumen (4 days of age), 8, Early blastocyst stage (approximately 4 1/2 days of age).
 - 9, Early phase of implantation (blastocyst approximately 6 days of age).
- * The ovary shows stages of transformation between a primary follicle and a graafian follicle as well as a corpus luteum.

- **proliferative** phase under influence of estrogen, & parallel growth of ovarian follicles.
- **Secretory** phase occurs 2-3 days after ovulation in response to progesterone produced by corpus luteum.
- **Menstrual** phase begins by shedding of endometrium.
- At the time of implantation, the mucosa of the uterus is in the secretory phase during which time uterine glands and arteries become coiled and the tissue becomes succulent. As a result, three distinct layers can be recognized in the endometrium: 1. superficial compact layer, 2. an intermediate spongy layer, and 3. a thin basal layer. Normally, the human blastocyst implants in the "endometrium along the posterior or anterior wall of the body of the uterus, where it becomes embedded between the openings of the glands

- If the oocyte is not fertilized, venules and sinusoidal spaces gradually become packed with blood cells, and an extensive diapedesis of blood into the tissue is seen.
- When the menstrual phase begins, blood escapes from superficial arteries, & small pieces of stroma & glands break away. During the following 3 or 4 days, the compact & spongy layers are expelled from the uterus, & the basal layer is the only part of the endometrium that is retained.
- This layer is supplied by its own arteries, the basal arteries, and functions as the regenerative layer in rebuilding again.



Changes taking place in the uterine mucosa, correlated with those in the ovary. note that implantation of the blastocyst has caused development of large corpus luteum. Secretory activity of the endometrium increases gradually as a result of large amounts of progesterone produced by corpus luteum of preg.



Changes taking place in the uterine mucosa(endometrium) during a regular menstrual cycle in which fertilization fails to occur. Note the corresponding changes in the ovary

THANK YOU

General Embryology,

Lecture VI,

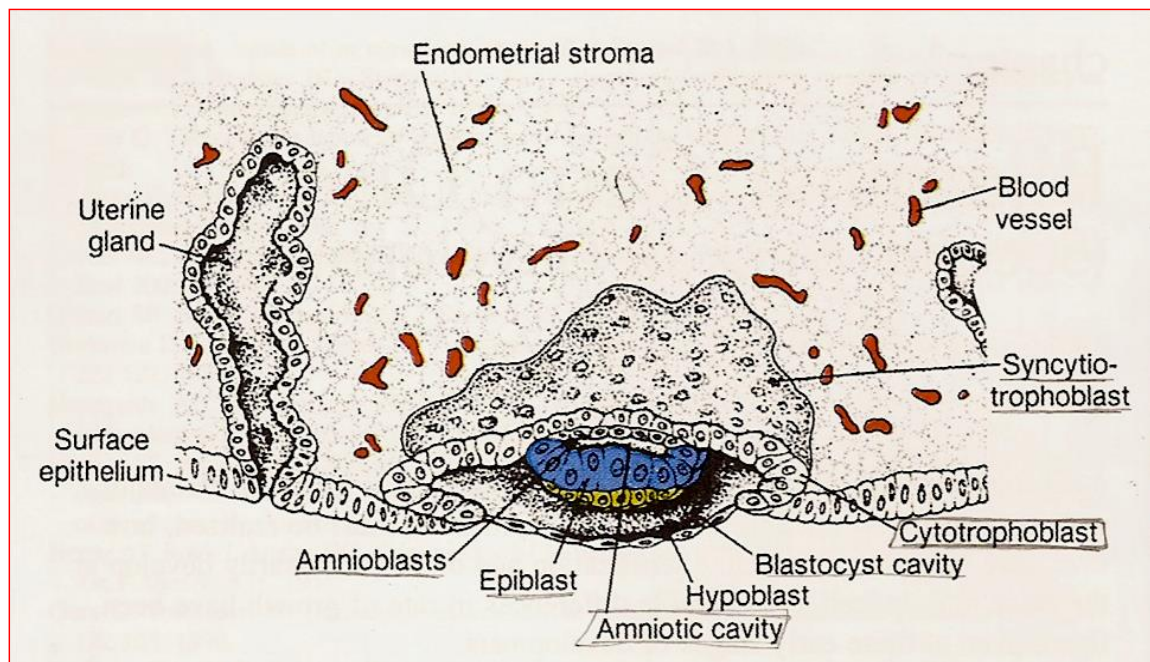
Second week of development, (Bilaminar Germ Disc)

Second week of development Bilaminar Germ Disc

Late Implantation/Uteroplacental Circulation

- Day 8 - The syncytiotrophoblast begins to invade the capillaries, glands & connective tissue of the endometrial wall of the uterus
- Day 9 - Spaces known as lacunae form in the syncytiotrophoblast; they fill with maternal blood and glandular fluid
- A closing plug covers the defect in the endometrial epithelium caused by implantation of the blastocyst; the epithelium will be regenerated by day 12
- A network of lacunae form (spaces in the placenta filled with maternal blood that comes into contact with fetal villi)

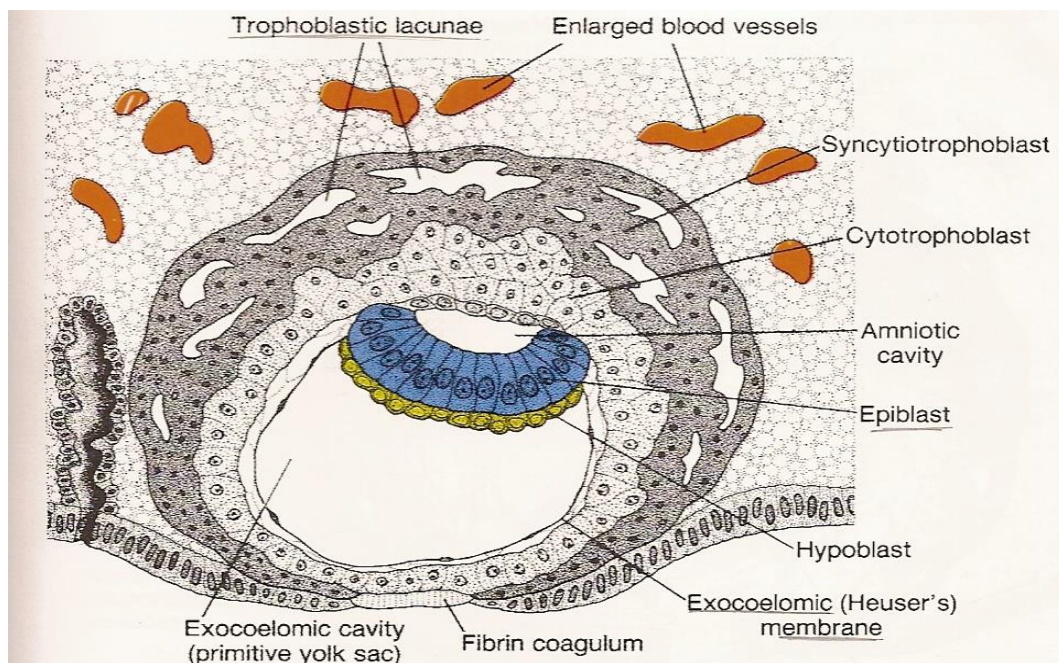
- **At the 8th day of development**, the blastocyst is partially embedded in the endometrial stroma.
- The syncytiotrophoblast begins to invade the capillaries, glands and connective tissue of the endometrial wall of the uterus
- In the area over the embryoblast, trophoblast has differentiated into two layers:
 - (a) An inner layer of mononucleated cells, the cytotrophoblast,
 - (b) An outer, multinucleated zone without distinct cell boundaries, the syncytiotrophoblast (see below).
- Cells of the inner cell mass or embryoblast also differentiate into two layers:
 - (a) a layer of small, **cuboidal cells** adjacent to the blastocyst cavity, known as the **hypoblast** layer;
 - (b) a layer of high **columnar** cells adjacent to the amniotic cavity, the **epiblast** layer (see below). Cells of each germ layer form a flat disc and together are known as the **bilaminar germ disc**.
- At the same time, a small cavity appears within the epiblast. This cavity enlarges to become the **amniotic cavity**. Those epiblast cells adjacent to the cytotrophoblast are called **amnioblasts** &, together with the rest of the epiblast, line the amniotic cavity (see below).



A 7 1/2-day human blastocyst, partially embedded in the endometrial stroma. The trophoblast consists of an inner layer with mononuclear cells, the cytotrophoblast, & an outer layer without distinct cell boundaries, the syncytiotrophoblast. The embryoblast is formed by the epiblast & hypoblast germ layers. The amniotic cavity appears as a small cleft.

Ninth Day of Development

- The blastocyst is more deeply embedded in the endometrium.
- Day 9 - Spaces known as **lacunae** form in the syncytiotrophoblast; they fill with maternal blood & glandular fluid
- The trophoblast shows considerable progress in development, particularly at the embryonic pole, where vacuoles appear in the syncytium. When these vacuoles fuse, they form large lacunae, & this phase of trophoblast development is therefore known as the **lacunar stage** (see below).
- At the abembryonic pole, meanwhile, flattened cells, originating from the hypoblast, form a thin membrane, known as the **exocoelomic (Heuser's) membrane**, that lines the inner surface of the cytotrophoblast (see below).
- This membrane, together with the hypoblast, forms the lining of the **exocoelomic cavity (primitive yolk sac)**,

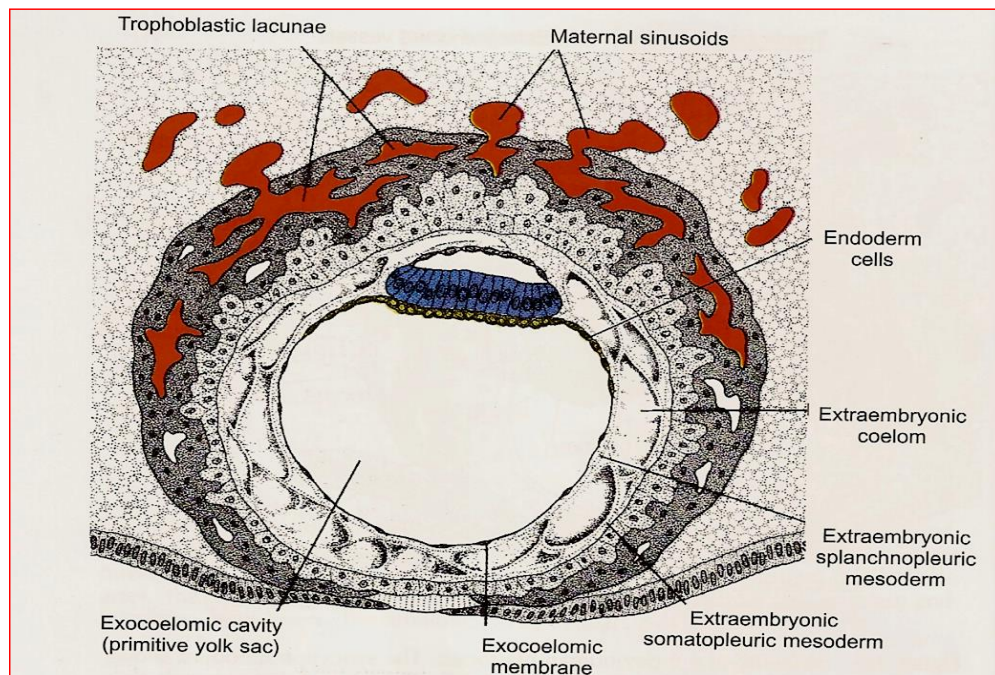
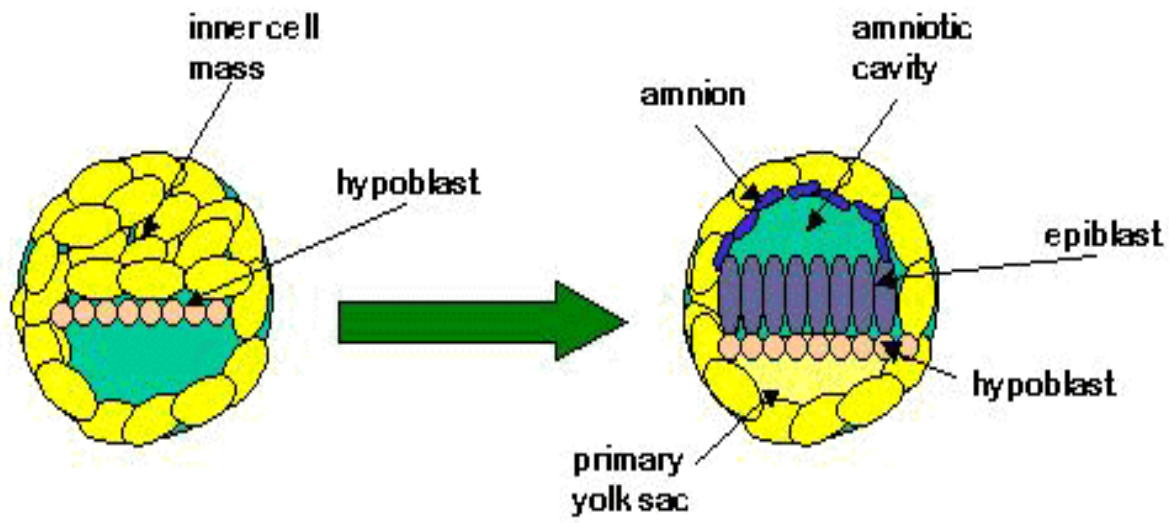


9-day human blastocyst. The syncytiotrophoblast shows a large No. of lacunae. Note i flat cells that form i exocoelomic membrane. The bilaminar germ disc consists of a layer of columnar epiblast cells & a layer of cuboidal hypoblast cells. The original surface defect is closed by a fibrin coagulum

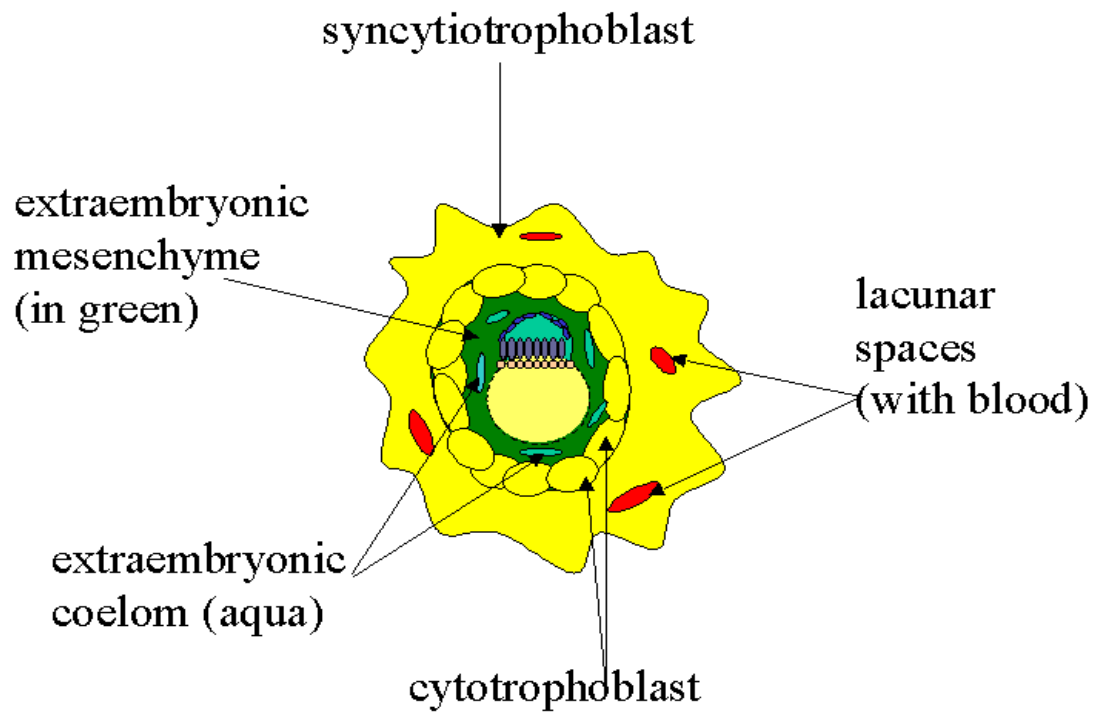
Eleventh to Twelfth Day of Development

- Days 11-12 - primitive utero-placental circulation forms with oxygenated maternal blood arriving via spiral arterioles, seeping into lacunae and leaving via endometrial venous capillaries.
- By the 11th to 12th day of development, the blastocyst is completely embedded in the endometrial stroma, & the surface epithelium almost entirely covers the original defect in the uterine wall. The blastocyst now produces a **slight protrusion** into the lumen of the uterus.
- Concurrently, cells of the syncytiotrophoblast penetrate deeper into the stroma & erode the endothelial lining of the maternal capillaries. These capillaries are congested & dilated & are known as **sinusoids**. The syncytial lacunae then become continuous with the sinusoids, & maternal bl. enters the lacunar system (see below).

- As the trophoblast continues to erode more & more sinusoids, maternal bl. begins to flow through the trophoblastic system, thus establishing the uteroplacental circulation.
- In the meantime, a new population of cells appears between the inner surface of the cytotrophoblast and the outer surface of the exocoelomic cavity. These cells are derived from yolk sac cells and form a fine, loose connective tissue, the **extraembryonic mesoderm**, which eventually fills all of the space between the trophoblast externally and the amnion and exocoelomic membrane internally. (see below)
- Soon, large cavities develop in the extraembryonic mesoderm, & when these become confluent, a new space known as the extraembryonic coelom (**chorionic cavity**) is formed. This space surrounds the primitive yolk sac and amniotic cavity except where the germ disc is connected to the trophoblast by the connecting stalk.
- The extraembryonic mesoderm lining i cytotrophoblast & amnion is called the extraembryonic somatopleuric mesoderm; that covering the yolk sac is known as the extraembryonic splanchnopleuric mesoderm (see below).



A human blastocyst of approximately 12 days. The trophoblastic lacunae at i embryonic pole are in open connection with maternal sinusoids in the endometrial stroma. Extraembryonic mesoderm proliferates & fills the space bet. i exocoelomic membrane & the inner aspect of i trophoblast.



These spaces fuse to form a fluid-filled cavity completely surrounding the amnion & yolk sac, except at the connecting stalk

THANK YOU

General Embryology, Lecture VII, Second week of development, (Bilaminar Germ Disc) continue

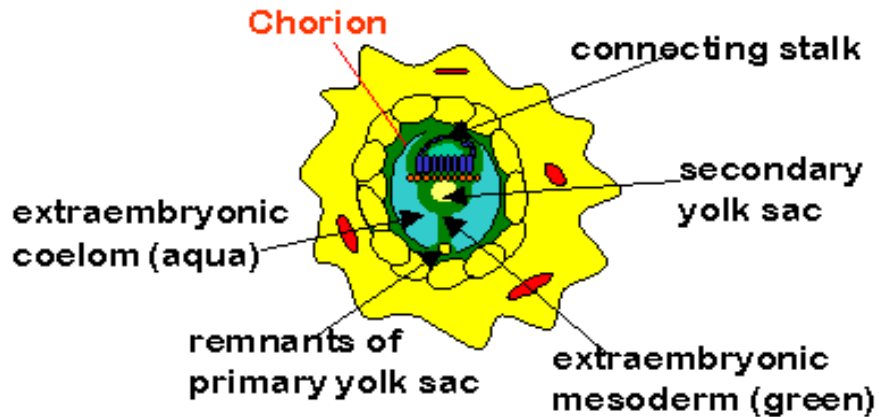
Days 13-14 - primary chorionic villi develop, will eventually become vascularized

- By the 13th day of development, the surface defect in the endometrium has usually healed. Occasionally, bleeding may occur at the implantation site as a result of increased blood flow into the lacunar spaces. Since this bleeding occurs near the 28th day of the menstrual cycle, it may be confused with normal menstrual blood.
- The trophoblast is characterized by the appearance of villous structures. Cells of the cytotrophoblast proliferate locally & penetrate into the syncytiotrophoblast, thus forming cellular columns surrounded by syncytium. Cellular columns with the syncytial covering become known as **primary villi** (see below).

- In the meantime, the hypoblast produces additional cells that migrate along the inside of the exocoelomic membrane (see above). These cells proliferate & gradually form a new cavity within the exocoelomic cavity. This new cavity is known as the **2ndry or definitive yolk sac** (see below). During its formation, large portions of the exocoelomic cavity are pinched off. These portions are represented by exocoelomic cysts, which are often found in the extraembryonic coelom or chorionic cavity (see below).
- Meanwhile, the extraembryonic coelom expands & forms a large cavity known as the **chorionic cavity**.
- The extraembryonic mesoderm lining the inside of the cytotrophoblast is then known as the **chorionic plate**. The only place where extraembryonic mesoderm traverses the chorionic cavity is in the connecting stalk (see below). With development of blood vessels, the stalk will become the **umbilical cord**.
- By the end of the 2nd week, the germ disc is represented by two apposed cell discs: the epiblast, which forms the floor of the continuously expanding amniotic cavity, and the hypoblast, which forms the roof of the secondary yolk sac. In its cephalic region the hypoblastic disc shows a slight thickening known as the **prechordal plate**.

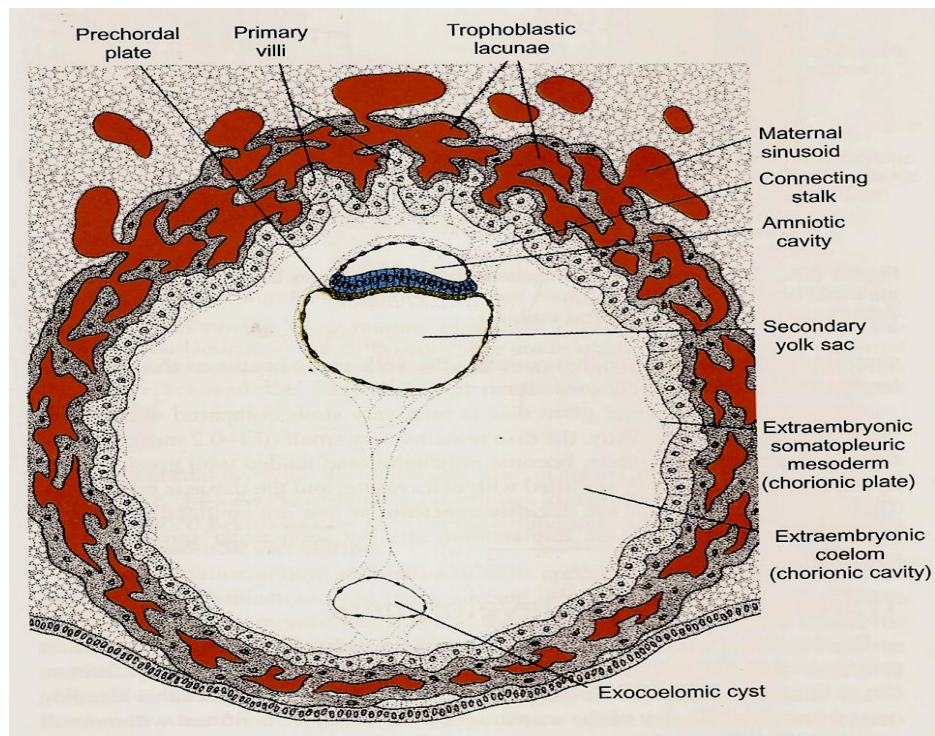
Formation of the chorion & definitive yolk sac:

- Endodermal cells from the hypoblast migrate to the primary yolk sac
- As the extraembryonic coelom grows, the large primary yolk sac pinches off, leaving behind a smaller, secondary yolk sac which is "permanent"



The extraembryonic fluid is actually surrounding i entire amnion and yolk sac, except at the connecting stalk

- The extra-embryonic coelom (future chorionic cavity) separates the extra-embryonic somatic mesoderm (lining the trophoblast and amnion) from the extra-embryonic splanchnic mesoderm (lining the yolk sac only)
- The embryo, surrounded by two cavities, floats in a large "bubble" (future chorionic cavity) (see above)



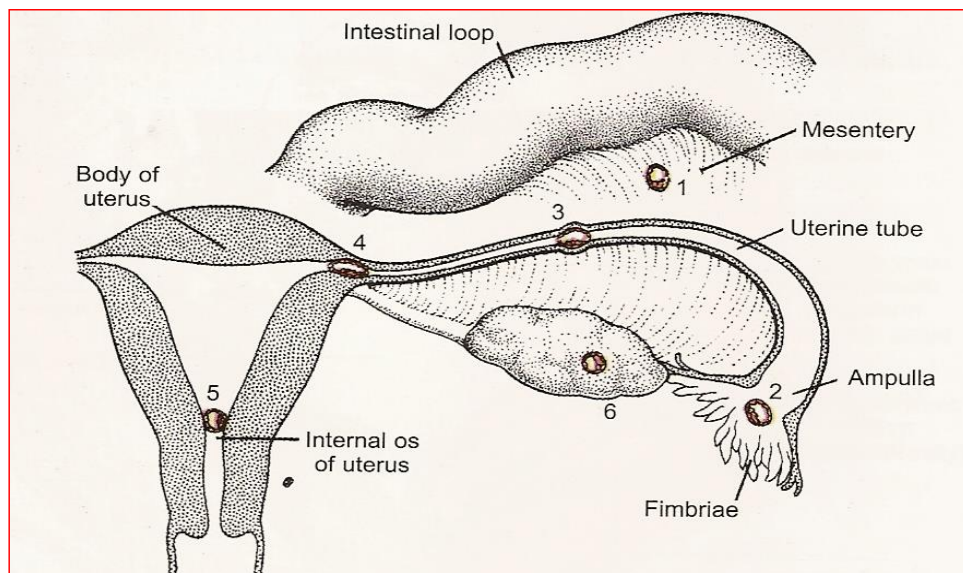
A 13-day human blastocyst. Trophoblastic lacunae are now present at the embryonic & abembryonic pole, & i uteroplacental circulation has begun. Note the 1ry villi & the extraembryonic coelom or chorionic cavity. The 2ndry yolk sac is entirely lined with endoderm.

Summary of Origin of Extraembryonic Membranes

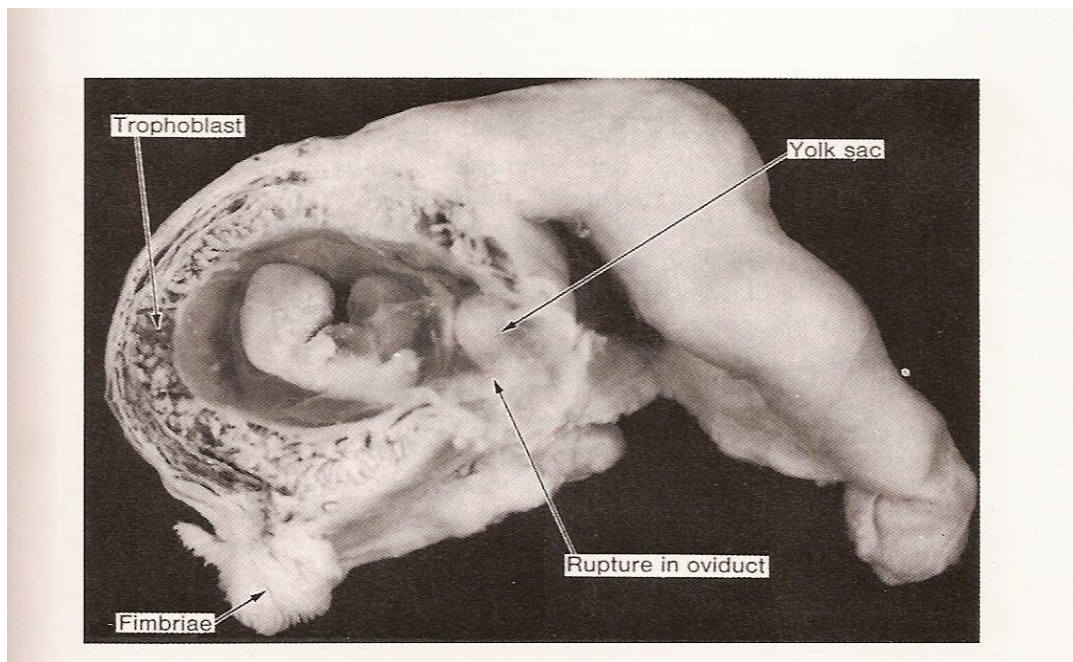
AMNION	bilayer	amniotic epithelium + extra-embryonic somatic mesoderm
CHORION	trilayer	extra-embryonic somatic mesoderm + cytotrophoblast + syncytiotrophoblast
YOLK SAC WALL	bilayer	yolk sac endoderm + extra-embryonic splanchnic mesoderm

CLINICAL CORRELATES

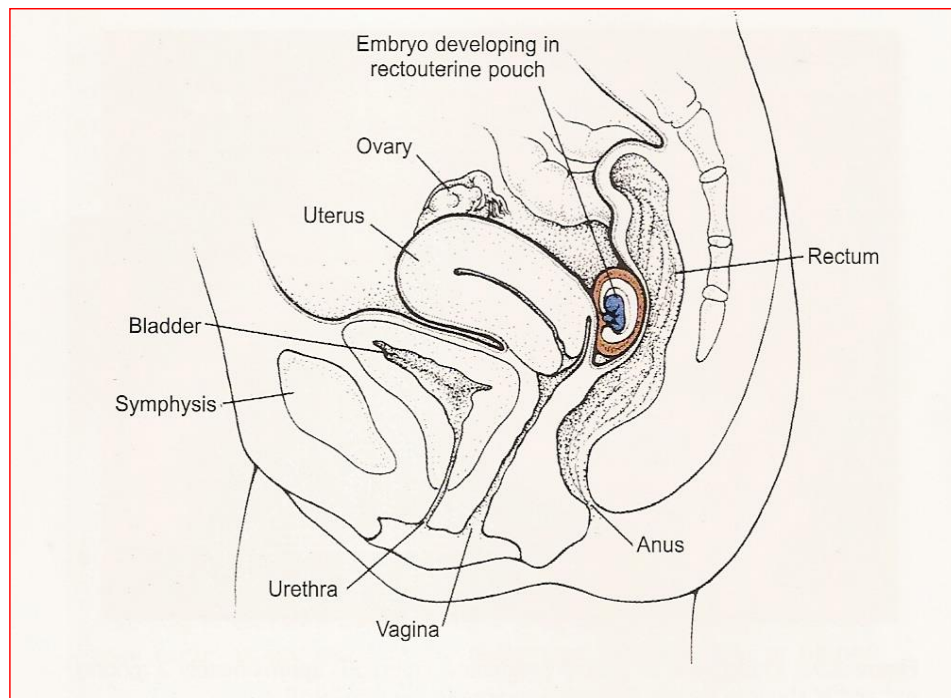
- **Rejection**, The syncytiotrophoblast is responsible for hormone production, including (hCG)
- Abnormal implantation sites sometimes occur even within the uterus.
- Normally, the human blastocyst implants along the post. or anterior wall of the body of the uterus.
- Not infrequently, implantation sites are found outside the uterus, Ectopic pregnancies may occur at any place in i abdominal cavity, ovary, or uterine.
- 95% of ectopic pregnancies occur in the uterine tube, & most of these are located in the ampulla (see below).
- Most abnormal blastocysts would not have produced any sign of pregnancy, since their trophoblast was of such inferior quality that the corpus luteum could not have persisted.
- Embryo probably aborted with i following menstruation.



Abnormal implantation sites of i blastocyst. 1, Implantation site in the abd. cavity. The ovum most frequently implants in the rectouterine cavity. 2, Implantation in the ampullary region of the tube. 3, Tubal implantation. 4, Interstitial implantation. 5, Implantation in the region of the internal os, resulting in placenta previa. 6, Ovarian implantation.



Photograph of a tubal pregnancy; Embryo is approximately 2 months old and is about to escape through a rupture in the tubal wall.



Drawing of midline section of bladder, uterus, & rectum to show an abd. pregnancy in i rectouterine (Douglas pouch).

THANK YOU

Trilaminar Germ Disc

Third Week of Development

part I

Gastrulation: Primitive Streak &
Cell migrations

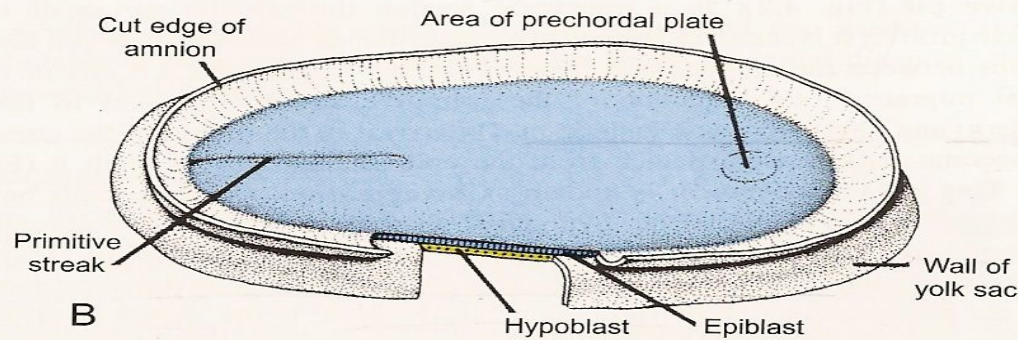
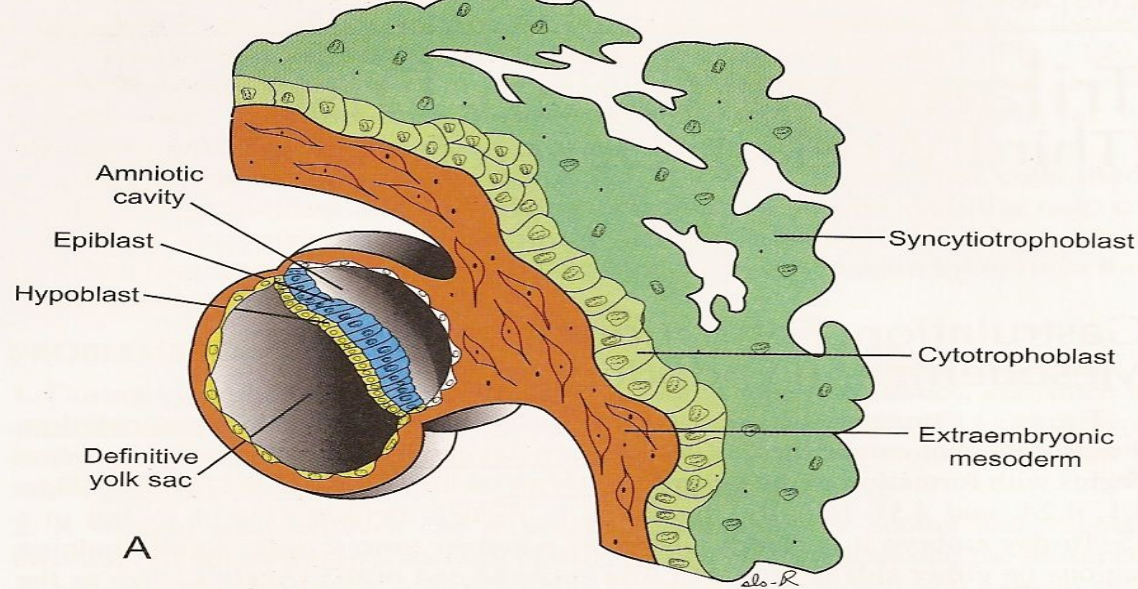
Gastrulation:



**Formation of Embryonic
Mesoderm & Endoderm**

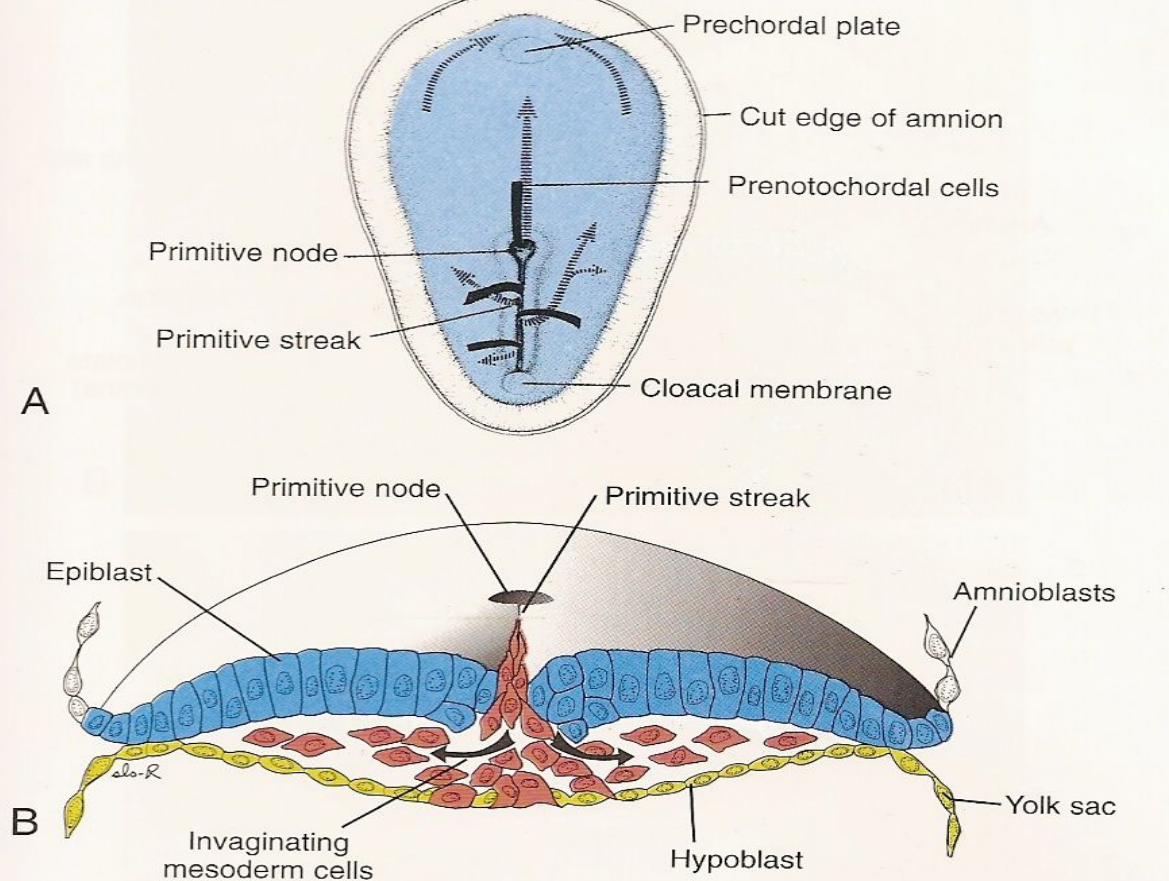
- The most characteristic event occurring during the 3rd week is **Gastrulation**, the process that establishes all three **germ layers** in the embryo.
- Gastrulation begins with formation of the primitive streak on the surface of the epiblast (see next 2 slides).
- The epiblast, through the Process of gastrulation, is the source of all, the germ layers in the embryo (i.e. ectoderm, mesoderm, and endoderm) (see below).
- As more and more cells move in between the epiblast and hypoblast layers, they begin to spread in lateral and cephalic directions (see bel.). Gradually, they migrate beyond the margin of the disc and establish contact with extraembryonic mesoderm covering the yolk sac and amnion. In the cephalic direction, they pass on each side of the prechordal plate to meet each other in front of this area, where they form the **cardiogenic or heart-forming plate** (see below).





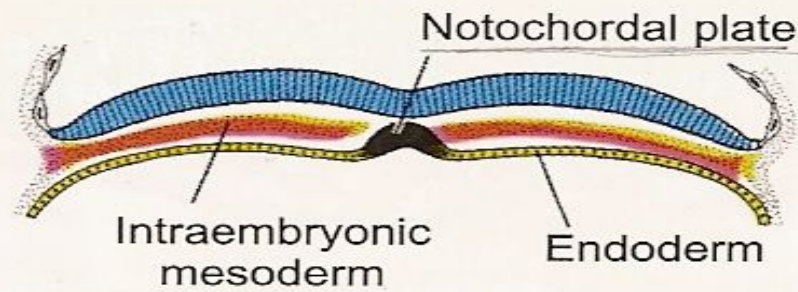
A. Schematic view of an implantation site at the end of the 2nd week.

B. Representative view of the germ disc at the end of the 2nd week of development. The amniotic cavity has been opened to permit a view on the dorsal side of the epiblast. Note that the hypoblast & epiblast are in contact with each other & that the primitive streak forms a shallow groove in the caudal region of the embryo.

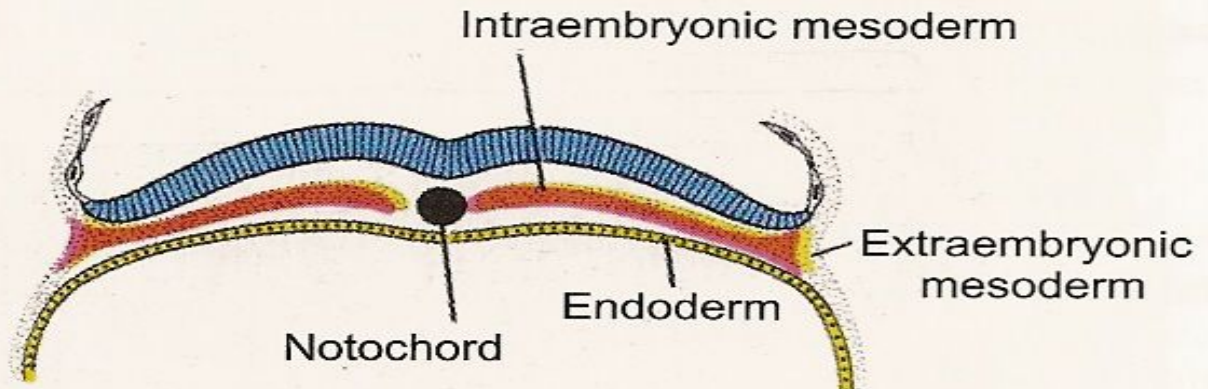


A. dorsal side of i germ disc from a 16-day embryo, indicating imovement of surface epiblast cells (solid black lines) through i primitive streak & node & i subsequent migration of cells bet.i hypoblast & epiblast (broken lines). **B.** Cross section through i cranial region of i streak at 15 days, showing invagination of epiblast cells. The 1st cells to move inward displace the hypoblast to create the definitive endoderm. Once definitive .endoderm is established, inwardly moving epiblast forms mesoderm

C



E



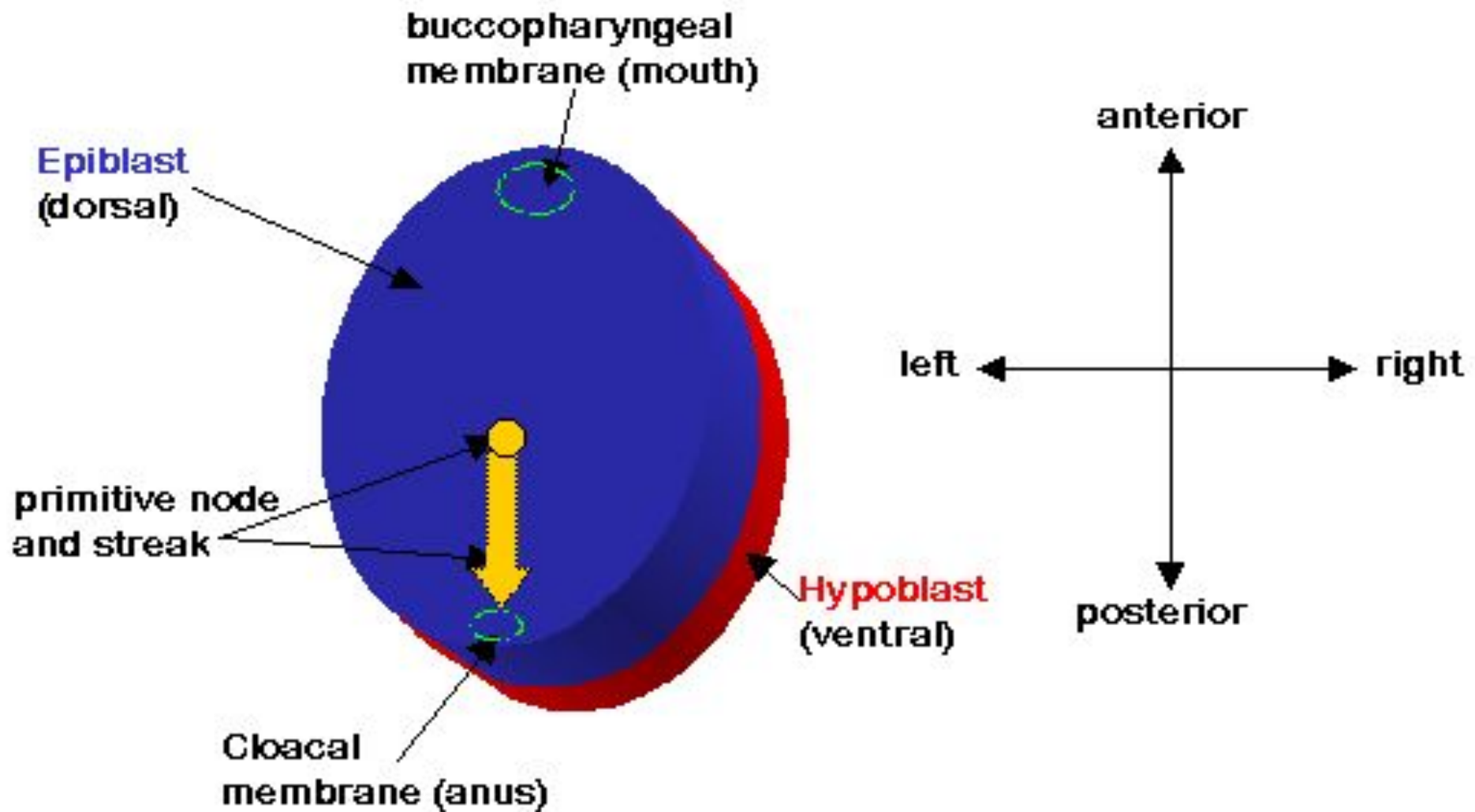
C. Cross section through the region of the notochordal plate. Soon, the notochordal plate will detach from the endoderm to form the definitive notochord.

.E. definitive notochord



- The primitive streak appears on the epiblast surface, migrating caudally from the primitive node (Hansen's node) to the cloacal membrane where it stops; it grows by the addition of cells at the "tail" end
- Embryonic orientation established: cranial/caudal since primitive streak migrates caudally, right vs. left, & dorsal vs. ventral since primitive streak occurs on dorsal side
- Cells migrate from i epiblast to i middle layer between it & the hypoblast; forming intra-embryonic mesenchyme (loose embryonic connective tissue)





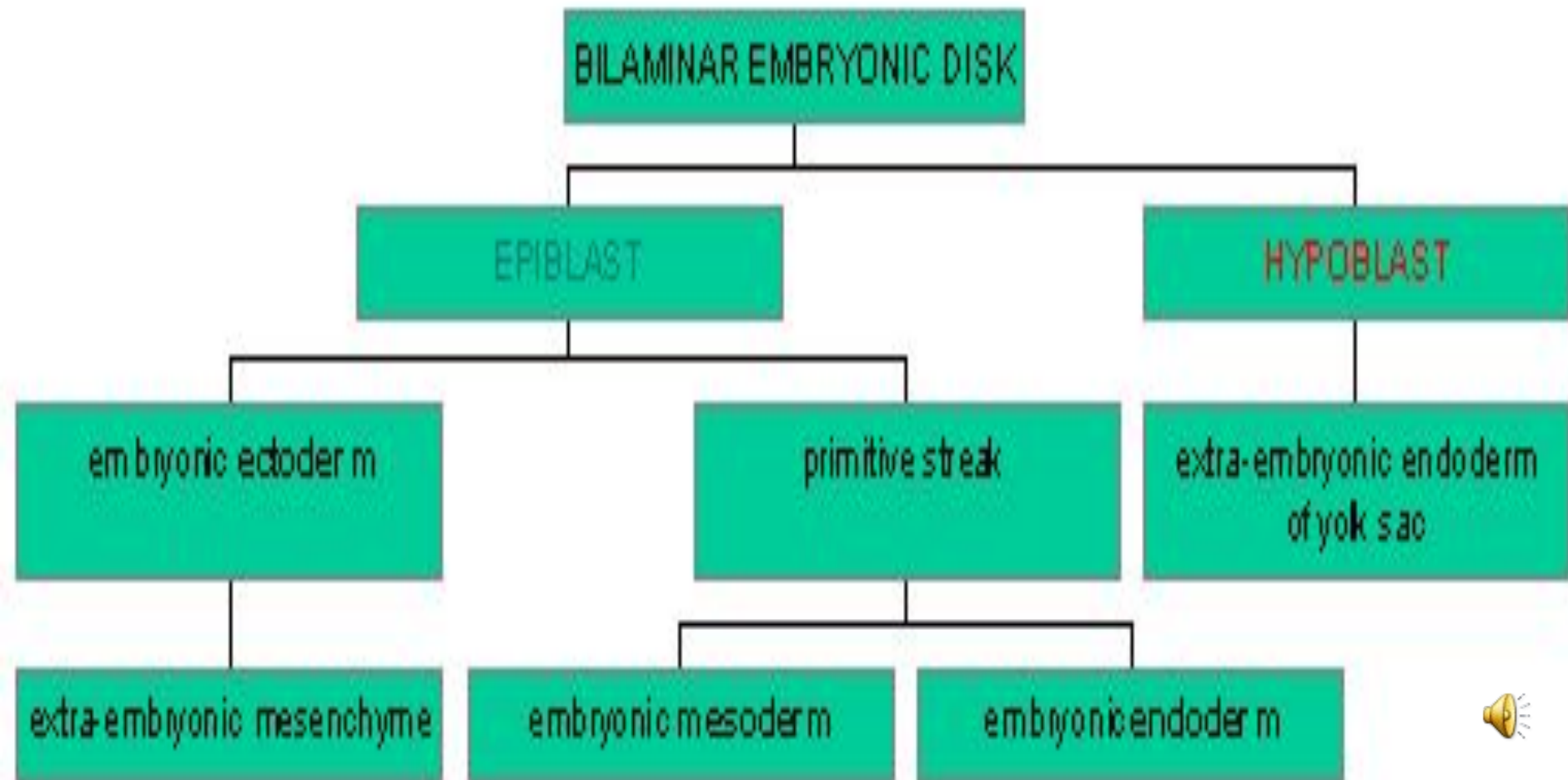
Cells migrate from the epiblast to the middle layer between it & the hypoblast; forming intra-embryonic mesenchyme (loose embryonic connective tissue) 📢

- Mesenchymal cells migrate from primitive streak cranially to form
 - 1)cardiogenic mesenchyme (most cranial point),
 - 2)the notochordal process (also in the cranial direction),
 - 3)lateral mesenchyme (to the lateral edges where it meets with extra-embryonic mesenchyme)
- The length of the primitive streak will decrease as the notochord increases and it will eventually degenerate, so that the caudal end of the embryo will decrease in size
- If the primitive streak does not degenerate, this undifferentiated tissue could result in a sacro-coccygeal teratoma.



Results of Gastrulation: Origin & Fate of the Germ Layers

Origin of the Germ Layers



Note: All three germ layers are derived from the epiblast.

Fate of the Germ Layers

ENDODERM	epithelial lining of respiratory and GI tract
MESODERM	<u>cardiovascular system</u> , reproductive/excretory organs , smooth and striated muscle, connective tissues, vessels, skeleton
ECTODERM	SURFACE ECTODERM - epidermis, and other external structures NEUROECTODERM - central & peripheral nervous system, <u>neural crest cells</u> & derivatives

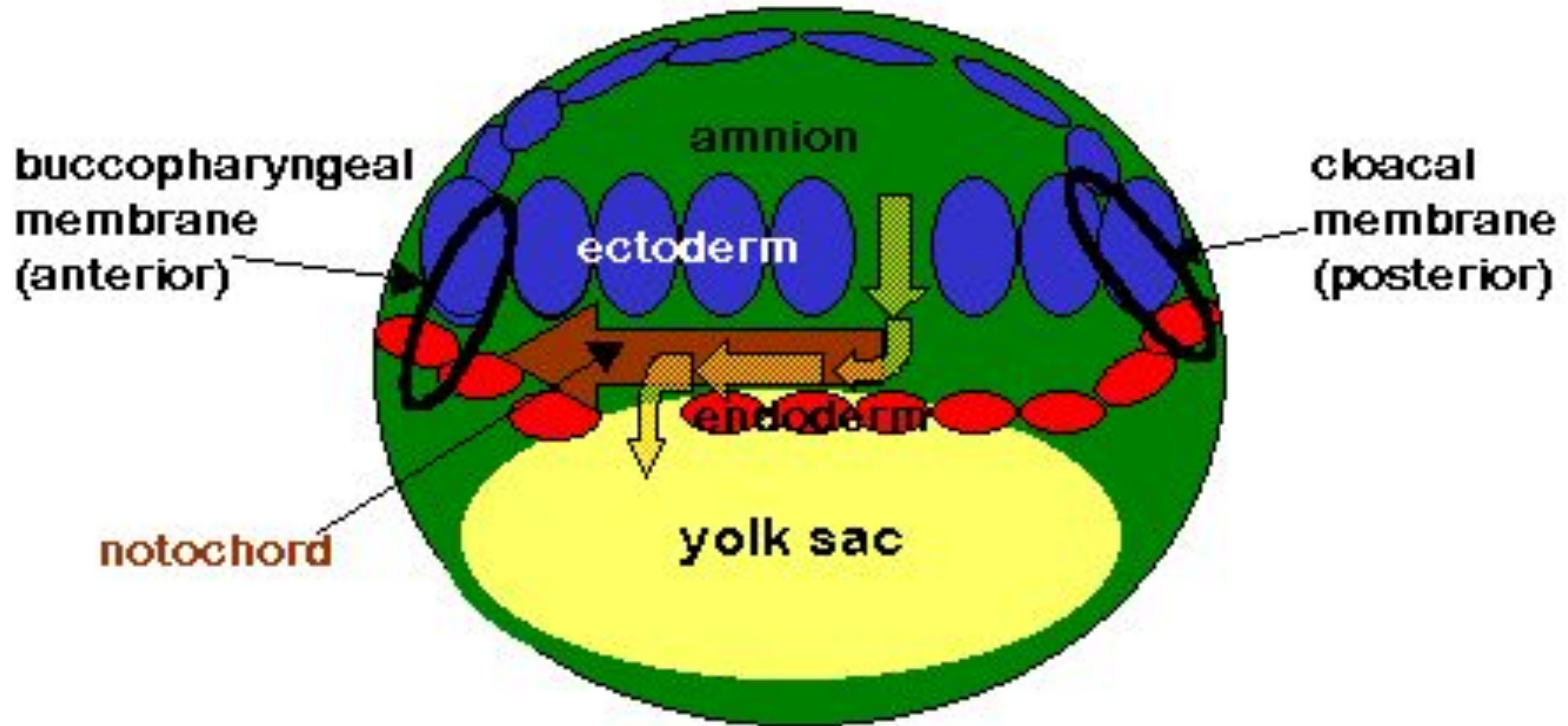
NOTE: Epithelium is derived from all three germ layers. 
examp. **endoderm** - epithelial lining inside viscera.
mesoderm - mesothelium lining outside of viscera.
ectoderm - skin epithelium.

Notochord: the Primary Inducer

- The notochordal process develops by the migration of mesenchymal cells cranially from the primitive node, eventually stopping at the bucco-pharyngeal membrane (a bilayer disk of endoderm/ectoderm)
- The floor of the notochordal process fuses with the intra-embryonic endoderm of the yolk sac
- The fused layers degenerate temporarily to form a transitory communication with the yolk sac (neurenteric canal)

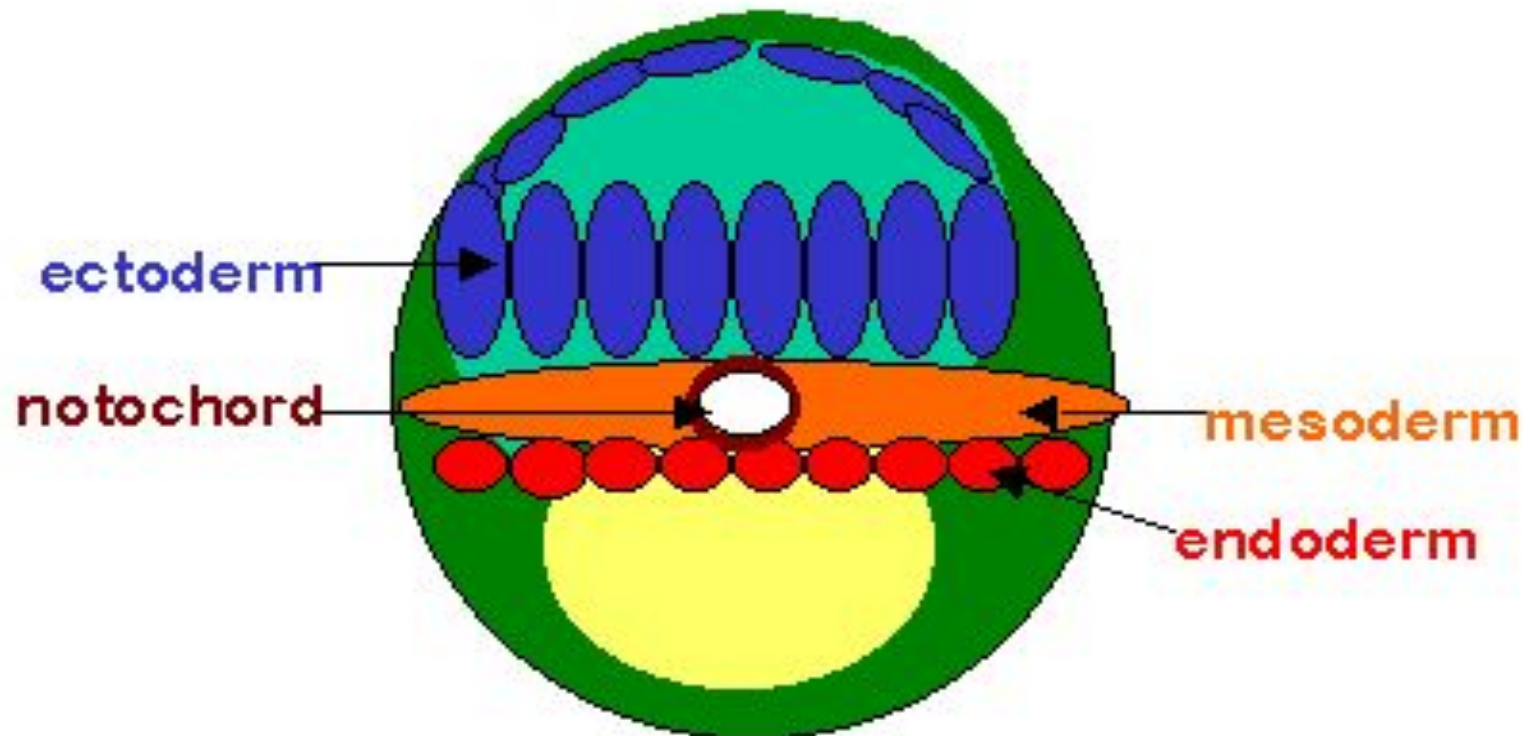


NEURENTERIC CIRCULATION (yellow arrows) flowing from the amnion, through the **notochordal** canal, to the yolk sac; embryo shown in *sagittal* section



- *The notochordal plate folds inward, to form a rod-shaped notochord
- *As the notochord closes as a tube, it detaches from the endoderm of the yolk sac
- *It is now located in i mesoderm, between the endoderm & ectoderm

*Transverse section thru
embryo, demonstrating
notochord in mesoderm*



■ **Functions of the Notochord:**

1. **Structure** - acts as a **rigid axis** around which the embryo develops
2. **Skeletal** - foundation upon which the **vertebral column** (vertebral bodies) will form
3. **Induction** - will bring about formation of the **neural tube** (future nervous system)

- **Fate of notochord:** It will eventually break up into section of weight-bearing intervertebral disks, known as **nucleus pulposus**.

A tumor can occur here, known as a chordoma, localized in the intervertebral disk, capable of causing nerve damage.



THANK YOU



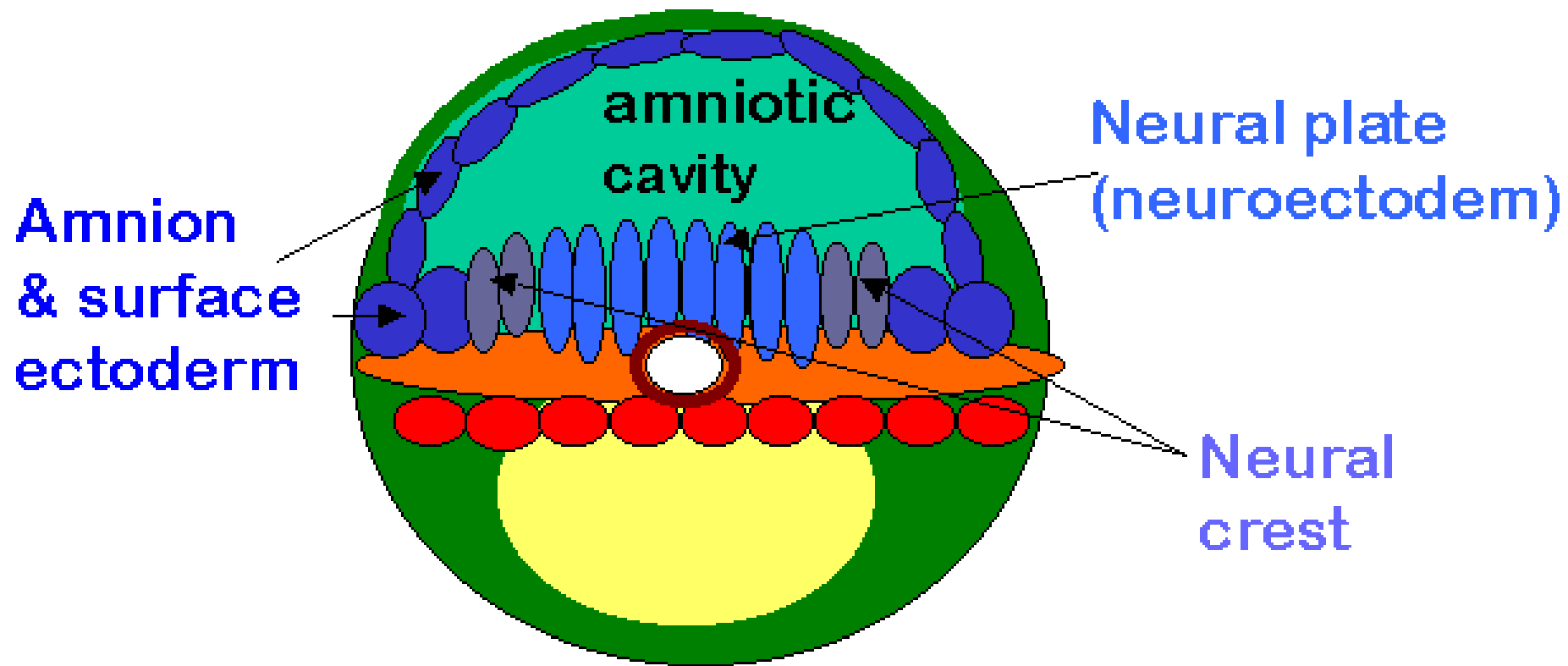
**General Embryology,
lecture IX,
3rd week development
(Gastrulation)
part II**



Neurulation: Neural Tube Formation

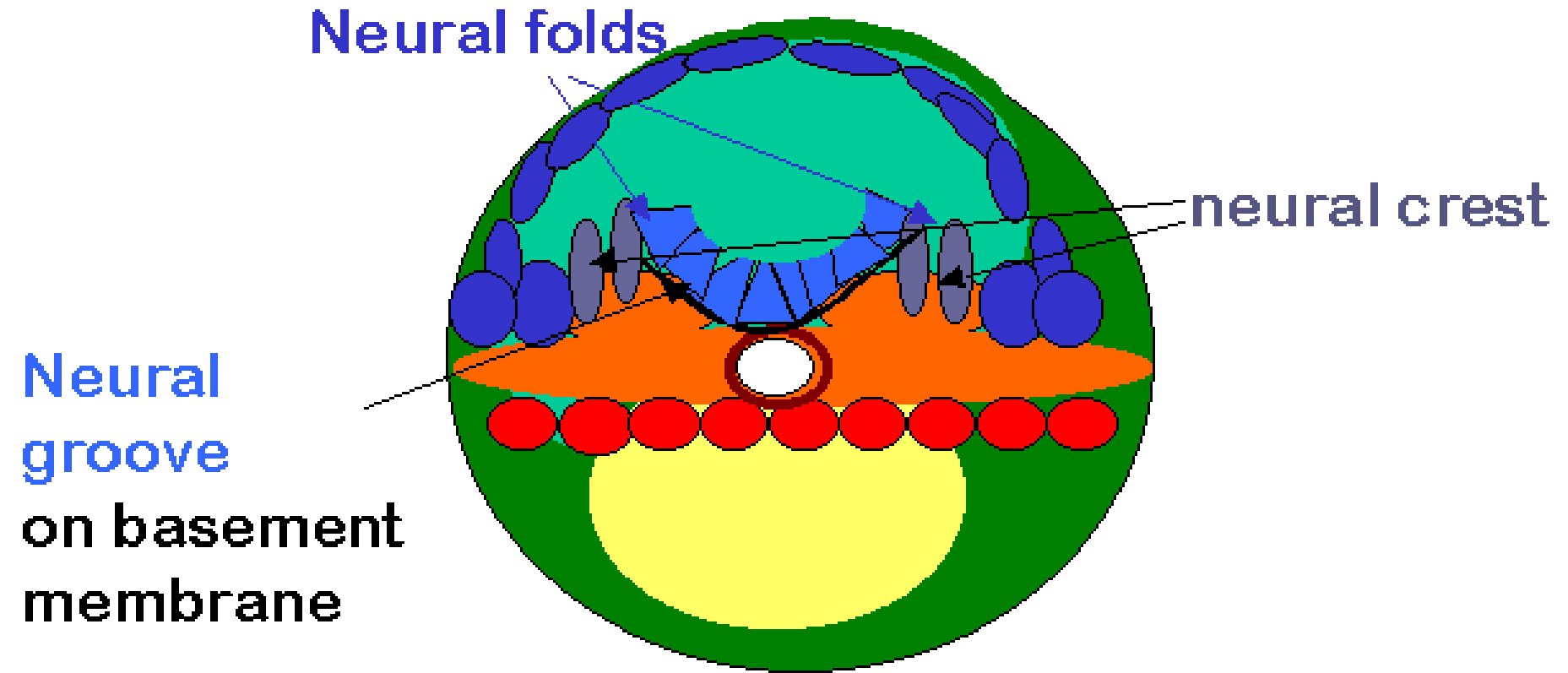
- Neurulation includes the formation of the neural plate (day 18-19), neural folds (day 20-21), and the neural tube (day 22-26); the latter will develop into the future **brain** and **spinal cord**
- The neural plate forms as a central strip of surface ectoderm cells, just above the notochord. It is induced to become neuroectoderm through changes in cell shape (cuboidal to columnar) and proliferation; the cells develop N-CAM adhesion molecules, disorganized filaments and elongated tubules; this flat layer of cells is referred to as the **neural plate**





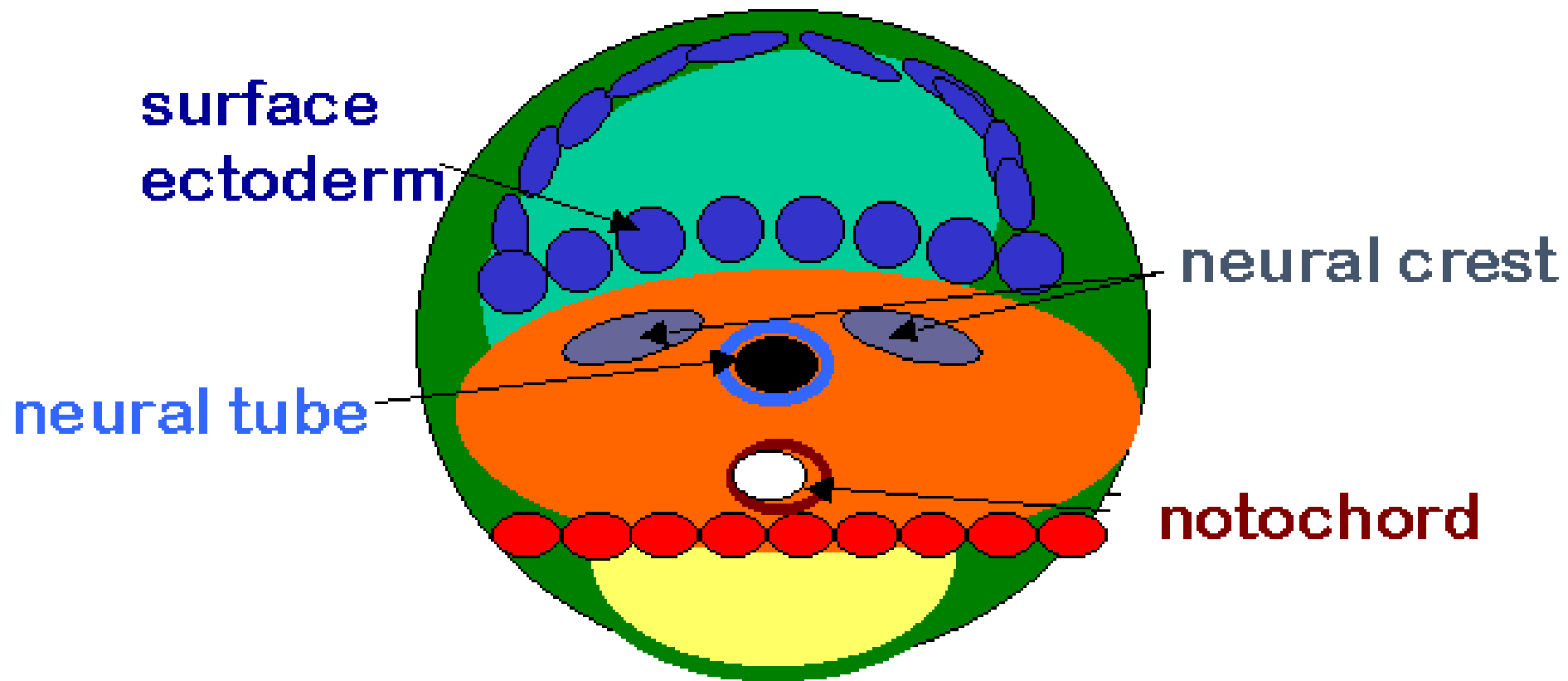
- The layer of cells between the regular surface ectoderm and the neuroectoderm possess characteristics of both cell types, such as the possession of both L-CAM (ectoderm) and N-CAM (neuroectoderm) adhesion molecules, and are called neural crest cells.
- At the neural plate, the cells continue to morph into pyramidal shaped cells with straight neuro-tubules, neuro-filaments concentrated at the apex of the cell, connected by desmosomes
- The change in cell shape and a decrease in cell number cause the neuroectodermal cells to gradually fold inward, forming neural folds (d 20-21)





The neural tube continues to grow in this manner, and eventually breaks free of the surface ectoderm which will be sealed off. Up to this point, it was supplied continuously with amniotic fluid.





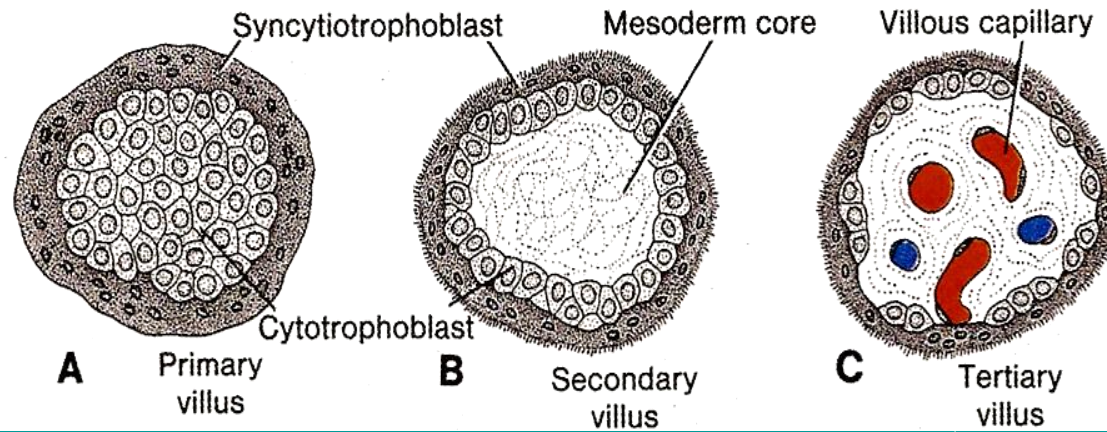
- As the neural tube forms, the closing process is critical, occurring from the cranial to the caudal end as the anterior neuropore closes around day 24, the posterior around day 26.
- This is a critical event, as defects in closure may result in [spina bifida](#) or other [neural tube defects](#).
- The risk of a neural tube defect can be decreased by folic acid supplements.
- Once the neural tube has closed completely, vertebral structures develop around it, as do meninges and finally, skin from the surface ectoderm



Neural Crest Cells and their Derivatives

- As the notochord induces the transformation of surface ectoderm to neuroectoderm, a multipotential middle cell layer develops with characteristics of both cell types.
- These neural crest cells migrate dorsolaterally to form the neural crest, a flattened irregular mass between the surface ectoderm & neuroectoderm
- This layer will separate into right and left portions and then migrate to different areas.
- **Remember**, teratomas form from disorganized, multipotential tissues such as the primitive streak, neural crest cells and primary germ cells.

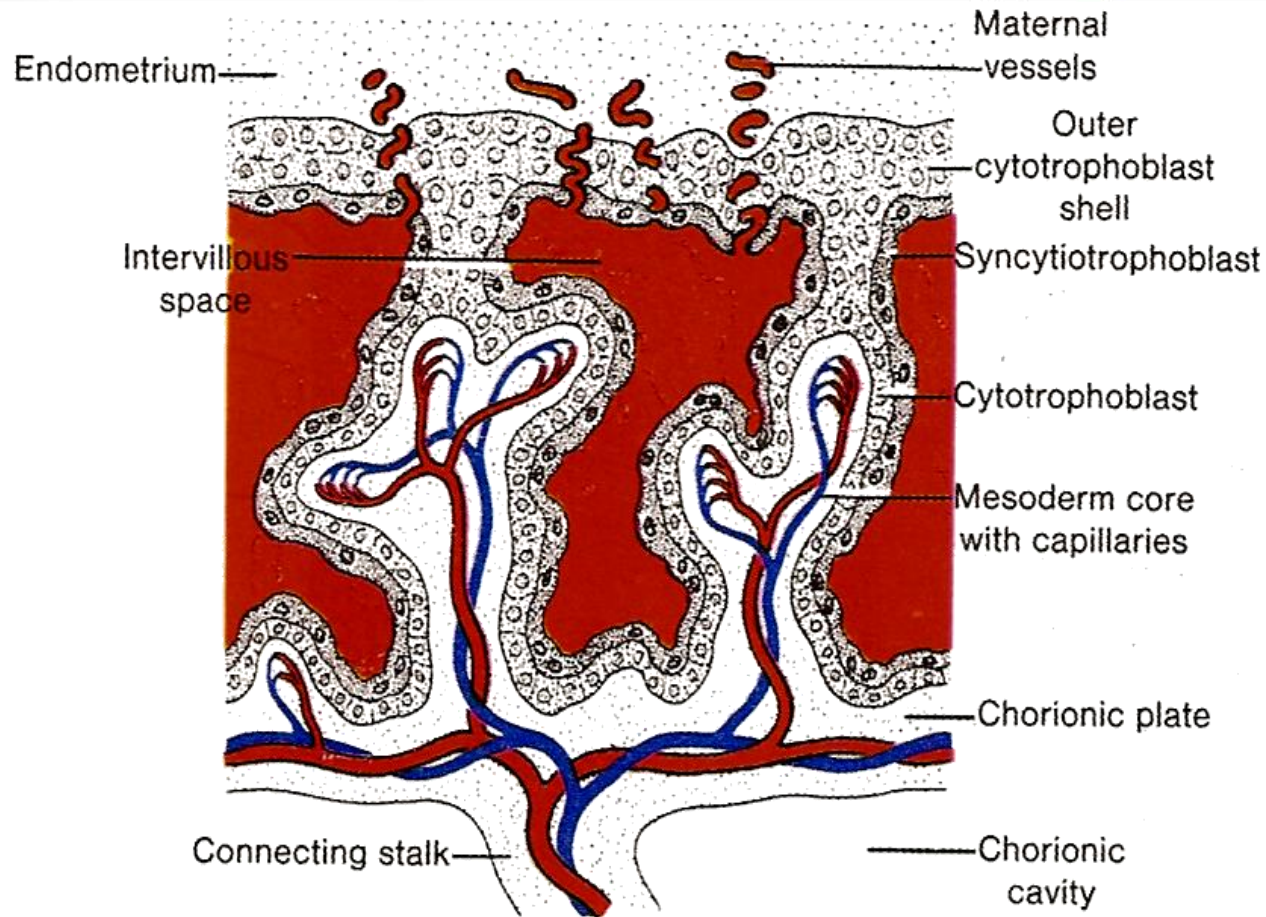




Further Development of the Trophoblast

By the beginning of the 3rd week, the trophoblast is characterized by **primary villi** that consist of a cytotrophoblastic core covered by a syncytial layer. During further development; mesodermal cells penetrate the core of primary villi forming a **secondary villus**.

- By the end of the 3rd week. Mesodermal cells in the core of the villus begin to differentiate into blood cells & small blood vessels, thus forming the villous capillary system, a **tertiary villus** or definitive placental villus. Capillaries in tertiary villi make contact with capillaries developing in mesoderm of the chorionic plate & in the connecting stalk.



Longitudinal section through a villus at i end of i 3rd week of development. Note that maternal vessels penetrate the cytotrophoblastic shell to enter intervillous spaces, which surround the villi. The capillaries in the villi, are in contact with vessels in i chorionic plate & in i connecting stalk, which, in turn, are connected to intraembryonic vessels.

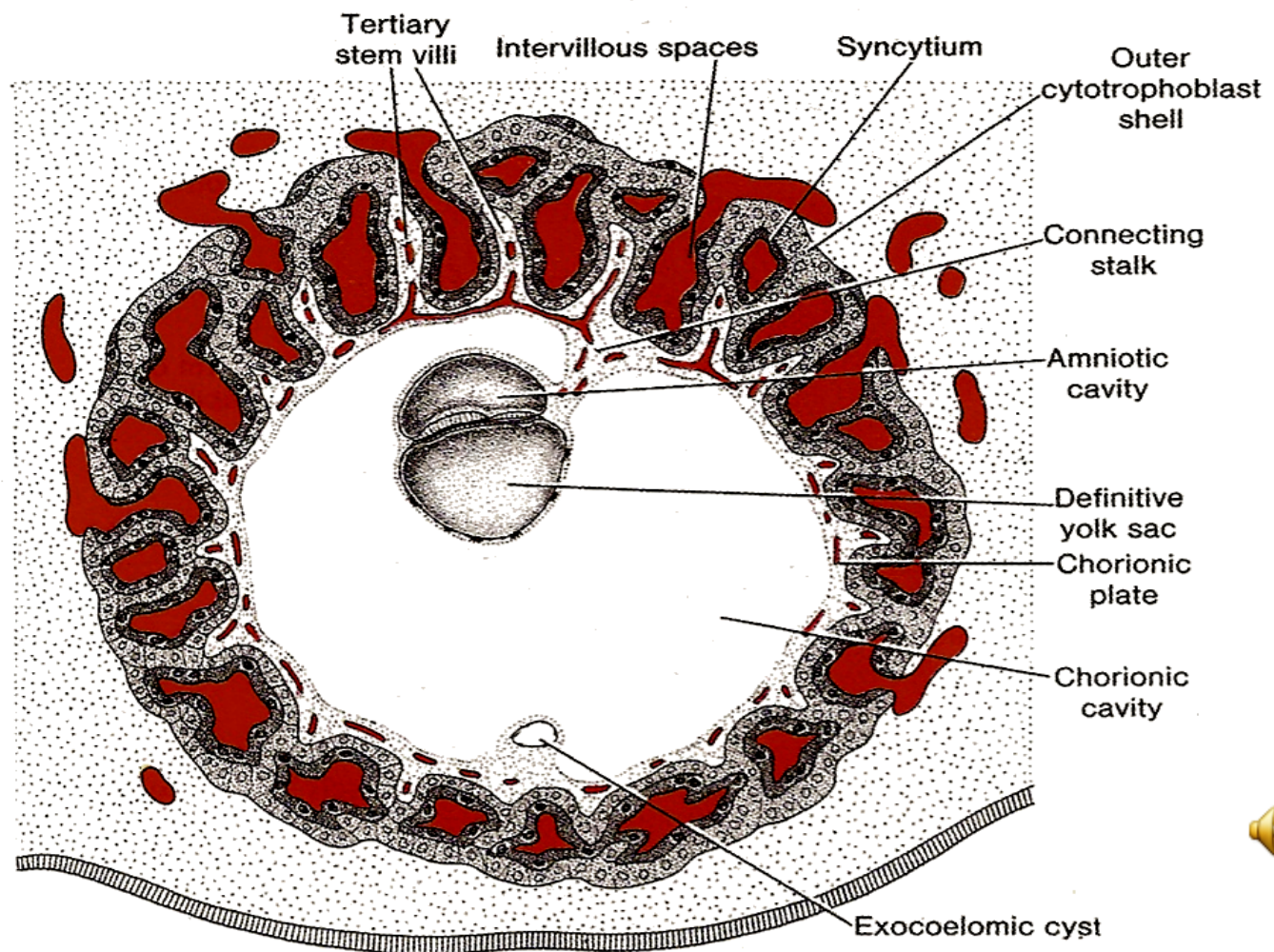


Diagram showing a presomite embryo and the trophoblast at the end of i 3rd week. Intervillous spaces are found throughout the trophoblast and are lined with syncytium. Cytotrophoblastic cells surround the trophoblast entirely and are in direct contact with the endometrium..

Clinical correlates

- This stage is highly sensitive for teratogenic insult, fate maps can be made for various organ systems, such as the eyes, ---etc.
- Cell populations may be damaged by teratogens. e.g., high doses of alcohol kill cells in the ant. Midline producing def. at midline in craniofacial structures & resulting in **holoprosencephaly** . .
- **Gastrulation** itself may be disrupted by genetic & teratogenic causes. **Caudal dysgenesis (sirenomelia)** is a syndrome contains insufficient mesoderm formed in the caudal most region of the embryo. Since this mesoderm contributes to formation of the lower limbs, urogenital system, & lumbosacral vertebrae, (see below).

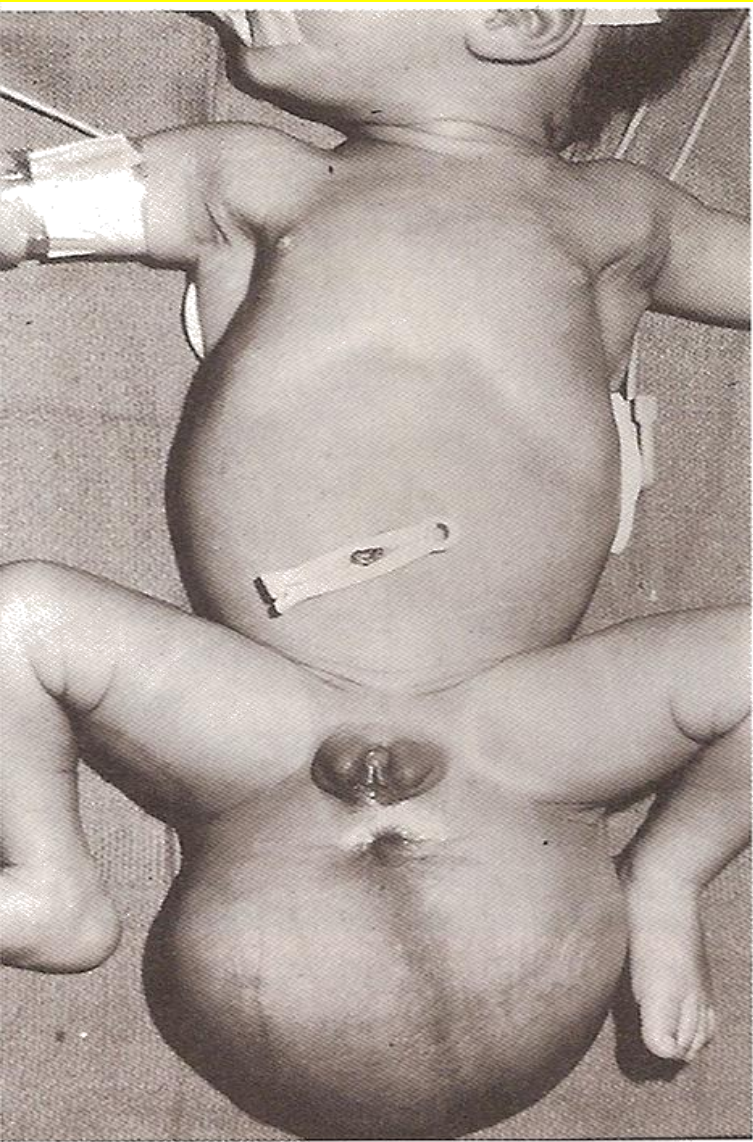


- Sometimes, remnants of the primitive streak persist in the sacrococcygeal region. These clusters of cells proliferate and form tumors, known as **sacrococcygeal teratomas**, that often contain tissues derived from all three germ layers (see below).





Sirenomelia (caudal dysgenesis). Loss of mesoderm in the lumbosacral region has resulted in fusion of the limb buds and other defects.



Sacroccocygeal teratoma resulting from remnants of the primitive streak. These tumors may become malignant and are more common in females.

THANK YOU



**General Embryology,
Lecture X,
Embryonic Period
(Third to Eighth Weeks)
Part I**



Embryonic Period

[Third to Eighth Weeks] (part I)

- During the 3rd to 8th weeks of development, a period known as the **embryonic period or period of organogenesis**, each of the three germ layers gives rise to a number of specific tissues and organs.
- By the end of the embryonic period, the **main organ** systems have been established. Major features of the external body form are recognizable.



Derivatives of the Ectodermal Germ Layer

- The ectodermal germ layer has the shape of a flat disc, broader in the cephalic than the caudal region (see below).
- With appearance of the notochord , ectoderm overlying the notochord thickens to form the **neural plate** (see below).
- Cells of the plate make up the neuroectoderm, which represents the initial event in the process of neurulation.
- **The induction process is complex**, involving stimulation of a responding tissue or group of cells by an inducing tissue. It is a process that occurs repeatedly during organogenesis (genes). 
- **Once induction has occurred**, elongated, slipper-shaped neural plate expands toward the primitive streak. By the end of the 3rd week, the lateral edges of the neural plate become more elevated to form neural folds, the depressed midregion forms a groove, the **neural groove** (see below).

- Gradually, the neural folds approach each other in the midline, where they fuse (Fig. 5.3C). This fusion begins in the region of the **future neck** (4th somite) and proceeds in cephalic and caudal directions (Figs. 5.5).
- As a result, the neural tube is formed. Until fusion is complete, the cephalic and caudal ends of the neural tube communicate with the amniotic cavity by way of the cranial and caudal **neuropores**, respectively. (Fig. 5.5).
- Closure of the cranial neuropore occurs approximately at day 25 (18-20somite stage), whereas the posterior neuropore closes at day 27 (25somite stage).
- **Neurulation is then complete.** & i CNS is represented by a closed, tubular structure with a narrow caudal portion, the spinal cord, and a much broader cephalic portion characterized by a number of dilations, the brain vesicles.



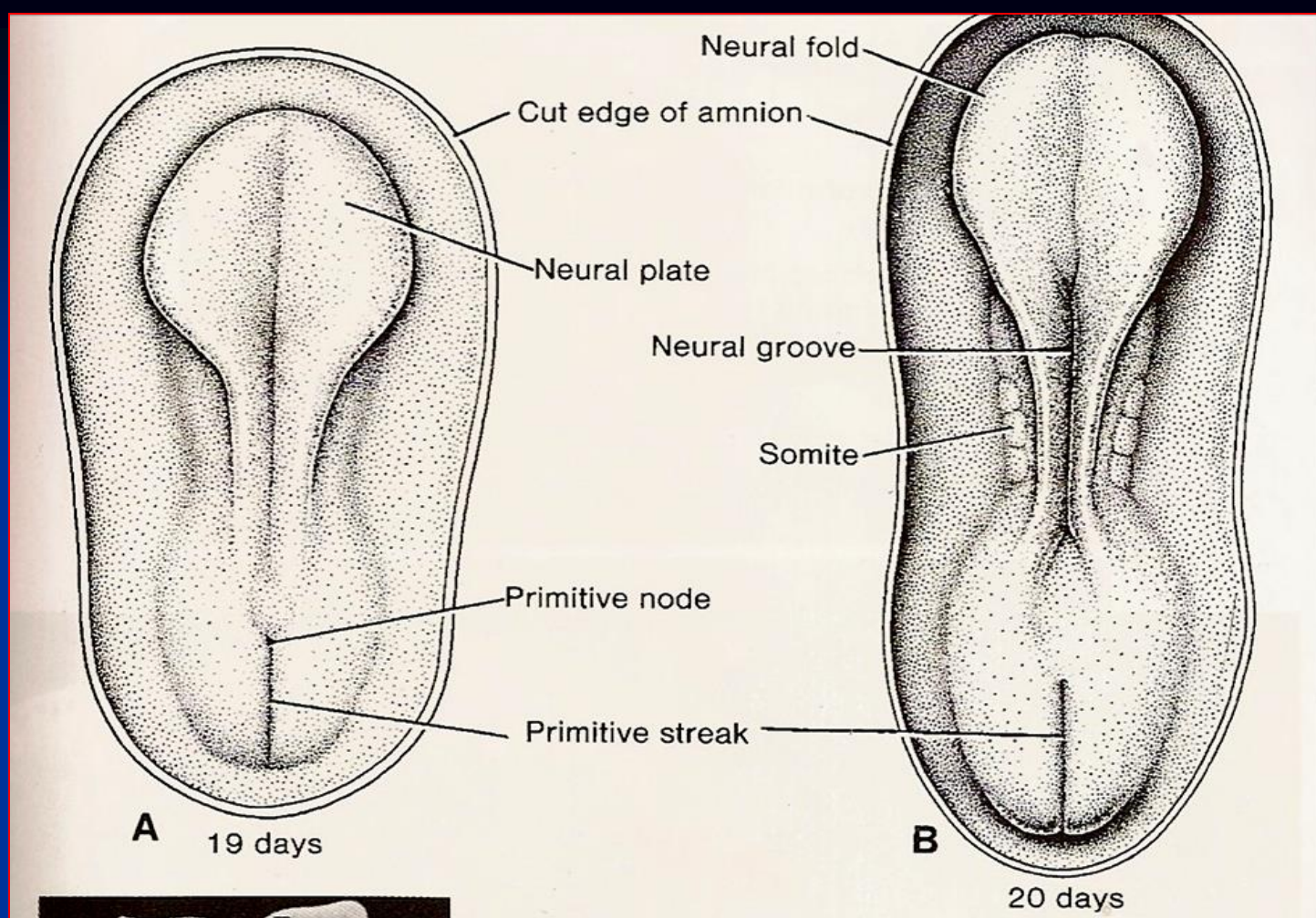


Figure 5.2. A. Dorsal view of a late presomite embryo (approx. 19 days). The neural plate is clearly visible. B. Dorsal view of a human embryo at approx. 20 days. Note the appearance of somites & formation of the neural groove and neural folds. C. neural folds have segregated themselves into forebrain (F), midbrain (M), hindbrain (H,) regions.

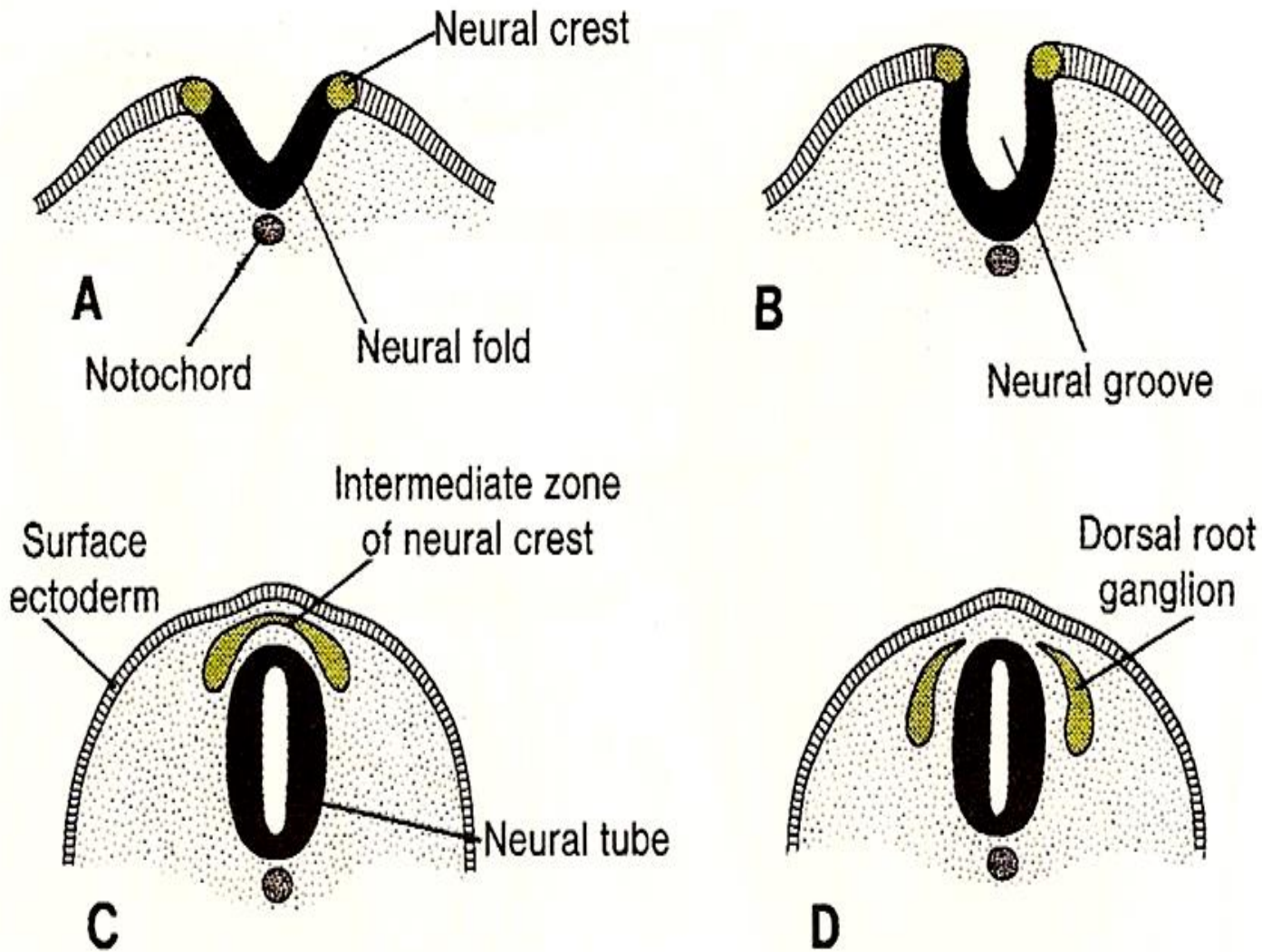


Figure 5.3. formation & migration of neural crest cells in the spinal cord, (A and B). Crest cells form at the tips of neural folds & do not migrate away from this region until neural tube closure is complete, (C and D).

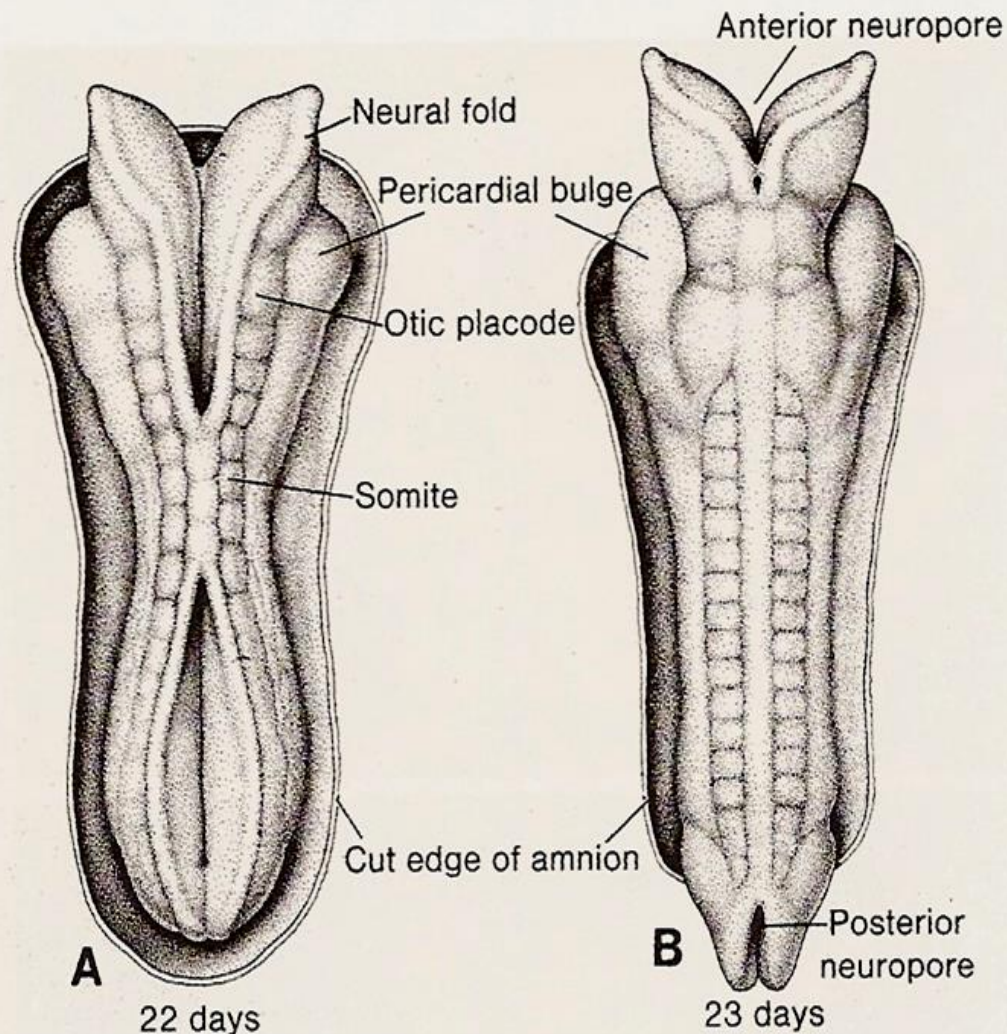


Figure 5.5. A. Dorsal view of a human embryo at day 22. Seven distinct somites are visible on each side of the neural tube. B. Dorsal view of a human embryo at approximately day 23. Note the pericardial bulge on each side of the midline in the cephalic part of the embryo

- **Neural crest** formed by elevation and fused of neural folds, then dissociation at the lateral border or crest of the neuroectoderm.
 - Crest cells then give rise to a heterogeneous array of tissues, including spinal (sensory) & autonomic ganglia; parts of the ganglia of cranial nerves V, VII, IX, and X; meninges; (adrenal) gland: bones and connective tissues of craniofacial structures.
- 
- By time, neural tube is closed, 2 bilateral ectodermal thickenings, i otic placodes & the lens placodes, become visible in i cephalic region (Fig.5.8B). Which invaginate to form i **otic vesicles** & **lenses** of the eyes respectively.

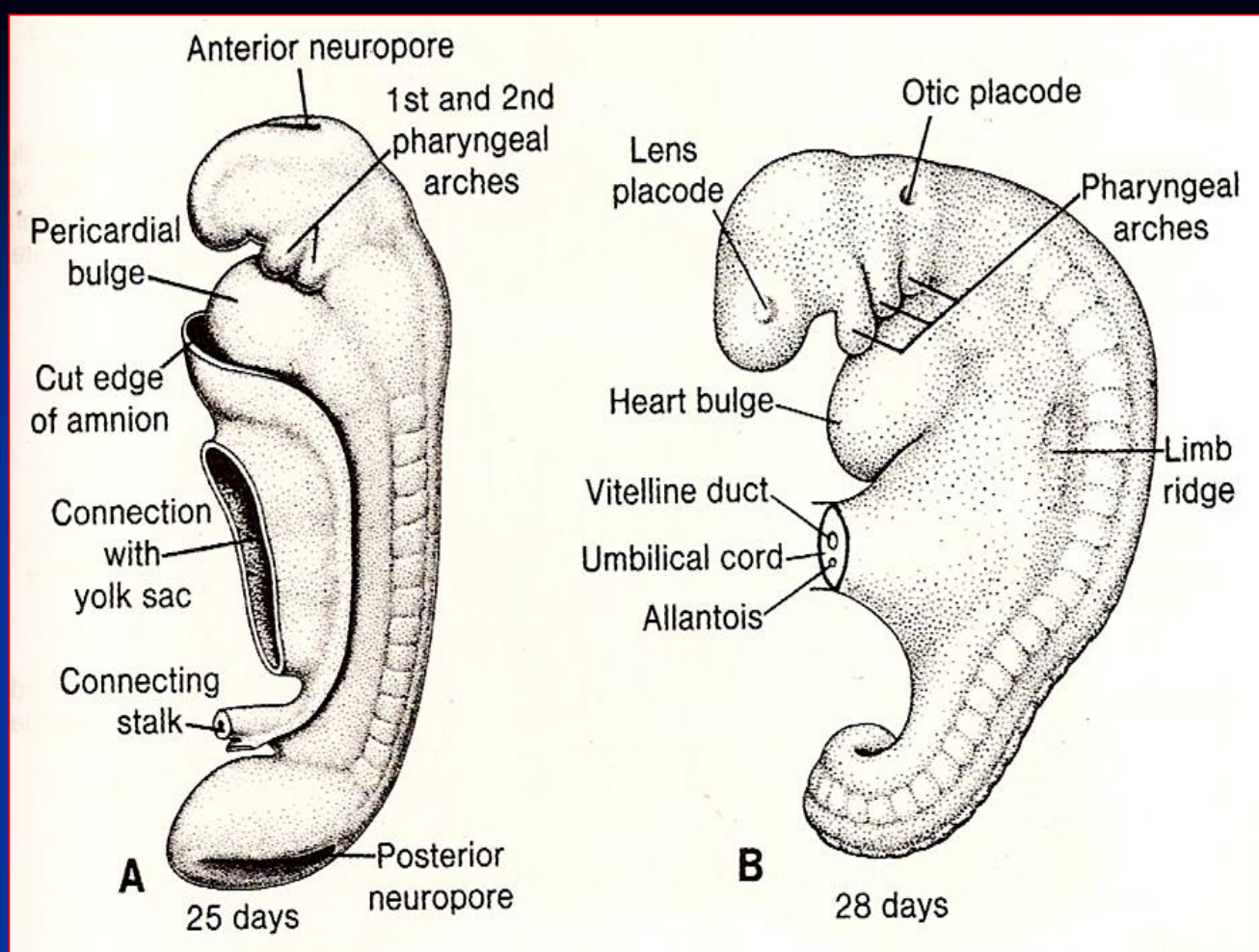


Figure 5.8. **A.** lateral view of a 14-somite embryo (approx. 25 days). Note i bulging pericardial area & the 1st & 2nd pharyngeal arches. **B.** left side of a 25-somite embryo approx. 28 days old. The 1st three pharyngeal arches & lens & otic placodes are visible.

In general terms the ectodermal germ layer gives rise to those organs and structures:

- (a)* the central nervous system:
- (b)* the peripheral nervous system;
- (e)* the sensory epithelium of the ear, nose, and eye.
- (d)* the epidermis, including the hair and nails.

In addition, it gives rise to subcutaneous glands, the mammary gland, the pituitary gland, and the enamel of the teeth.



Derivatives of the Mesodermal Germ Layer

- Initially, cells of the mesodermal germ layer form a thin sheet of loosely woven tissue on each side of the midline (Fig. 5.9A).
- By about the 17th day, cells close to the midline proliferate and form **paraxial mesoderm** (Fig. 5.9B). More laterally, the mesoderm layer remains thin, **the lateral plate**. , this tissue is divided into two layers (Fig. 5.9. B and C):
 - (a) a layer continuous with mesoderm covering the amnion. known as **the somatic or parietal mesoderm layer**.
 - (b) a layer continuous with mesoderm covering the yolk sac. known as the **splanchnic or visceral mesoderm layer** (Figs. 5.9, C and D,).



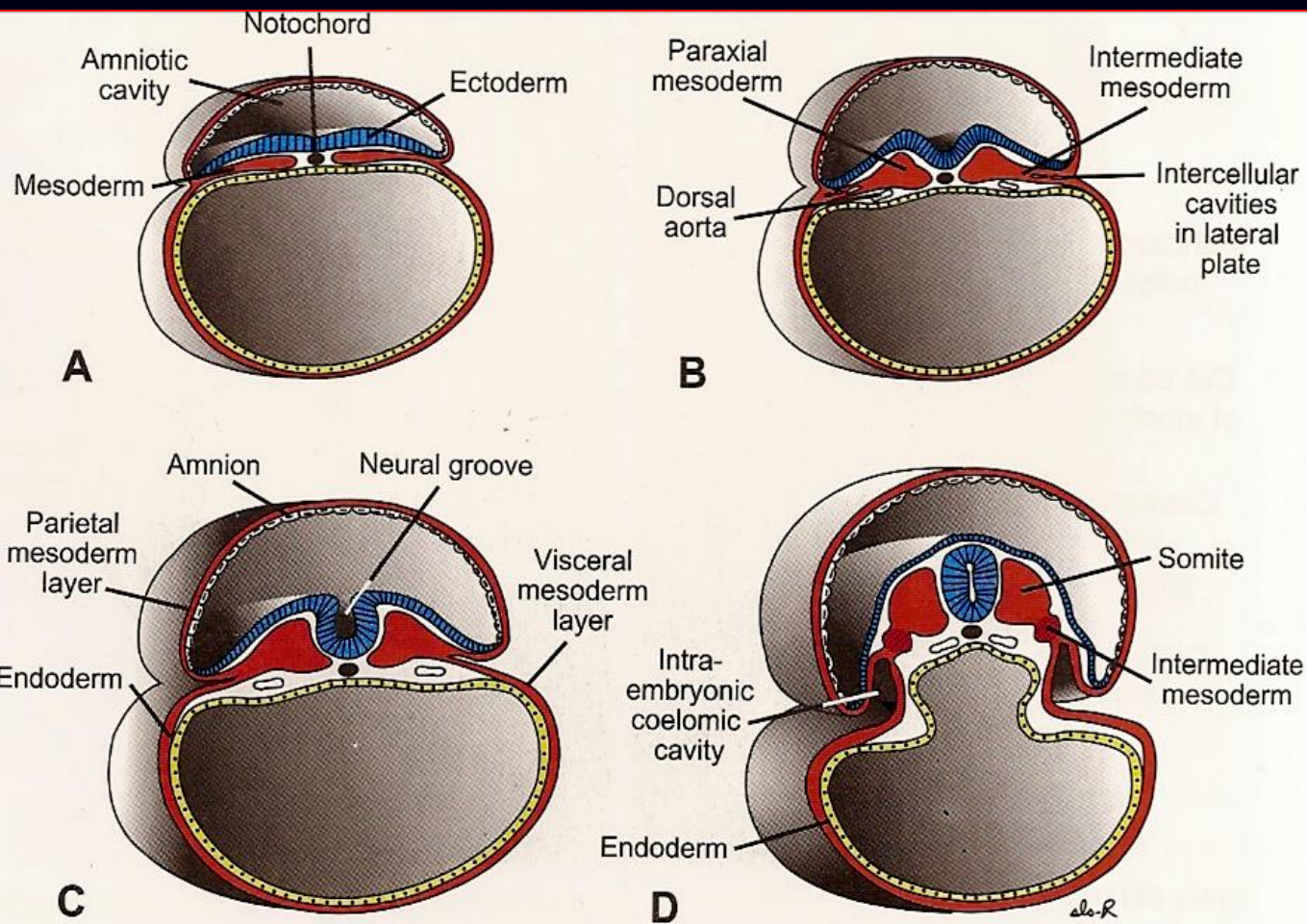


Figure 5.9 Transverse section showing development of i mesodermal germ layer. A. Day 17. B. Day 19. C. Day 20. D. Day 21. The thin mesodermal sheet gives rise to paraxial mesoderm (future somites), intermediate mesoderm (future excretory units), and lateral plate, which is split into parietal and visceral mesoderm layers lining the intraembryonic coelomic cavity.

- By the beginning of the 3rd week. paraxial mesoderm becomes organized into segments. These segments, known as **somitomeres**, which form **neuromeres** & then **somites**.
- Somites form a loosely tissue known as mesenchyme which form the **vertebral column**, **musculature** & form **dermis & subcutaneous tissue of the skin** (fig. 5.11) 

Table 5.1.

Number of Somites Correlated to Approximate Age in Days

Approximate Age (days)	No. of Somites
20	1-4
21	4-7
22	7-10
23	10-13

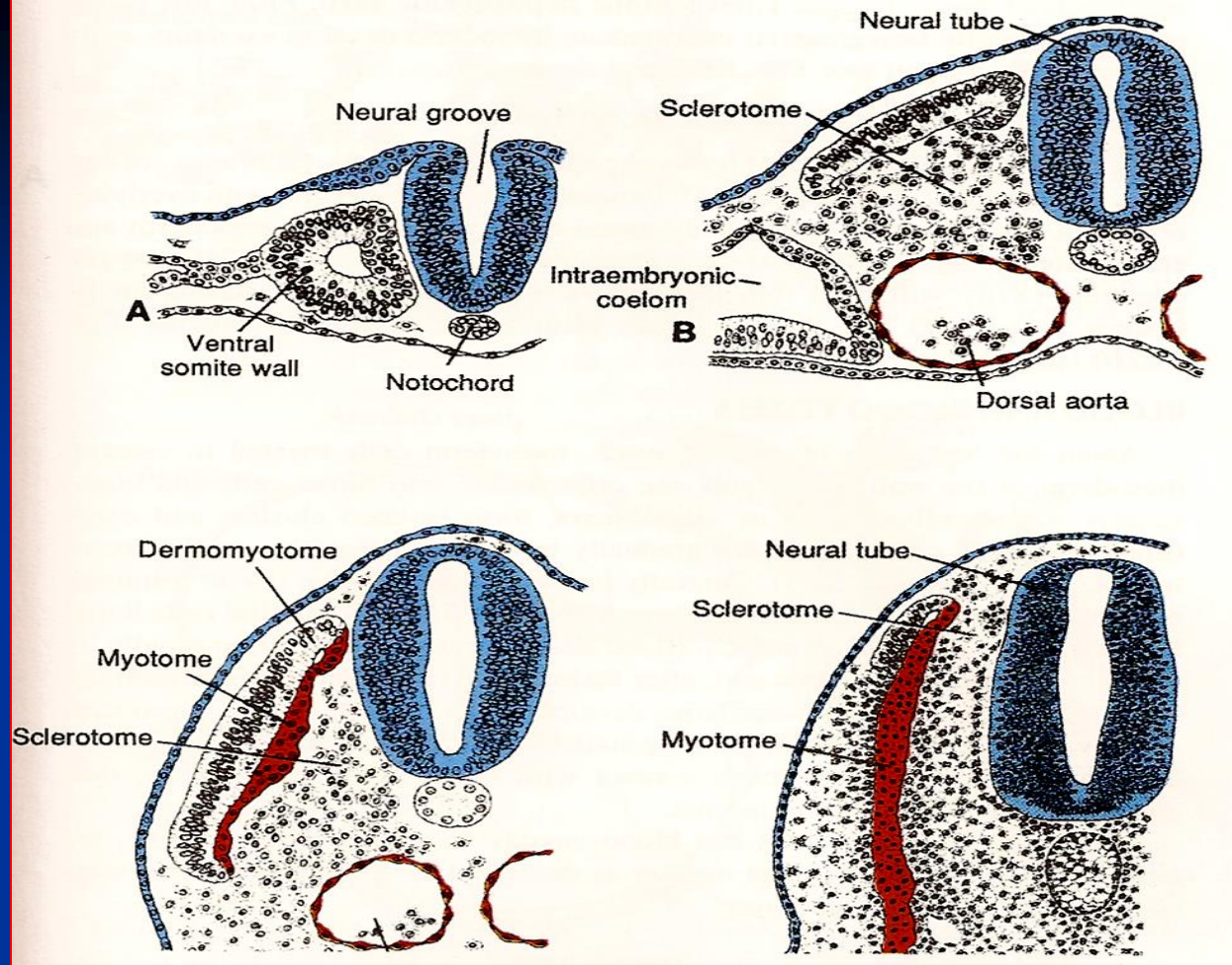


Figure 5.11. Successive stages in development of a somite. A. Mesoderm cells are arranged around a small cavity. B. Cells of the ventral & medial walls of the somite. These cells are collectively referred to as the sclerotome. C. The dorsal somite wall gives rise to a new cell layer, the myotome. D. After extension of the myotome in a ventral direction, dermatome cells form dermis.

■ **In summary**, the following tissues & organs are considered to be of mesodermal origin:

- (a) Supporting tissues such as connective tissue, cartilage, and bone.
- (b) Striated and smooth musculature;
- (c) Blood and lymph cells and the walls of the heart. blood. and lymph vessels.
- (d) Kidneys. gonads, and their corresponding ducts;
- (e) The cortical portion of the suprarenal gland;
- (f) The spleen.



THANK YOU



**General Embryology,
Lecture XI,
Embryonic Period
(Third to Eighth Weeks develop.)
(part II)
+ Fetal Period
(Third Month to Birth)**



Derivatives of the Endodermal Germ Layer

- The gastrointestinal tract is i main organ system derived from the endodermal germ layer.
- Formation of i tube-like gut is a passive event & consists of i inversion & incorporation of part of i endoderm-lined yolk sac into i body cavity.
- The endodermal germ layer covers i ventral surface of the embryo & forms the roof of i yolk sac (Fig. 5.15A).
- In the anterior part, the endoderm forms the **foregut**; in the tail region, it forms the **hindgut**. The part between foregut and hindgut is known as the **midgut**.
- Allantois into the body of the embryo forms the **cloaca** (Fig.5.17)



- Endodermal germ layer initially forms the epithelial lining of the primitive gut and the intraembryonic portions of the allantois and vitelline duct (Fig. 5.17A).
- During further development. it gives rise to
 - (a) the epithelial lining of the respiratory tract;
 - (b) the **parenchyma** of the thyroid, parathyroids, liver, and pancreas;
 - (c) the reticular stroma of the tonsils and thymus.
 - (d) the epithelial lining of the urinary bladder and urethra;
 - (e) the epithelial lining of the tympanic cavity and auditory tube.



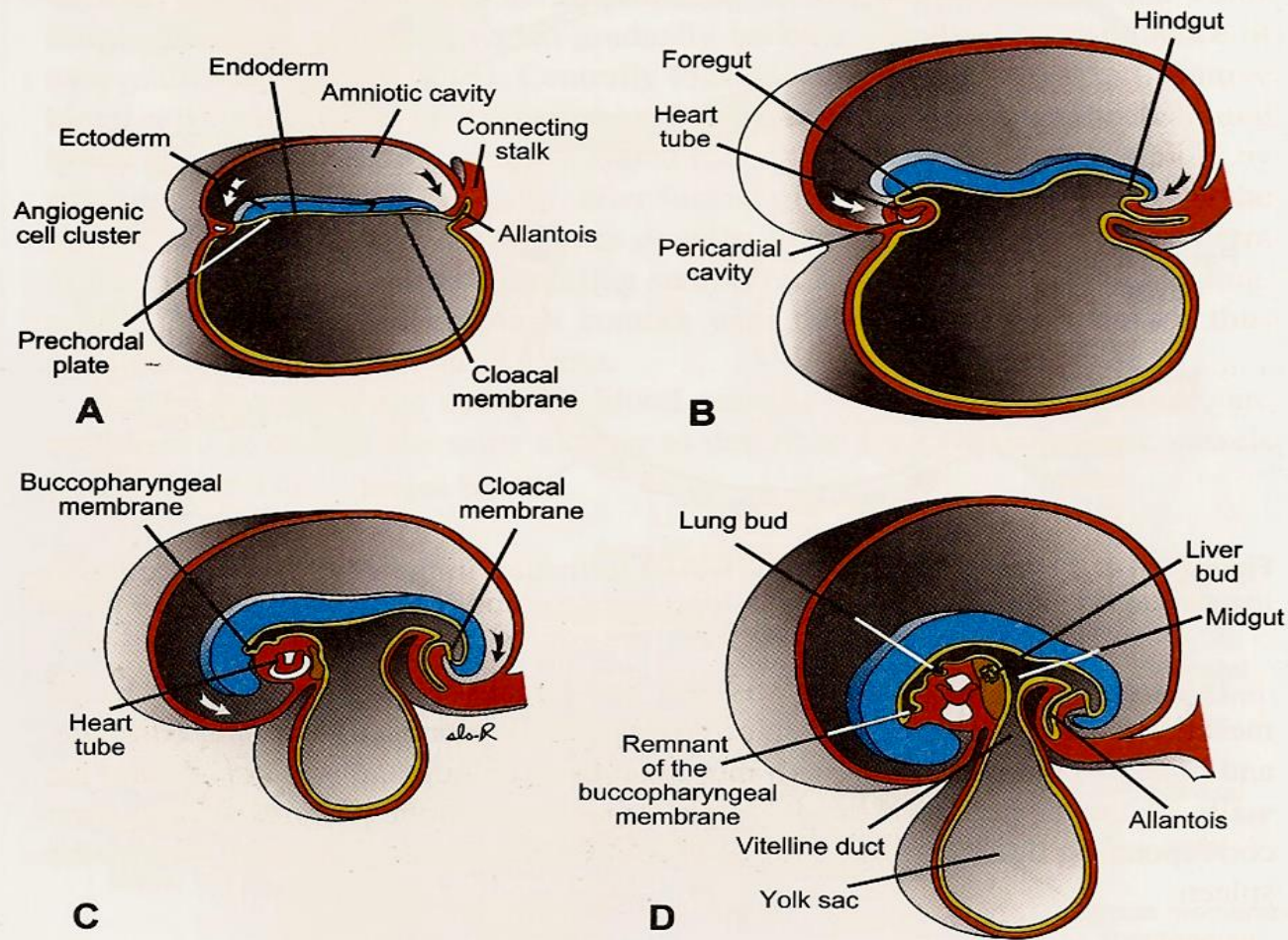


Figure 5.15. Drawings of sagittal midline sections of embryos at various stages of development to demonstrate cephalocaudal folding & its effect on position of the endoderm-lined cavity. A. Presomite embryo. B. Seven-somite embryo. C. Fourteen somite embryo. D. At the end of the 1st month. Note the angiogenic cell clusters in relation to the prechordal (buccopharyngeal membrane) plate.

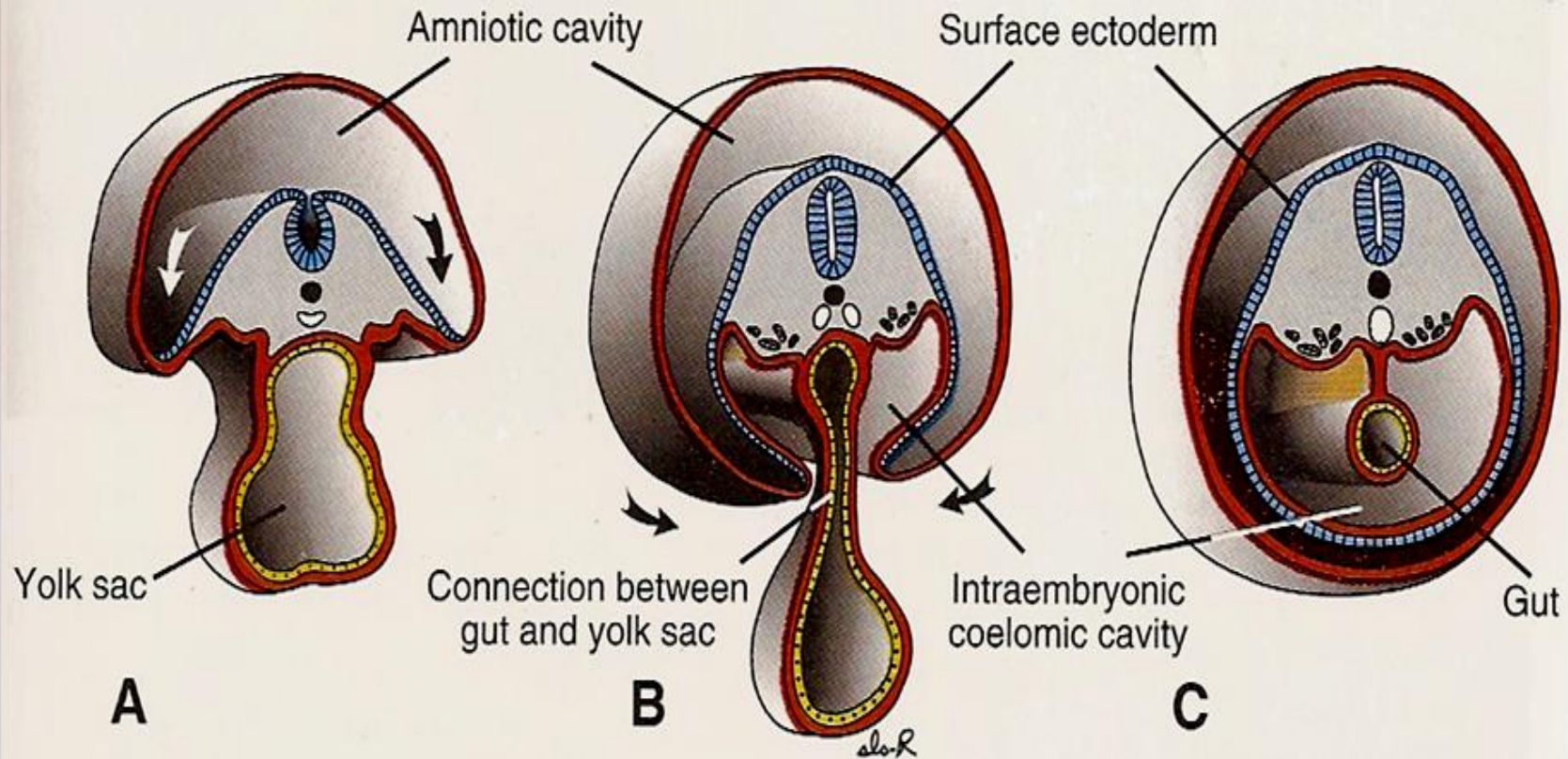


Figure 5.16. Transverse sections through embryos at various stages of development to show the effect of lateral folding on the endoderm-lined cavity. **A. folding is initiated. **B.** Transverse section through the midgut to show the connection between the gut & yolk sac. **C.** Section just below the midgut to show the closed ventral abdominal wall & gut suspended from the dorsal abdominal wall by its mesentery.**

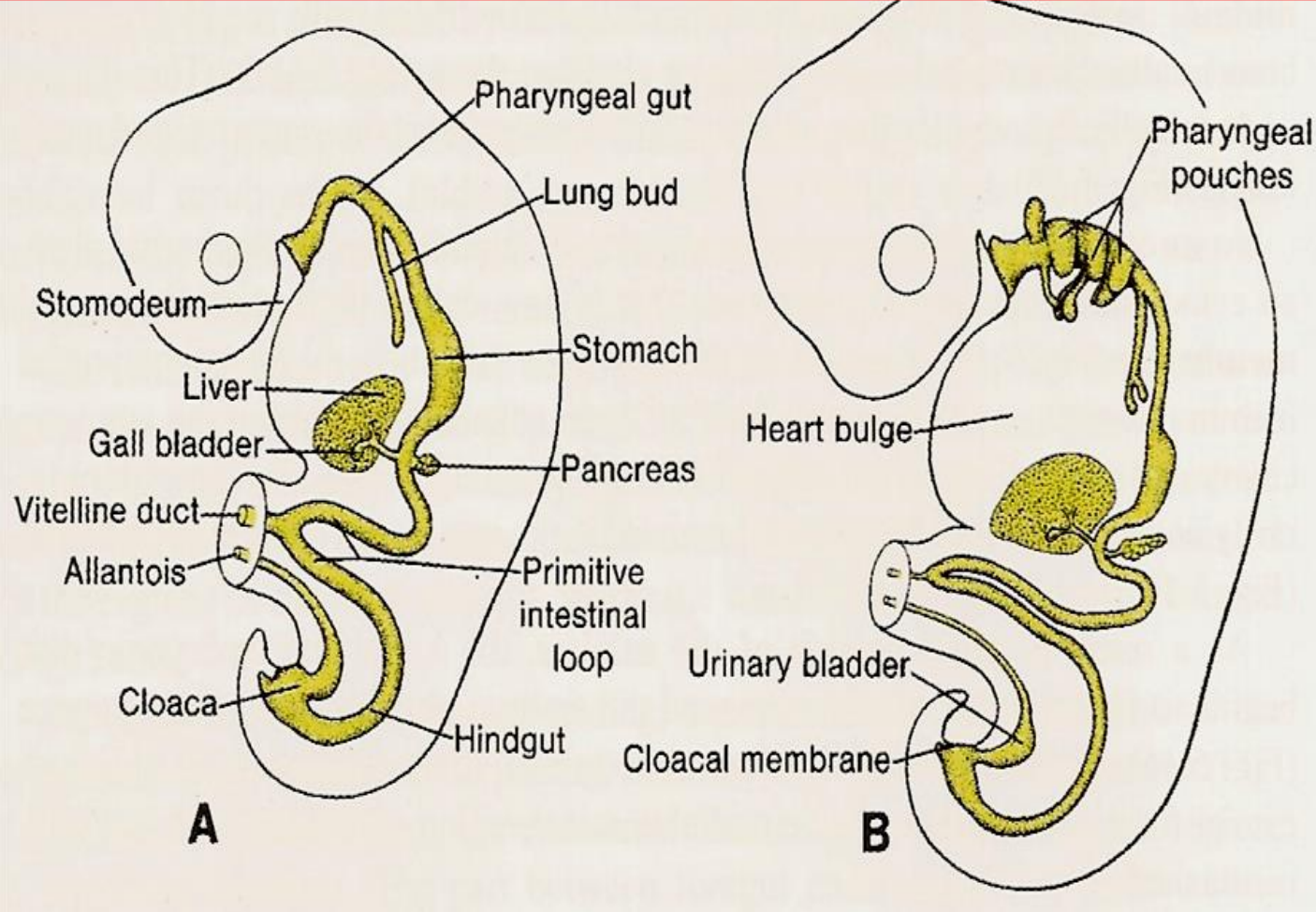


Figure 5.17. Sagittal sections through embryos at various stages of development to show derivatives of the endodermal germ layer. Note i pharyngeal pouches & epithelial lining of i lung buds & trachea. Note i liver, gallbladder, & pancreas. The urinary bladder is derived from the cloaca &, at this stage of development, is in open connection with the allantois.

Fetal Period (Third Month to Birth)

Development of the Fetus:

- **Fetal period** is a period from the beginning of the 3rd month to the end of intrauterine life.
- Characterized by maturation of tissues & organs & rapid growth of the body. Few malformations arise during this period.
- length of pregnancy is considered to be 280 days or 40 Weeks; or, more accurately, 266 days or 38 weeks after fertilization



Monthly Changes:

- At beginning of **3rd month**, i head constitutes approximately one-half CRL (Fig. 6.1).
- At beginning of **5th month**, i size of i head is about (one-third CHL. **At birth**, it is approximately one-fourth CHL (Fig. 6.2).
- During i 3rd month, i face becomes more human-looking (Figs. 6.3 & 6.4). **eyes**, initially directed laterally & then located on i ventral aspect, **the ears** come to lie close to their definitive position (Fig. 6.3).
- **Limbs** reach their relative length. **1ry ossification centers** are present in i long bones & skull by the 12th week.
- **external genitalia** develop (sex of fetus can be determined by external examination (ultrasound).



Table 6.1.

Growth in Length and Weight During the Fetal Period

Age (weeks)	CRL (cm)	Weight (gm)
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	900-1300
29-32	28-30	1400-2100
33-36	31-34	2200-2900
37-38	35-36	3000-3400



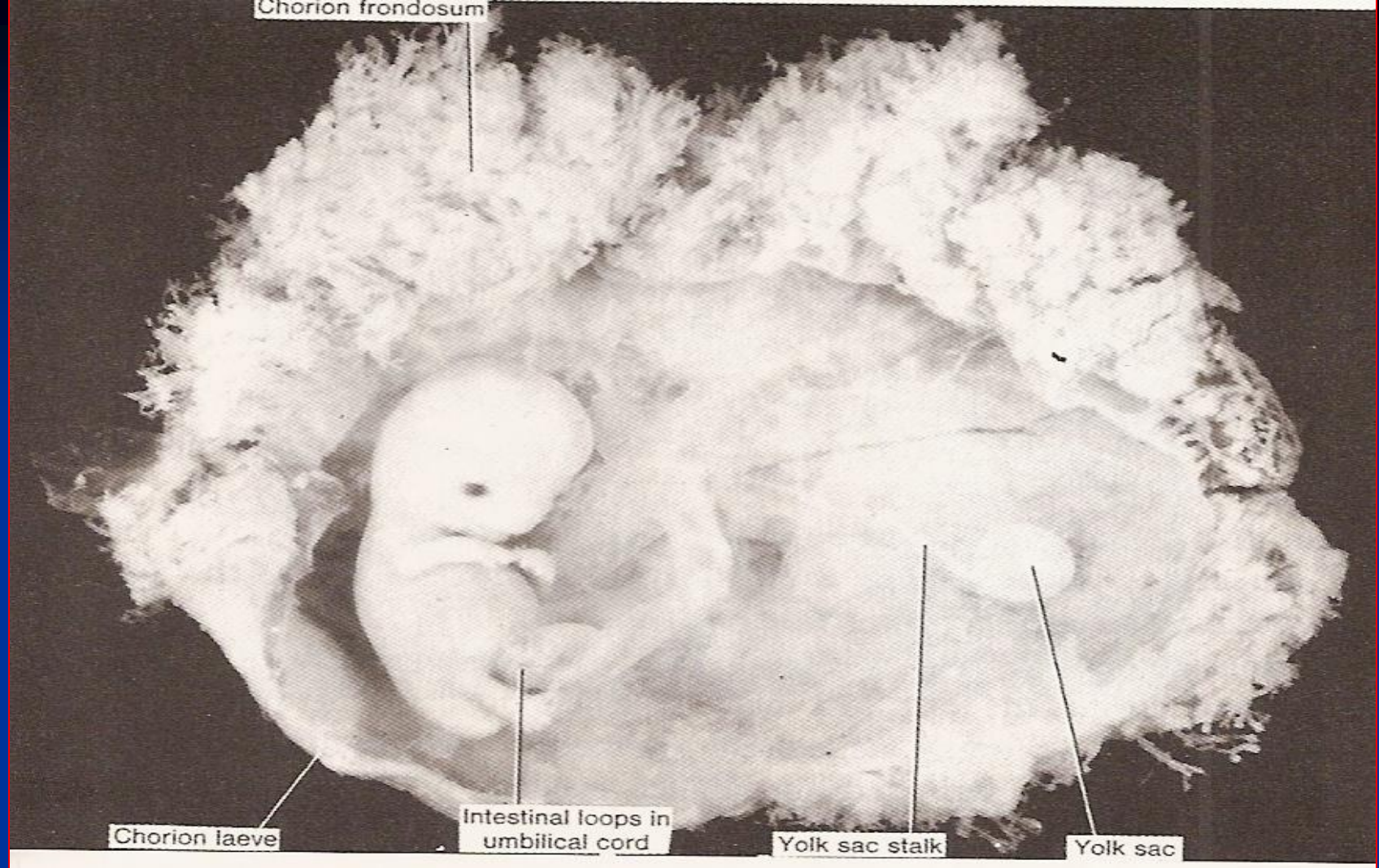


Figure 6.1. Photograph of a 9-week fetus. Note the large size of the head compared with that of the remaining part of the body. The yolk sac is visible in the chorionic cavity. Note the umbilical cord and herniation of intestinal loops. 🔊

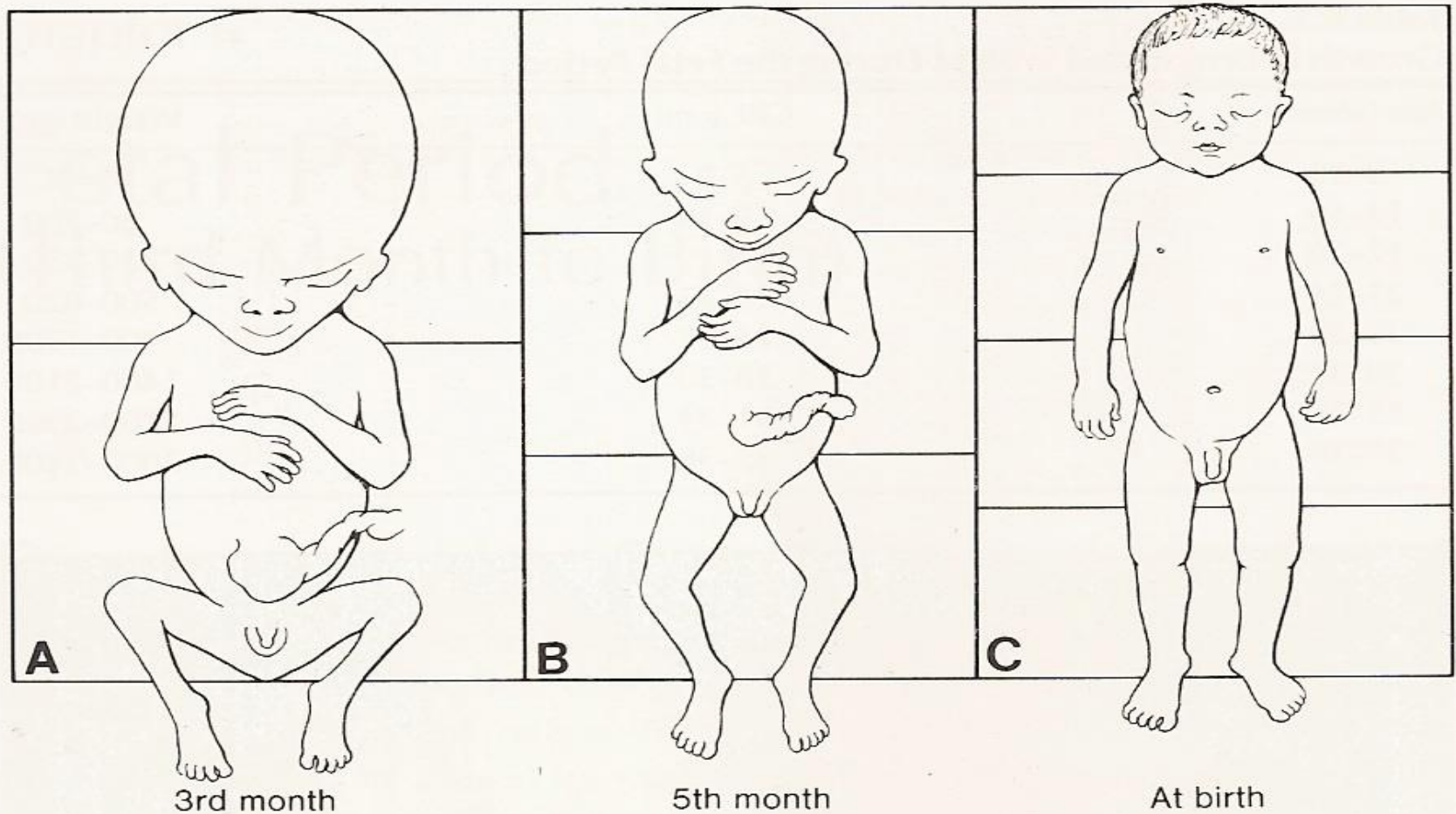


Figure 6.2. Schematic drawings showing the size of the head in relation to the rest of the body at various stages.

- During the **4th** and **5th** months, the fetus **lengthens** rapidly (Fig. 6.5 and Table 6.1), & at i end of the 1st half of intrauterine life its crown rump length (CRL) is approximately 15 cm,
- Regard **weight**, i end of 5th mo. is still less than 500 gm.
- During the 5th month, **movements** of i fetus are usually clearly recognized by the mother.
- During the **second half** of intrauterine life, **wt.** increases considerably. particularly during the last 2 1/2 months, when 50% of the full-term weight (approximately 3200 gm) is added.
- During the 6th mon., the **skin** of the fetus is reddish & has a wrinkled appearance. (if delivered premature)





Figure 6.3. Photograph of 11-week fetus. The umbilical cord still shows a swelling at its base, caused by herniated intestinal loops. Toes are developed, and the sex of the fetus can be recognized.

- **At last 2 months.** fetus obtains well-rounded contours as i result of deposition of subcutaneous fat (Fig. 6.6).
- **At the end of the 9th month,** the skull has the largest circumference of all parts of the body.
- **At the time of birth.** the weight of a normal fetus is 3000--3400 gm: its CRL about 36 cm; and its CHL about 50 cm.



Time of Birth

- The date of birth is most accurately indicated as 266 days or 38 weeks after fertilization.
- The obstetrician calculates the date of birth as 280 days or 40 weeks from the first day *of* the last normal menstrual period.
- The time bet. ovulation & the succeeding menstrual bleeding is constant (14 d). but the time bet. ovulation & the preceding menses is highly variable.
- **In** general, most fetuses are born within 10-14 days of the calculated delivery date.
- Ultrasound provide an accurate measurement of i baby, head, abdominal circumference, and femur length. An accurate determination of fetal size and age is important for managing pregnancy.





Fig 6.4. Photo of 12-wk fetus in utero. Note i extremely thin skin & underlying blood vessels. face has all the human characteristics, but the ears are still primitive. Movements begin at this time but are usually not felt by the mother.



Clinical correlates

- IUGR- SGA; 1 in 10
- Several approaches are now available for assessing growth & development of i fetus in utero. these techniques are designed to detect malformations, chromosomal abnormalities.
- Ultrasonography; Amniocentesis with alpha fetoprotein, & chorionic villus sampling

Indications for employing these tests include:

- (A) Advanced maternal age, i.e., 35 years or older;
- (B) History of neural tube defects in the family;
- (C) Previous child with a chromosome abnormalities., i.e., Down Syndrome.
- (D) Chromosome abnormalities in either parent.
- (E) A mother who is a carrier of X-linked recessive disorders.



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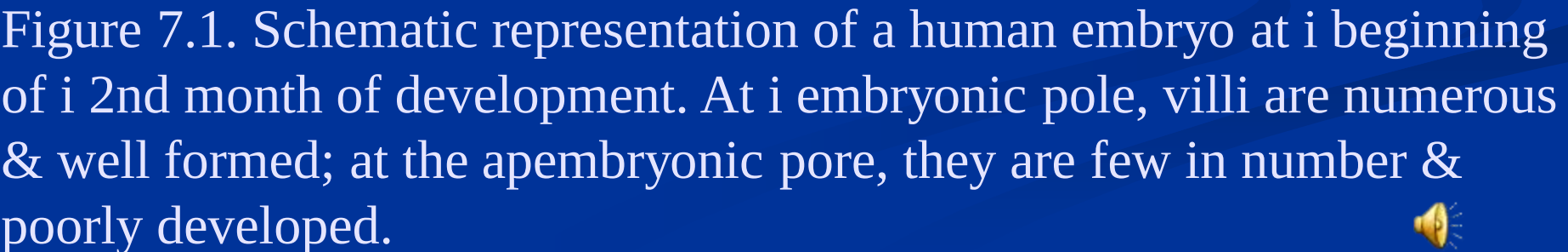
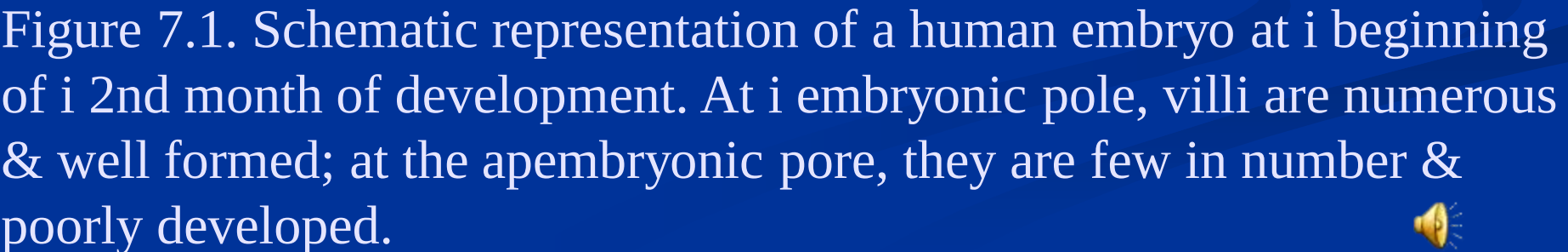
**General Embryology,
Lecture XII,
Fetal Membranes & Placenta,
part I**



Fetal membranes & Placenta

- By the beginning of the 2nd month, the trophoblast is characterized by a great number of 2ry & tertiary villi that give it a radial appearance (Fig. 7.1).)
- 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. (Fig.7.2, A,C).
- **During the following months**, numerous small extensions sprout from existing villous stems into the surrounding lacunar or intervillous spaces. The syncytium & endothelial wall of the blood vessels are then the only layers that separate the maternal & fetal circulations (Fig. 7.2, *B & D*).
- Frequently, the syncytium becomes very thin, & large pieces containing several nuclei may break off & drop into the intervillous blood lakes. These pieces, known as **syncytial knots**





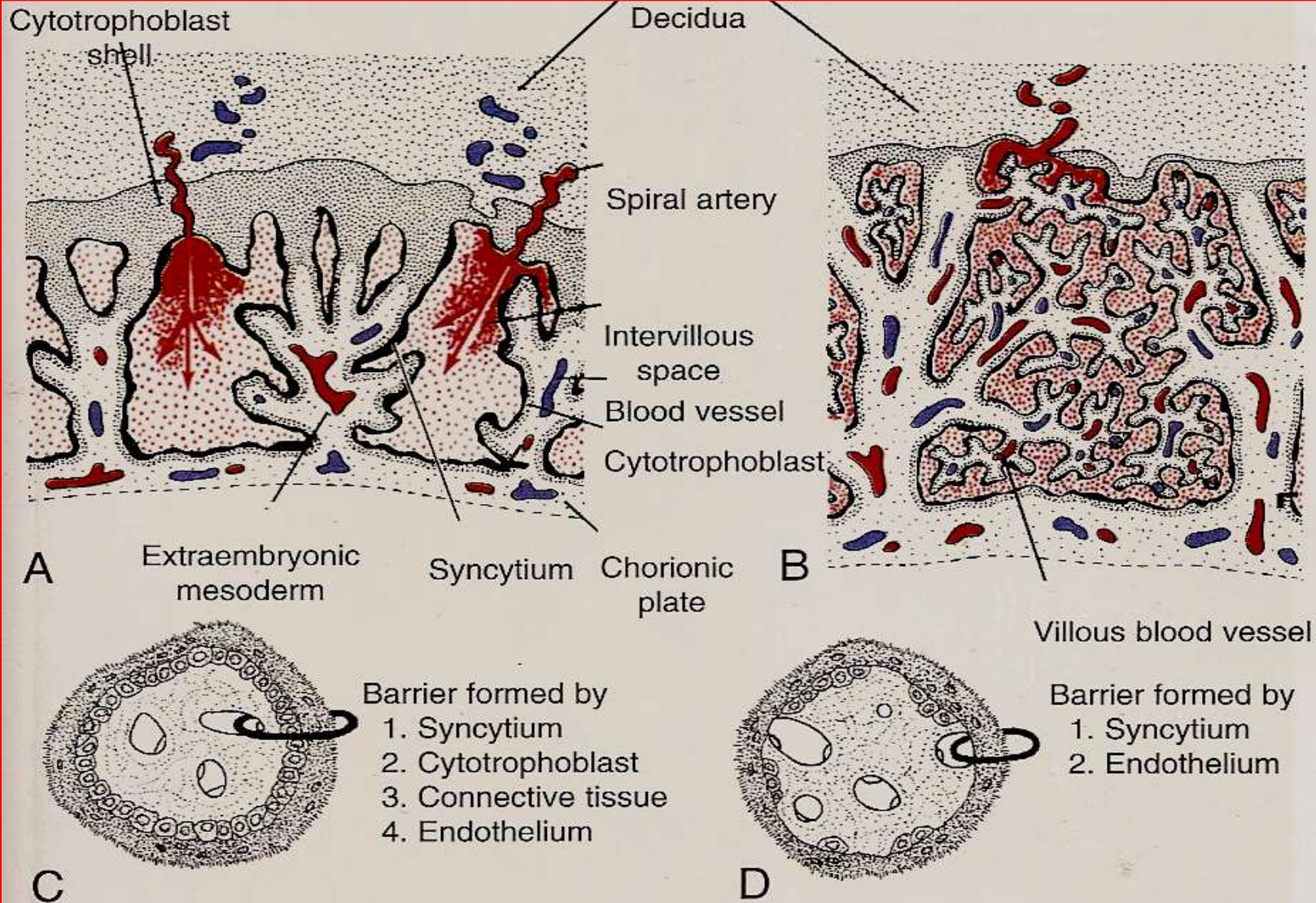


Figure 7.2. Structure of villi at various stages of development. **A.** During the 4th week **B.** During the 4th month. In many small villi the wall of the capillaries is in direct contact with the syncytium. **C** and **D.** Enlargement of the villus as shown in A and B, respectively. 🔊

Chorion Frondosum and Decidua Basalis

- As pregnancy advances, villi on the embryonic pole continue to grow and to form **chorion frondosum** (bushy chorion).
- By the 3rd month the side of the chorion is smooth & is known as the **chorion laeve** (Figs. 7.3 and 7.4 A).
- The **decidua basalis**, which is over the chorion frondosum, has a layer, the **decidual plate**, is tightly connected to the chorion.
- The decidual layer over the abembryonic pole is known as the **decidua capsularis** (Fig. 7.4A). Which becomes stretched & degenerates later.
- Subsequently, the chorion laeve comes into contact with the uterine wall (**decidua parietalis**), and the two fuse (Figs. 7.4-7.6), thereby obliterating the uterine lumen. Hence, the only portion of the chorion participating in the exchange process is the chorion frondosum, which, together with the decidua basalis, makes up the placenta. 
- Similarly, fusion of the amnion and chorion to form the amniochorionic membrane obliterates the chorionic cavity (Fig. 7.4, A & B).

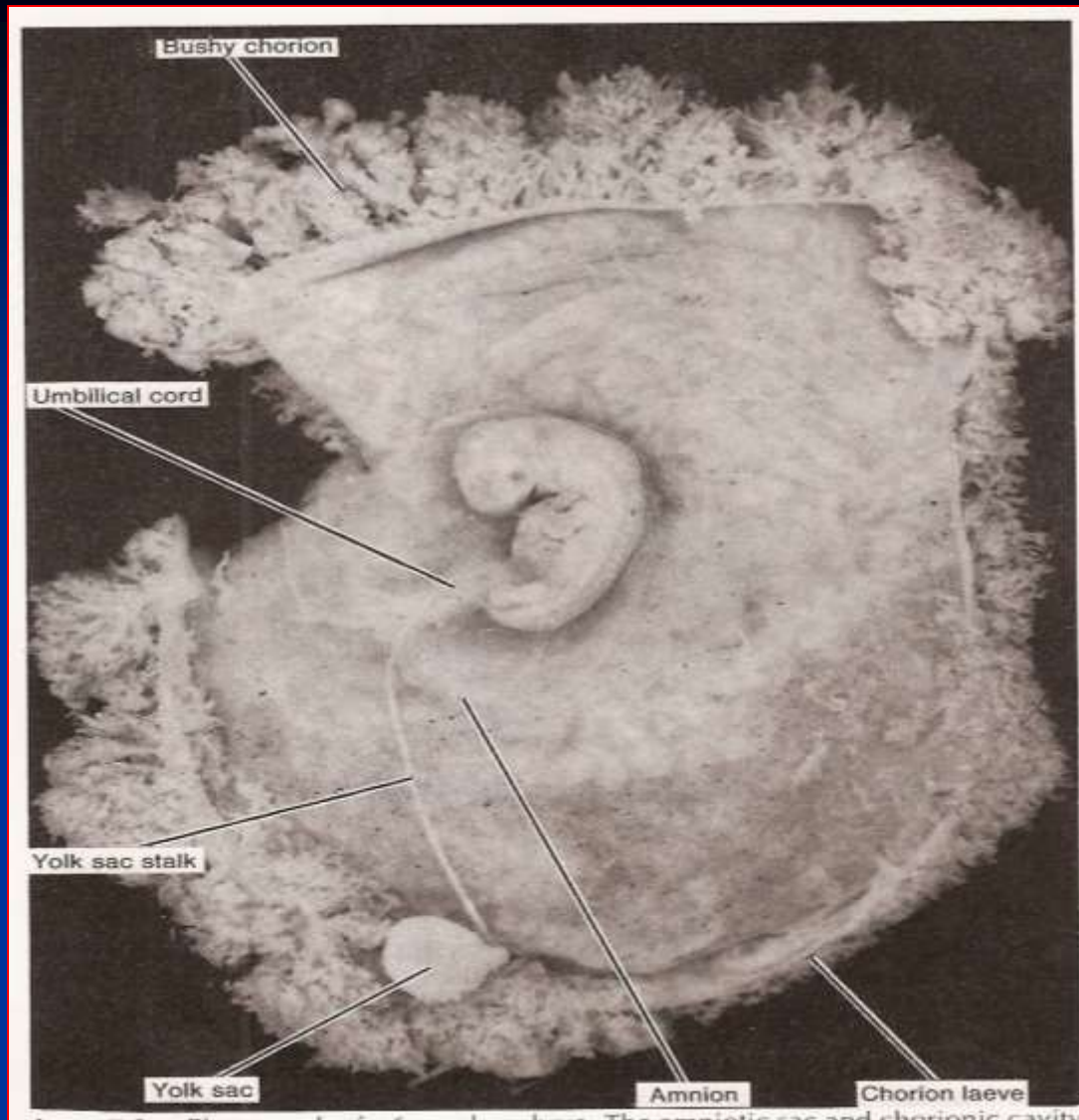


Figure 7.3. Photograph of 6-week embryo. The amniotic sac and chorionic cavity have been opened to expose the embryo. Note the bushy appearance of the trophoblast at the embryonic pole in contrast to small villi at the abembryonic pole. Note also i connecting stalk and yolk sac with its extremely long duct.

Structure of the Placenta

- By the beginning of the 4th month, the placenta has 2 components :
 - (a) A fetal portion, formed by the chorion frondosum;
 - (b) A maternal portion, formed by the decidua basalis **Fig.7.4B** On the fetal side, the placenta is bordered by the chorionic plate (Fig.7.7); on its maternal side, it is bordered by the decidua basalis, of which the decidual plate is incorporated into the Placenta.
- During 4th & 5th months, the decidua forms a number of septa, the decidual septa, which project into intervillous spaces but do not reach the chorionic plate (Fig. 7.7). As a result of this septum formation, the placenta is divided into a No. of compartments or cotyledons (Fig. 7.8).
- The placenta enlarges with growth of the fetus. Its increase in surface area roughly parallels that of the expanding uterus, & throughout pregnancy it covers approximately 15-30%.

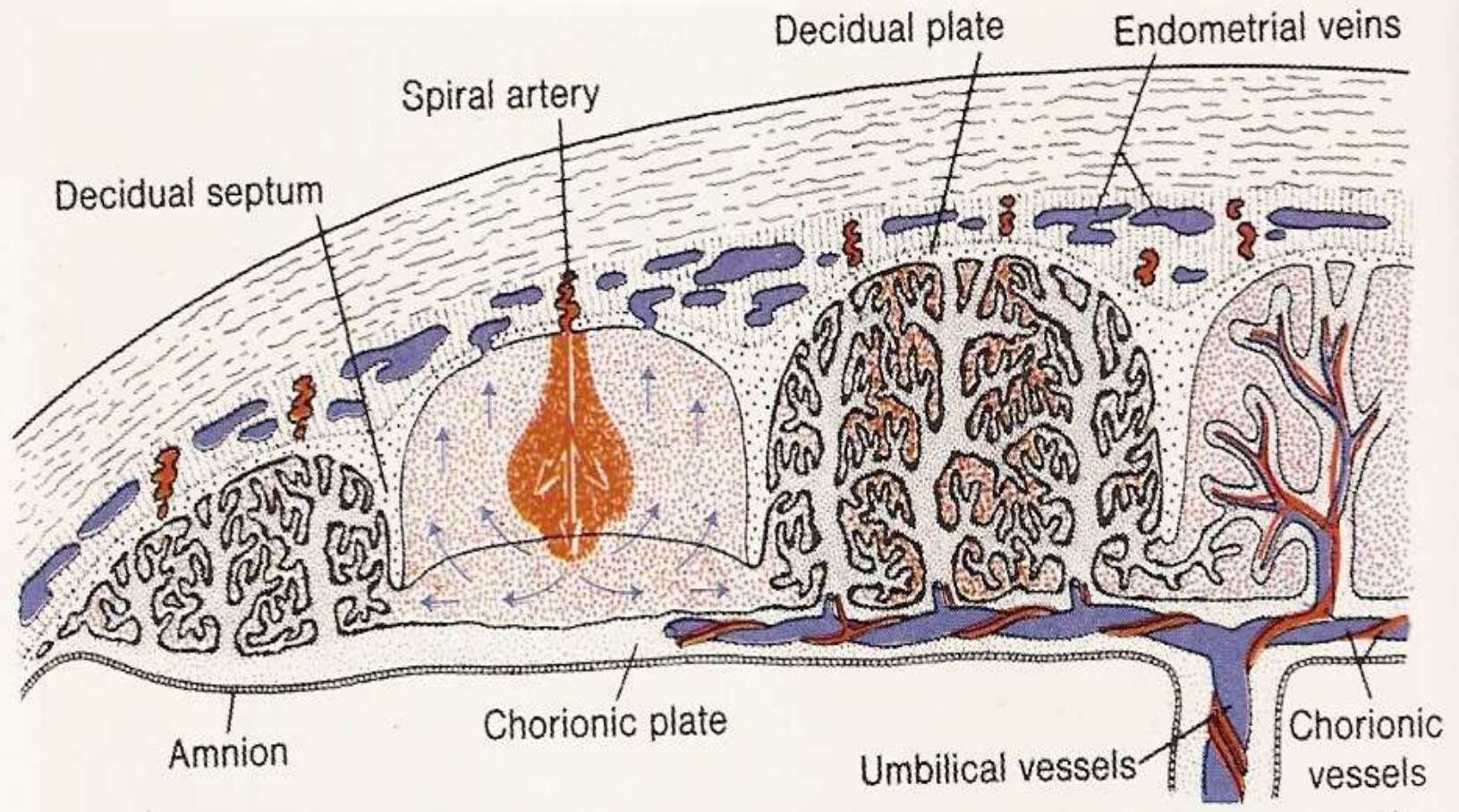
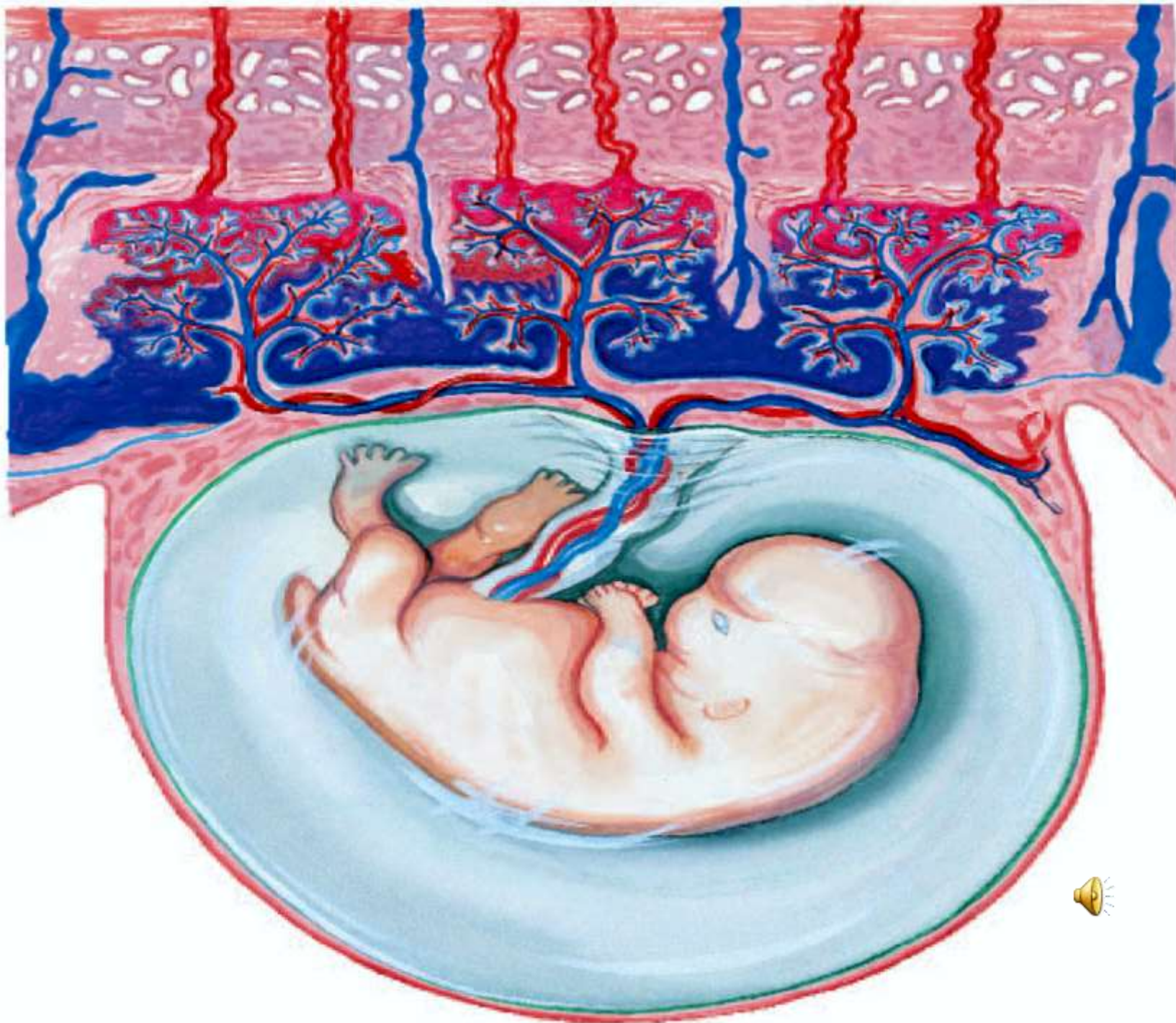


Figure 7.7. Composite drawing of the placenta in the second half of pregnancy. The cotyledons are partially separated from each other by the decidual (maternal) septa. Note that most of the intervillous blood returns to the maternal circulation by way of the endometrial veins.



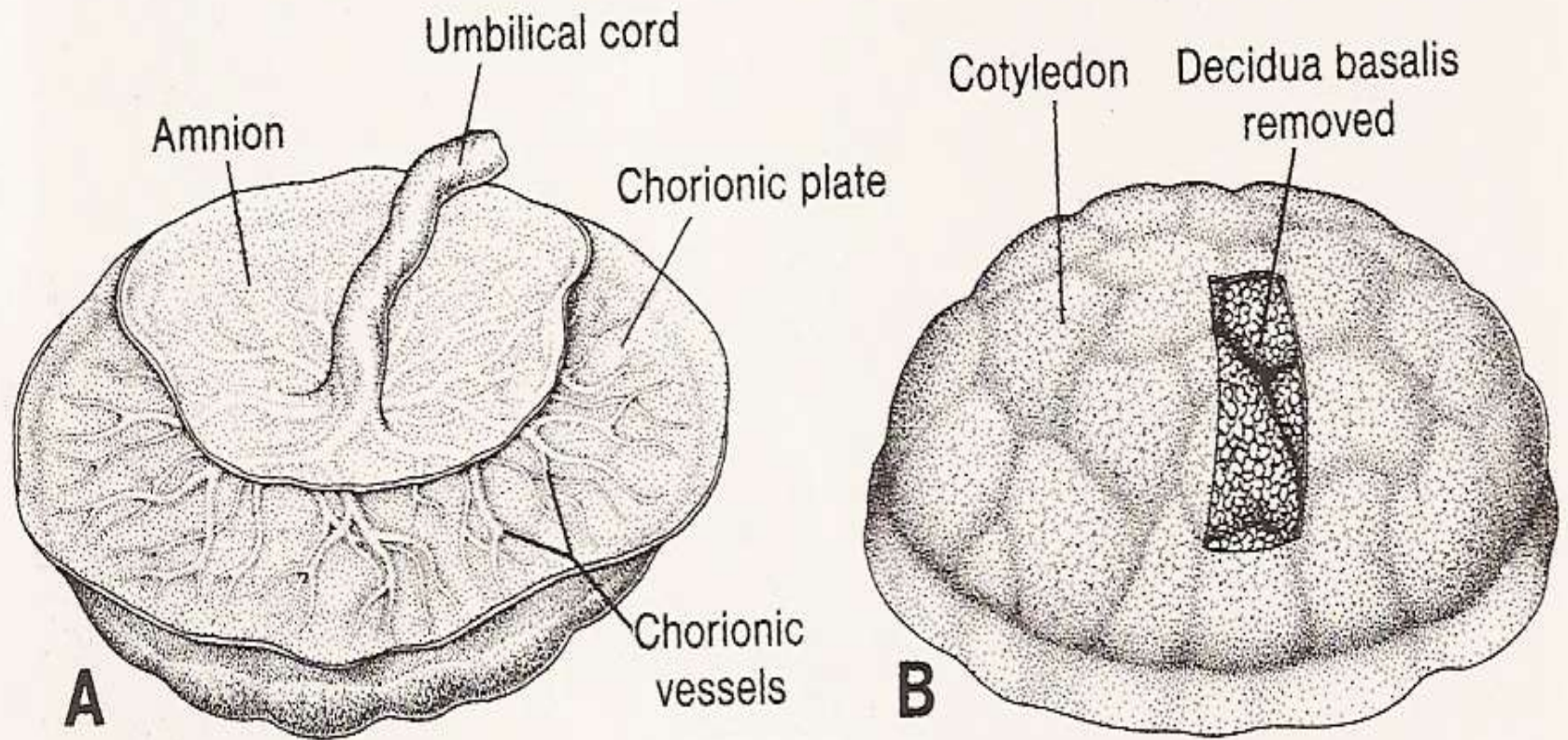


Figure 7.8. Full-term placenta. **A.** As seen from the fetal side. Note that the chorionic plate and umbilical cord are covered by amnion. **B.** As seen from the maternal side. Note the cotyledons. In one area, the decidua has been removed. The maternal side of the placenta is always carefully.

Full-Term Placenta

- At full term, the placenta has a discoid shape, a diameter of 15-25 cm, is approximately 3 cm thick, and weight of about 500-600 gm.
- At birth, it is torn from the uterine wall and, approximately 30 minutes after birth of the child, is expelled from the uterine cavity.

(Fig. 7.8B) (Fig. 7.8A).



THANK YOU



**General Embryology,
Lecture XIII,
Fetal Membranes & Placenta,
Part II**



Circulation of the Placenta

- Cotyledons receive their blood through 80--100 spiral arteries that pierce the decidual plate and enter the intervillous spaces at more or less regular intervals (Fig. 7.7).
- The lumen of the spiral artery is narrow, resulting in an increased blood pressure when entering the intervillous space. 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, 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/minute. This blood moves along the chorionic villi.
- The placental membrane separates maternal & fetal bl. & 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; & *(d)* the syncytium (Fig. 7.2C).
- From the 4th month on, the placental membrane becomes much thinner. since the endothelial lining of the vessels comes in intimate contact with the syncytial membrane, thus greatly increasing the rate of exchange (Fig. 7.2D). Sometimes called the **placental barrier**.



Function of the Placenta

■ EXCHANGE OF GASES

Exchange of gases. such as oxygen, carbon dioxide, and carbon monoxide. Is done by simple diffusion. At term, the fetus extracts 20-30 mL of oxygen per minute from the maternal circulation

■ EXCHANGE OF NUTRIENTS AND ELECTROLYTES

Exchange of nutrients and electrolytes, such as amino acids. free fatty acids, carbohydrates. and vitamins

■ TRANSMISSION OF MATERNAL ANTIBODIES

Maternal antibodies are taken up by the syncytiotrophoblast and subsequently transported to fetal capillaries. Specially IgG

■ HORMONE PRODUCTION

Probably, all hormones are synthesized in the syncytial trophoblast
By the end of the 4th month, the placenta produces progesterone
estrogenic hormones

Syncytiotrophoblast also produces gonadotropins (hCG),
Another hormone produced by the placenta is somatomammotropin (placental lactogen). It is a growth hormonelike substance



CLINICAL CORRELATES

- Rh incompatibility

Erythroblastosis fetalis or hemolytic disease of the newborn (HDN)

- Most maternal hormones do not cross the placenta.

- Some synthetic progestins that cross the placenta at a rapid rate and may cause masculinization in female fetuses.

- Dangerous has been the use of the synthetic estrogen diethylstilbestrol, which easily crosses the placenta. This compound produces carcinoma of the vagina and abnormalities of the testes



- Placental barrier 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.
- Most drugs & drug metabolites traverse the placenta without difficulty & many cause serious damage to the embryo.



Amnion and Umbilical Cord

- The line of reflection between the amnion & embryonic ectoderm (amnioectodermal junction) is oval and is known as the **primitive umbilical ring**.
 - At the 5th week of development, the following structures pass through the ring (Fig. 7.9, A and C):
 - (a) The connecting stalk, containing the allantois & the umbilical vessels consisting of two arteries & one vein;
 - (b) The yolk stalk (vitelline duct) accompanied by the vitelline vessels;
 - (c) the canal connecting the intraembryonic & extraembryonic coelomic cavities (Fig. 7.9C).
- The yolk sac proper occupies a space in the chorionic cavity, i.e. the space bet. the amnion & chorionic plate (Fig. 7.9B).



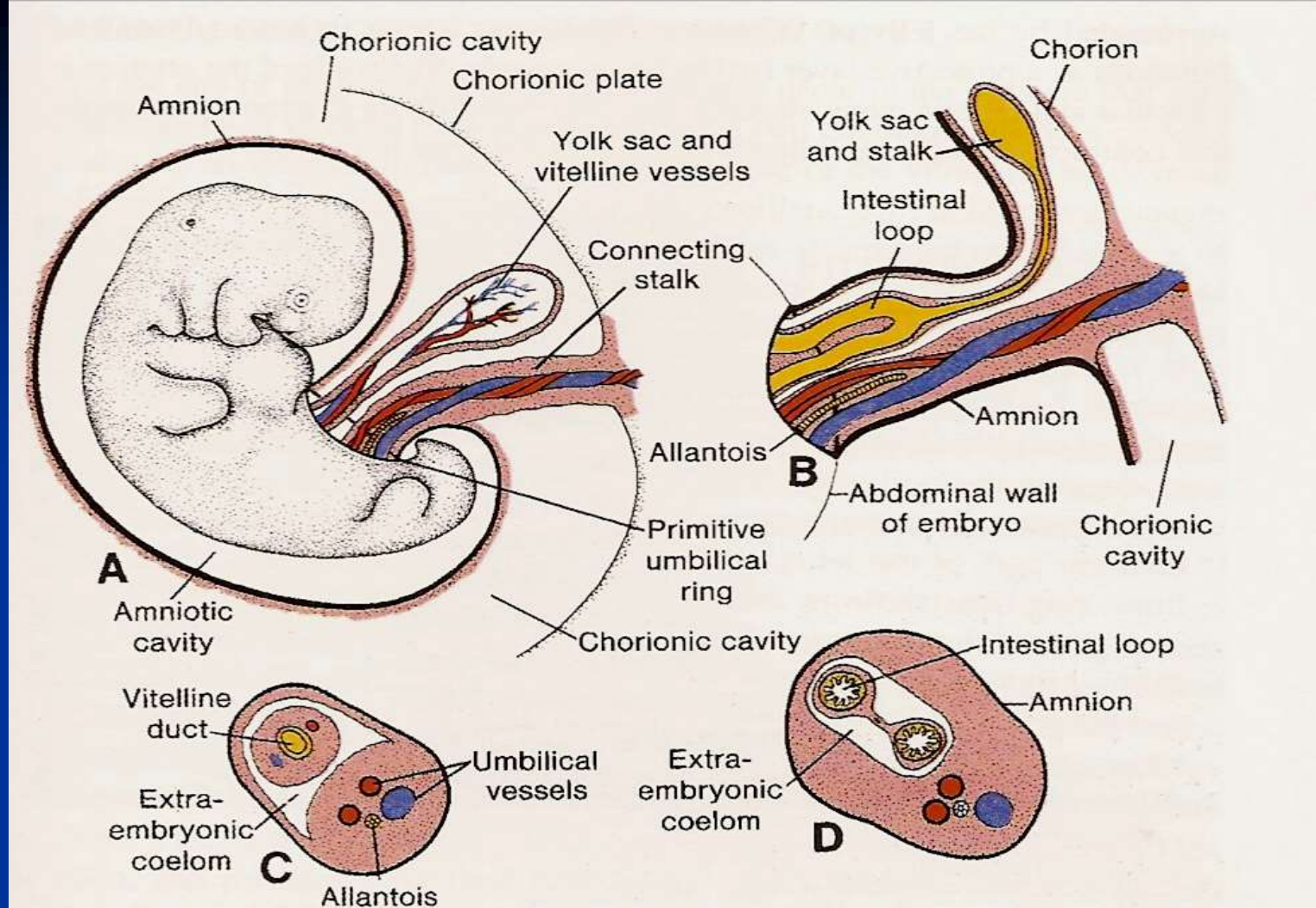


Figure 7.9. **A.** 5-week embryo to show structures passing through the primitive umbilical ring. **B.** primitive umbilical cord of a 10-week embryo. **C.** Transverse section through the structures at the level of the umbilical ring. **D.** Transverse section through the primitive umbilical cord, showing intestinal loops protruding in the cord.

CLINICAL CORRELATES

- Normally, there are two arteries and one vein in the umbilical cord.
- In 1 in 200 newborns, only one artery is present, & these babies have an approximately (20 %) chance of having cardiac and other vascular defects.
- Occasionally, tears in the amnion result in **amniotic bands** that may encircle part of the fetus, particularly the limbs & digits. Amputations, **ring constrictions**, & other abnormalities may result, including craniofacial deformations (Fig.7.10)
- Origin of the bands is probably from infections or toxic insults that involve either the fetus, fetal membranes, or both. Bands then form from the amnion, like scar tissue, constricting fetal structures.



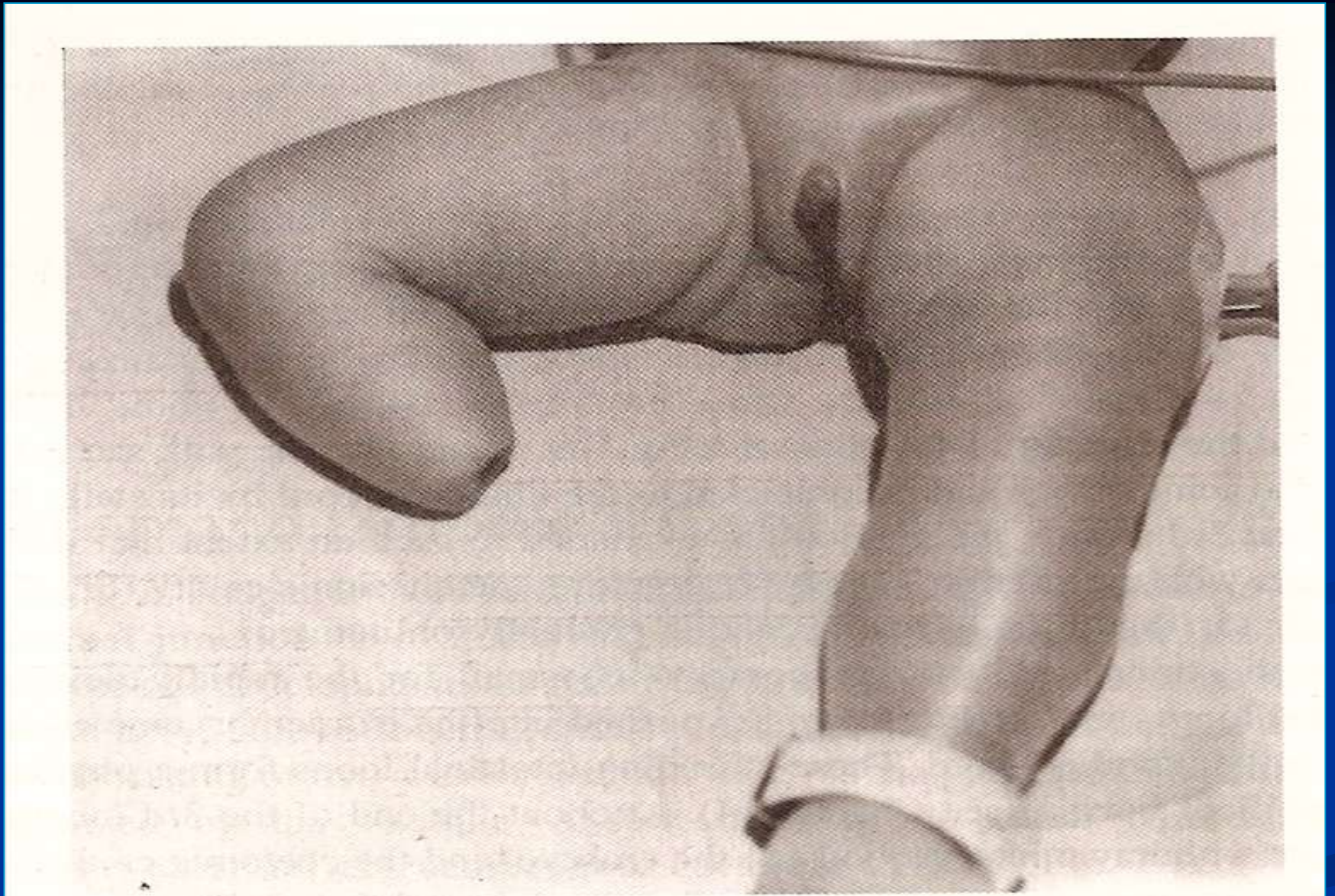


Figure 7.10. Photograph of infant showing limb amputation resulting from otic bands 

Placental changes at the end of pregnancy :

- At the end of pregnancy, a number of changes occur in the placenta. These changes include:
 - (a) Increase in fibrous tissue in the core of the villus,
 - (b) Increase in thickness of basement membranes in fetal capillaries,
 - (c) Obliterative changes in small capillaries of the villi.
 - (d) Deposition of fibrinoid on the surface of the villi in the junctional zone and in the chorionic plate, which frequently causes infarction of an intervillous lake or of an entire cotyledon.
- At birth, the umbilical cord is approximately 2 cm in diameter and 50--60 cm long. It is tortuous, causing false knots.



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. Amount of fluid increases from 30 ml at 10 weeks gestation, to 350 ml at 20 weeks, to 800--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, (c) allows for fetal movements. The volume of amniotic fluid is replaced every 3 hours..
- Fetal urine is added daily to the amniotic fluid in the 5th month, but this urine is mostly water, since the placenta is functioning as an exchange for metabolic wastes.



CLINICAL CORRELATES

- Premature rupture of the amnion occurs in 10% of pregnancies & represents the most common cause of preterm labor.
- Clubfoot & lung hypoplasia may be caused by **oligohydramnios** (amount less than 400 mL) following amnion rupture.
- Causes for rupture are largely unknown, but in some cases, trauma plays a role.
- **Hydramnios or polyhydramnios** is the term used to describe an excess of amniotic fluid (1500-2000 ml),
- Both conditions are associated with an increased incidence of birth defects.
- Primary causes of hydramnios include idiopathic causes (35%),  maternal diabetes(25%), & congenital malformations.

THANK YOU



**General Embryology,
Lecture XIV,
Fetal Membranes & Placenta,
Part III**



Fetal Membranes in Twins

- Arrangement of fetal membranes in twins varies considerably and is dependent on the type of twins as well as on the time of separation of monozygotic twins.



DIZYGOTIC TWINS

- Approximately two-thirds of twins are **dizygotic or fraternal**, and their incidence of 7-11/1000 births increases with increasing maternal age.
- They result from simultaneous shedding of two oocytes and fertilization by two different spermatozoa., the twins have no more resemblance than brothers or sisters. They may or may not be of different sex.
- Both zygotes implant individually in the uterus, and each develops its own placenta, amnion, and chorionic sac (fig.7 .11A).



MONOZYGOTIC TWINS

- The 2nd type of twins develops from a single fertilized ovum and is known as **monozygotic or identical twins**. The rate is 3-4/1000.
- 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.
- Both blastocysts implant separately, and each embryo has its own placenta and chorionic sac (Fig. 7.12A).
- In most cases, splitting of the zygote occurs at the **early blastocyst stage**. The inner cell mass splits into 2 separate groups of cells within the same blastocyst cavity (Fig. 7.12B).
- The 2 embryos have a common placenta, & a common chorionic cavity but have separate amniotic cavities (Fig. 7.12B).



- Rarely, i separation occurs at the **bilaminar germ disc stage** just before i appearance of the primitive_streak (Fig.7.12c).
- This method of splitting results in form. of 2 partners with a single placenta & a common chorionic & amnion sac.



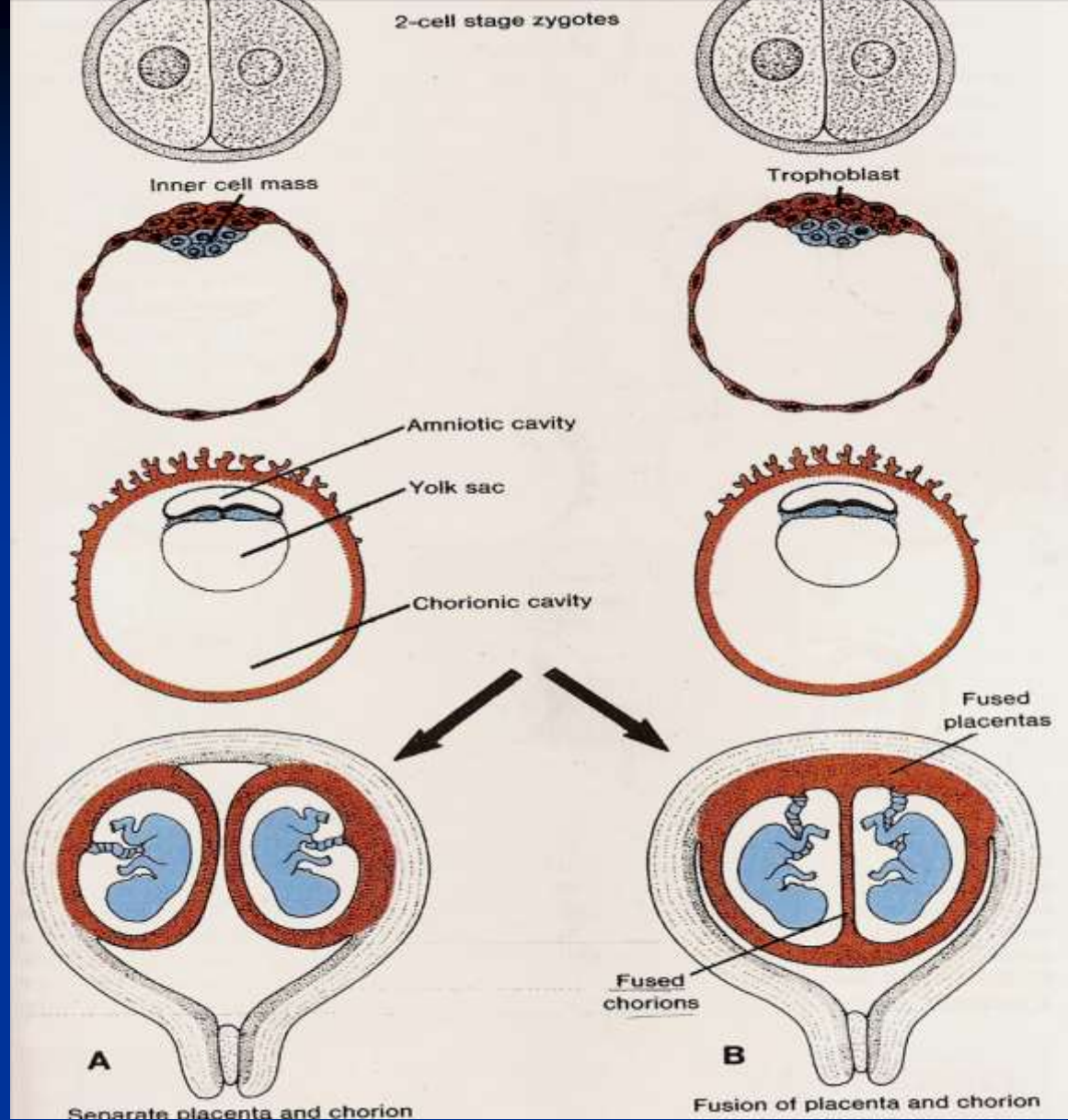


Figure 7.11. development of dizygotic twins. Normally, each embryo has its own amnion, chorion, & placenta **(A)**, but sometimes the placentas are fused **(B)**, Each embryo usually receives an appropriate amount of bl.

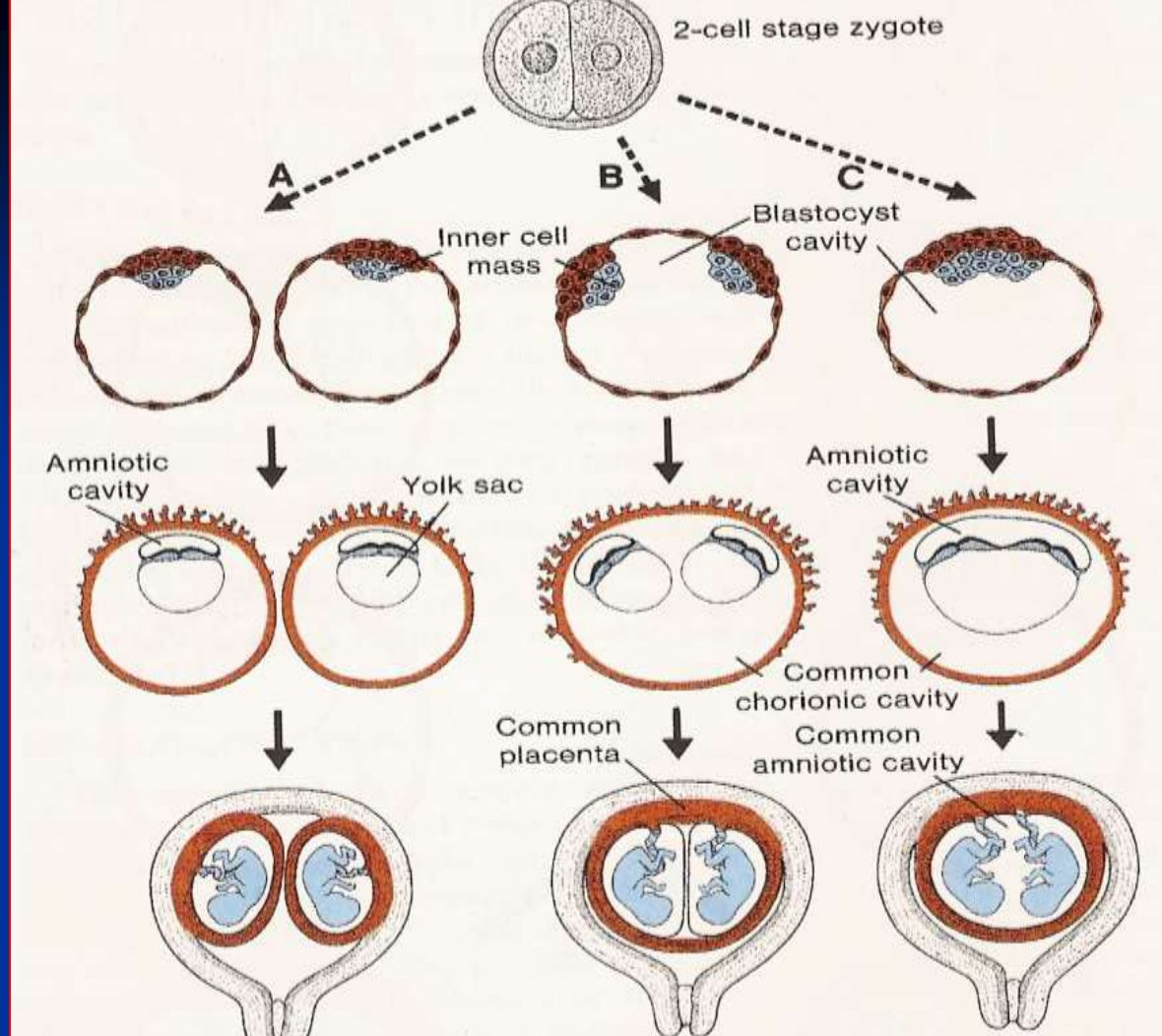


Fig 7.12. Possible relations of fetal membranes in monozygotic twins. **A**, Splitting occurs at i 2-cell stage & each embryo has its own placenta, amniotic & chorionic cavity. **B**, Splitting of i inner cell mass into 2 completely separated groups. The 2 embryos have a common placenta & a common chorionic sac but have separate amniotic cavities. **C**, Splitting of i inner cell mass at a late stage of develop. The embryos have a common placenta ,a common amniotic & common chorionic cavit.

CLINICAL CORRELATE

- Twin pregnancies have a higher incidence of perinatal mortality & morbidity & tendency toward preterm delivery.
- Nearly 12% of premature infants result from twin pregnancies, & twins are usually smaller at birth.
- Low birth weight & prematurity place infants of twin pregnancies at great risk, & about 10-20% of them will die compared with only 2%, of infants from single pregnancies.
- 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 occurs in the 1st trimester or early 2nd trimester & may result from resorption or formation of a fetus **papyraceus** (Fig. 7.13).



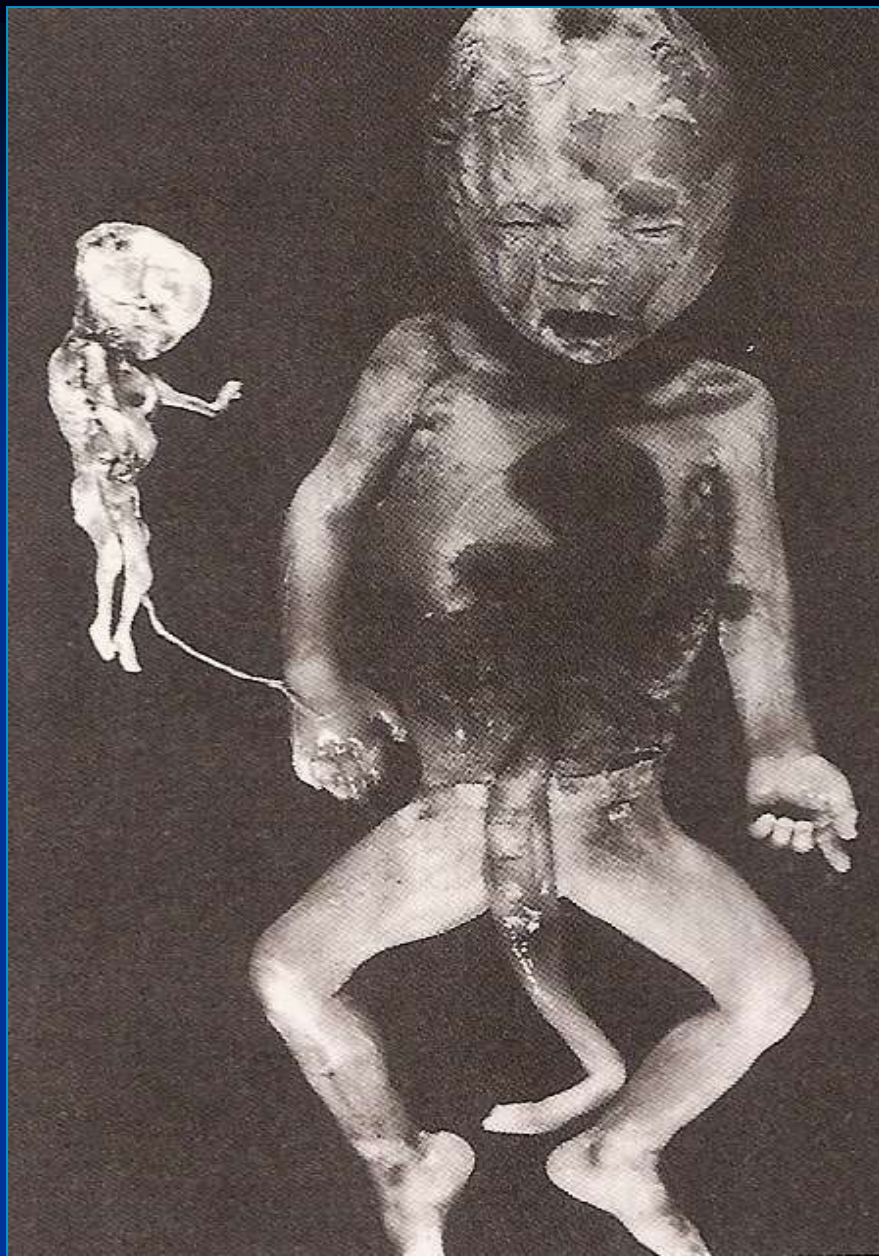


Figure 7.13 fetus papyraceus . One twin is larger , while the other has been compressed and mummified, hence the term papyraceus

- **Twin transfusion syndrome**, increased mortality among twins which occurs in 5-15%, of monochorionic monozygotic pregnancies.
- In this condition, placental vascular anastomoses, which occur in a balanced arrangement are disturbed, one twin receives most of the blood flow (Fig. 7.14). Death of both twins occurring in 60-100% of cases.
- Splitting of the zygote during later stages of development may result in an abnormal or incomplete splitting of the axial area of the germ disc. Such incompletely separated discs lead to formation of conjoined (**Siamese**) **twins**. According to the nature & degree of the union, they are classified as **thoracopagus**, **pygopagus**, & **craniopagus** (Figs.7.15 & 7.16)





**Fig. 7.14; Monozygotic twins with twin transfusion syndrome. Placental vascular anastomosis produced unbalanced blood flow to i
2 fetuses**

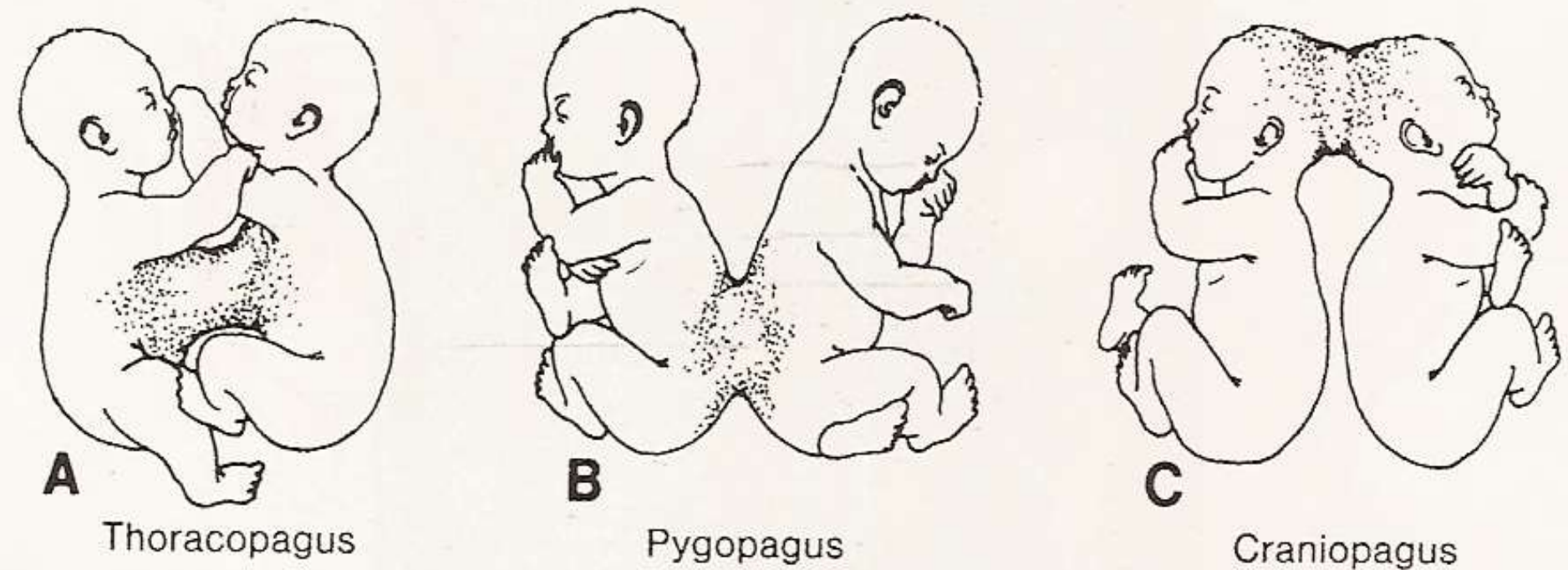


Figure 7.15. Schematic drawings of thoracopagus, pygopaus, and craniopagus twins. Conjoined twins can be separated only if they have no vital parts in common.

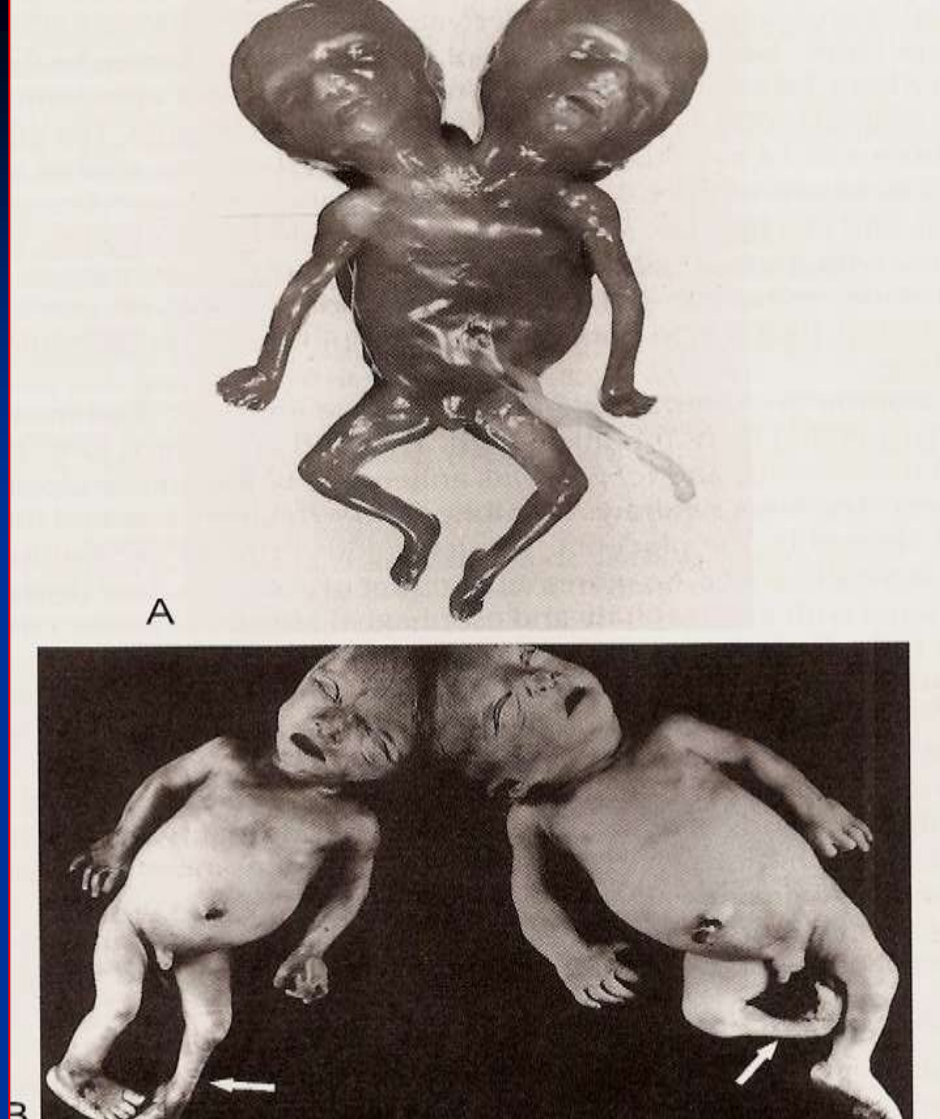


Figure 7.16. Examples of conjoined twins. A. Twins with 2 heads, a broad thorax, two spines, two partially fused hearts, four lungs, & a duplicated gut down to the ileum. B. Twins joined at the head (craniopagus) with multiple deformations of the limbs



THANK YOU

