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الفصل الدراسي الاول

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Lec. 1

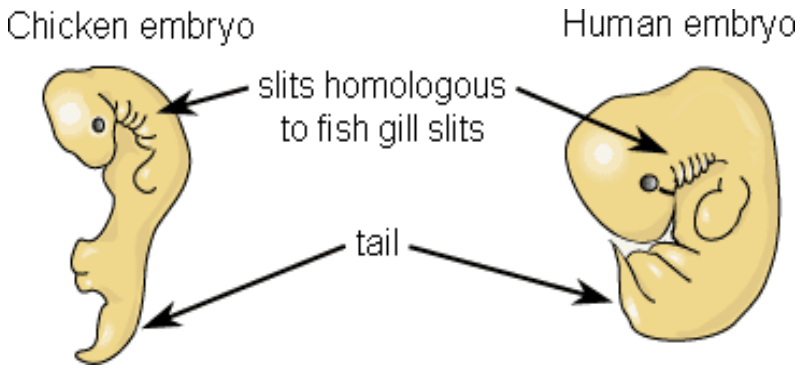
Introduction to embryology

The survival of each species of virus, bacteria, fungi, plants and animals requires its individual members multiply to produce new individual to replace the one killed by natural death in old age or by predators, parasites, environmental pollution or any ecological hazards such hot,loss of water or food, oxygen, light, etc.

The multiplication of new species is achieved by two basic process, called asexual reproduction, and sexual reproduction

- **In the asexual reproduction**, the progeny arises from single existing organism which splits, buds or fragments from the body of the organism, to give rise to two or more offspring's, all of which have hereditary traits identical to those of the parental organisms.
- **In the sexual reproduction**, the progeny arises from the fusion of the two genetically identical gametes (sperms & eggs) in the multicellular animals; each of them is derived from different sex of the organisms with genome different from the parent, the resultant cell called **fertilized egg or zygote** has a genomic different from that of their parents. The process which transform zygote or somebody rudiment of parent somatic cells (i.e; asexual and sexual reproduction respectively) into a multicellular organism constitute two different aspects of **Ontogenetic development** and phylogenetic development. The ontogenetic development differ from the phylogenetic development, In biology, phylogenetic is the study of the evolutionary history and relationships among individuals or groups of organisms that are derived from a common ancestor, while the ontogenetic development of a species include developmental history of an organism means, embryogenesis, development of a new individual from the fertilized egg and then to blastogenesis or development of a new organism from a sexual reproduction

body(bud, body fragments,etc.) . By studying ontogeny (the development of embryos), scientists can learn about the evolutionary history of organisms. Ancestral characters are often, but not always, preserved in an organism's development. For example, both chick and human embryos go through a stage where they have slits and arches in their necks that are identical to the gill slits and gill arches of fish. This observation supports the idea that chicks and humans share a common ancestor with fish. Thus, developmental characters, along with other lines of evidence, can be used for constructing phylogenies.



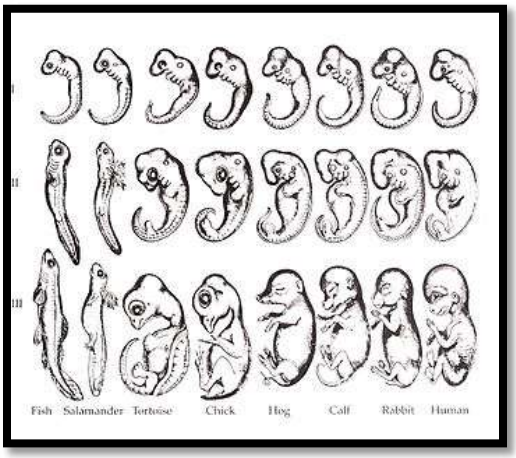
Historical review of the embryology

pre-20th century, Embryology was not easily separated from Medicine, Anatomy and Physiology and other biological sciences. Embryology has a long history. Aristotle proposed the currently accepted theory of epigenesis, that organisms develop from seed or egg in a sequence of steps. The alternative theory, preformationism, that organisms develop from pre-existing miniature versions of themselves,
as the 18th century, the prevailing notion in western human embryology was preformation : the idea that semen contains an embryo – a preformed, miniature infant, or *homunculus* – that simply becomes larger during development, As microscopy improved during the 19th century, biologists could see that embryos took shape in a

series of progressive steps, and epigenesis displaced preformation as the favored explanation among embryologists.

Biogenetic law, also called **Recapitulation Theory**, postulation, by Ernst Haeckel in 1866, that ontogeny recapitulates phylogeny—*i.e.*, the development of the animal embryo and young traces the evolutionary development of the species. The theory was influential and much-popularized earlier but has been of little significance in elucidating either evolution or embryonic growth.

biogenetic law, in biology, a law stating that the earlier stages of embryos of species advanced in the evolutionary process, such as humans, resemble the embryos of ancestral species, such as fish. The law refers only to embryonic development and not to adult stages; as development proceeds, the embryos of different species become more and more dissimilar. An early form of the law was devised by the 19th-century Estonian zoologist von Baer, **who observed that embryos resemble the embryos, but not the adults, of other species**. A later, but incorrect, theory of the 19th-century German zoologist Ernst Heinrich Haeckel states that the embryonic development (ontogeny) of an animal recapitulates the evolutionary development of the animal's ancestors (phylogeny).



The development of an organism involves all changes it undergoes from its beginning until death, most metazoan animals include two distinct periods in their life history:

1- Embryonic period or called Pre-natal period

This represents the period in the egg or inside the body of the mother.

2-Postembryonic period or called Post-natal period

extend from hatching or birth up to the natural death of the organism due to aging. Thus all the developmental events and changes which occur from the time of fertilization of the egg through formation of the embryo or foetus up to hatching or birth belong to the pre-natal or embryonic period of the life history of the animal are included in embryogenesis, so the study of embryogenesis is called embryology. So we can define the embryology is: all the developmental events and changes which occur from the time of fertilization of the egg through formation of the embryo or fetus until the belong to the pre-natal or embryonic period

Embryological development does not end at birth but continuous during the post-natal period also. the newly born or hatched young animal is in size and developed both structurally and physiologically. During later days, weeks or years many changes occur lead the individual capable of reproduction this period called (progressive nature), then after the animal reach to maximum of development this time called (degenerative in nature) leads to death.

In biology the field which deals with the study of those embryogenetic and blastogenetic process by which organism undergoes progressive changes in structure and function during its life history is called developmental biology.

In fact, developmental biology, unlike embryology because does not restricted to the study of the embryogenesis of the organism but deals with all aspects (genetic, biochemical, physiological and morphological).

Therefore the different in the concept between the embryogenesis and the development is that the development is a wider term than the embryogenesis,

Review of chordate embryogenesis stages

The embryogenesis of an animal species includes the following stages or phases:

1) Gametogenesis

This stage is started from the time of development and specialization of haploid male & female sex cells, from diploid somatic cells of each parent during a process called **Gametogenesis**. Gametogenesis includes **spermatogenesis** in male tests and **oogenesis** in female ovaries.

2) Fertilization

This second phase of embryogenesis is fertilization, which is the union of spermatozoon (sperm) and the ovum and then activation of egg to begin the embryogenesis of a new individual.

3) Cleavage

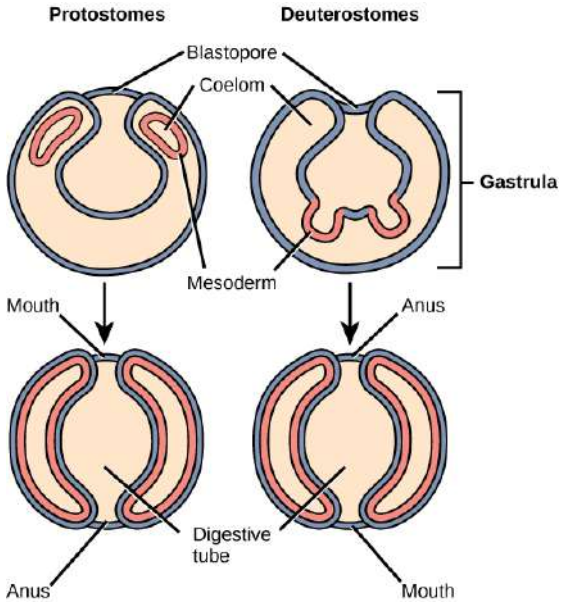
During third phase of embryogenesis, the cleavage, **no growth** of egg cytoplasm(ooplasm) occur, but rate of synthesis of some macromolecule such as DNA, protein, glycogen, fats and yolk, so the fertilized egg undergoes repeated mitotic cell divisions and produces a compact mass of cells (blastomeres), called **morula**. The morula soon get arranged in hollow spherical mass, called **blastula**, with a layer of **blastomeres** called blastoderm surrounding a fluid-filled central space or cavity, and

called the **blastocoel**. The process of conversion of a fertilized egg into multicellular blastula called **blastulation**.

4) Gastrulation

In this phase, there are an extensive movements and rearrangements of cells of blastula, called (morphogenetic movements) transforming the one-layered thick embryo (blastula) into a two or three-layered thick embryo, called Gastrula. From the gastrula the **three primary germ layers** are formed, the outer layer called ectoderm, the middle layer called mesoderm, and the inner layer called endoderm; from these three germ layers various organs of animal body are formed. so they called primary germ layers

In the middle center of the gastrula found a central cavity called the **archenteron (gastrocoel)**, which is lined by endoderm and communicates to the outer environment by an opening called **blastopore**. During later stages of the development, the archenteron becomes the cavity of the alimentary canal, while the blastopore becomes **mouth opening in all invertebrates**, **except echinoderms and hemichordates**, these animals in embryology called **protostomia**. But in the other groups of animals includes echinoderms, hemichordates and all chordates the blastopore becomes the anal opening (anus)**,** therefore called **duterostomia**.(notice the figure below).



5) Organogenesis

During the fifth phase of embryogenesis, the organogenesis or named the formation of the organs. The continuous growing of the masses of the three germ layers will split up into smaller groups of cells, called primary organ rudiments, each of which is destined to produce a certain organ or part of the adult body. The primary organ rudiments further subdivided into secondary organ rudiments which are the rudiments of the simple organs, with the appearance of primary and secondary rudiments the embryo begins to show some similarity to the adult animal or larva if the development includes larval stage

6) Growth

The simplest definition of the growth in embryology is the **increase in the body mass of the animal**. This increase in the body mass is achieved by synthesis of new nuclear material and cytoplasm and cell multiplication, thus during growth period the organ rudiments of the embryo begin to grow and greatly increase their volume.

7) Differentiation

The differentiation refers to the events by which parts become different from one another and also different from their origin. During development differentiation includes following kinds:

a- Morphological differentiation

When the cells of the organ rudiments multiply, the individual cells and group of cells become structurally different from another (cytodifferentiation) e.g; the nerve cells and epidermal cells originate from a common starting point (ectoderm) later they acquire different feature of size, shape.

b- Behavioral (physiological) differentiation

All cells have common basic activity such as metabolism, synthesis of DNA,RNA, proteins, lipids, carbohydrates, etc. but after later development these cells acquire special function, nerve cells come to transport electric impulses, muscle cells to contract, gland cells to secret and so on.

c- Chemical differentiation

The cytodifferentiation and physiological differentiation are the products of chemical differentiation which in turn depends on enzymes which direct the synthesis of the organic compounds that give the specialty of the cells, this production of chemicals is under genetic control of the cell.

Morphogenesis

The morphogenesis refers to that tissues and organs are take a special shape and size that make the special form of the organism body. The **form** of an organism depends on two main factors:-

- the form of the cells (differentiation)
- the position of the different cells

the process of the morphogenesis depend on the communication between the growing cells physically and chemically .the embryonic cells capable to motile so that the same type of cells become reassociated together. morphogenes are chemicals

produced during development to determine the morphogenesis and differentiation of cells, tissues or organs.

The morphogenes are two types :

1- Intra-cellular morphogenes

Found within a oocyte determinate the fate of the early embryo found in insects, nematodes and tunicates

2- Extra-cellular morphogenes

Found in particular regions of late embryos, they acquire activity when the embryo has become multicellular (i.e; after 2-cell stage of egg)these are analogous chemicals to hormones, During development, retinoic acid, a metabolite of vitamin A, is used to stimulate the growth of the posterior end of the organism.[12] Retinoic acid binds to retinoic acid receptors that acts as transcription factors to regulate the expression of Hox genes (group of genes that regulate the body plane of the embryo along head—tail axis) Exposure of embryos to exogenous retinoids especially in the first trimester results in birth defects.

8) Metamorphosis

The growth, differentiation and morphogenesis transform the embryo into a young animal. After hatching from the egg morphological features are similar to the adult animal except in being of small and sexually immature, so this will called **juvenile stage** or not similar with adult animal because may found different types of organs which serve the young animal during certain period and disappear later, this is called **larval stage**. The young larva later passes through an important development process called the metamorphosis **means:**

morphological and physiological changes of the larva during normal development causes transforms it into an animal similar to the adult, the metamorphosis is regulated by hormones. Most invertebrates pass through metamorphosis during their life cycle, but some vertebrates, such as frogs, also go through this process before reaching adulthood

Branches of Embryology

1- **Descriptive embryology**

For centuries observation and descriptive of different embryonic stages of the ontogenetic development of a species depend on notices.

2- **Comparative embryology**

Comparative study is made between the embryology of most animals types.

3- **Experimental embryology**

This is youngest and most modern field in embryology, study the fertilization, cleavage, and gastrulation in the vivo.

4- **Chemical embryology**

Study the embryology phases in molecular terms.

Lec. 2

Cell cycle and Chromosomes

All cells are produced by divisions of pre-existing cells, growth and development of any organism depend in large part on multiplication, enlargement and differentiation of its cells beginning with the zygote.

Cell cycle

The cell cycle is the life history of a cell ,each cell capable of division passes through a cycle called interphase cycle or cell cycle which can be defined as a sequence of events happening from the one nuclear division to the beginning of the next.

The total time of the cell cycle in the animal cells varies with the species, maturation , tissue and many physical conditions like temperature, and the type of the cell. The cell cycle divided into 4 stages, G1,S and G2 phases forming the interphase and M phase forming the mitotic phase :-

1- G1 phase

Is the first gap or growth stage of the interphase begins immediately following the cell division, many events happen in this phase ;

* the nucleus and cytoplasm are enlarging, chromatin is fully extended not recognized as chromosomes under light microscope

* this time is considered the time of the active synthesis of RNA and protein and reactive all the metabolic pathways that slowed during the cell division.

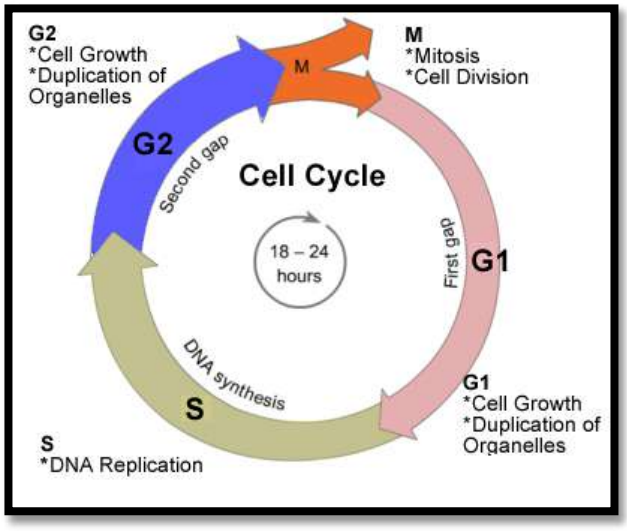
G1 is very variable in its duration; it may occupy 30-50% of the total time of the cell cycle or may lacking in rapidly dividing cells (e.g. those of early mammalian cells) because the rapid cell division just after fertilization, while the differentiated somatic cells that no longer divide (e.g. neurons) are arrested in the G1 stage which often referred to as G0 phase, type of these cells called postmitotic cells during

2- S phase

Called the synthetic phase, the events that happen; replication of DNA and synthesis of histones occur. DNA molecule of each chromosome becomes doubled in its amount, so that each chromosome will carry double set of the genes or two DNA molecules , at the end of this phase each chromosome is composed of two sister chromatids sharing one centromere, thus te cell retains the original diploid (2n) chromosome number but now has duplicate set of genes. Cells in early eukaryotic embryonic cells are completely locate in S phase because the short generation time have, and these cells have no G1 and G2 like the prokaryotic cells, this means that total genome DNA is replicated 100 times faster in early embryos than in late embryos or in adults tissues.

3- G2 phase

This is the second gap, or called the growth phase two, represent the less time of the cell cycle, new DNA is rapidly complexes with chromosomal proteins and synthesis of RNA and proteins continues, it may occupy 10-20% time of the cell cycle. At the end of this stage, the cell now is ready to inter the mitotic division or M phase.



The cell cycle in mature cell

Regulation of cell cycle

1- Regulation of the Cell Cycle by External Events

External factors can influence the cell cycle by inhibiting or initiating cell division. Unlike the life of organisms, which is a straight progression from birth to death, the life of a cell takes place in a cyclical pattern. Each cell is produced as part of its parent cell. When a daughter cell divides, it turns into two new cells, which would lead to the assumption that each cell is capable of being immortal as long as its descendants can continue to divide. However, all cells in the body only live as long as the organism lives. Some cells do live longer than others, but eventually all cells die when their vital functions cease. Most cells in the body exist in the state of interphase, the non-dividing stage of the cell life cycle. When this stage ends, cells move into the dividing part of their lives called mitosis.

Both the initiation and inhibition of cell division are triggered by events external to the cell when it is about to begin the replication process. An event may be as simple as the death of a nearby cell or as sweeping as the release of growth-promoting hormones, such as human growth hormone (HGH). A lack of HGH can inhibit cell division, resulting in dwarfism, whereas too much HGH can result in gigantism. Crowding of cells can also inhibit cell division. Another factor that can initiate cell division is the size of the cell; as a cell grows, it becomes inefficient due to its decreasing surface-to-volume ratio. The solution to this problem is to divide.

We can summarize the external events that can affect cell cycle regulation:

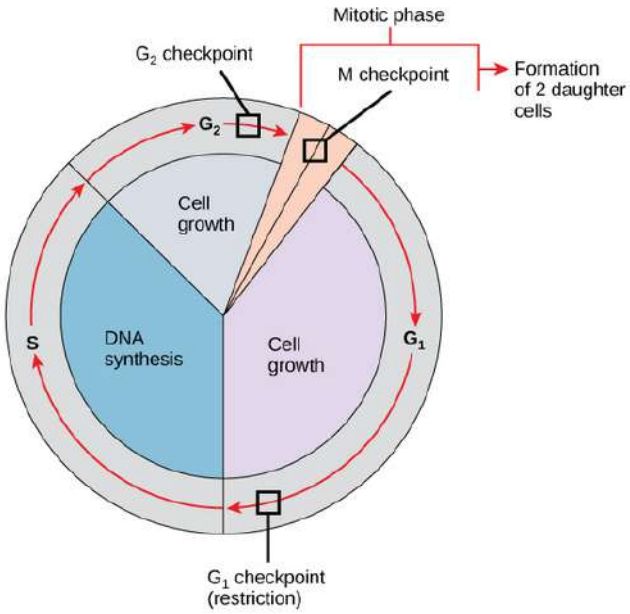
- The death of nearby cells and the presence or absence of certain hormones can impact the cell cycle.
- The release of growth-promoting hormones, such as HGH, can initiate cell division, and a lack of these hormones can inhibit cell division.

- Cell growth initiates cell division because cells must divide as the surface-to-volume ratio decreases; cell crowding inhibits cell division.
- Key conditions must be met before the cell can move into interphase.

2- Regulation of the Cell Cycle at Internal Checkpoints

The cell cycle is controlled by three internal checkpoints that evaluate the condition of the genetic information.

- Damage to DNA and other external factors are evaluated at the G1 checkpoint; called restriction point if conditions are inadequate, the cell will not be allowed to continue to the S phase of interphase.
- The G2 checkpoint ensures all of the chromosomes have been replicated and that the replicated DNA without mistakes or damage before cell enters mitosis.
- The M checkpoint occurs near the end of the metaphase stage of mitosis The M checkpoint is also known as the spindle checkpoint because it determines whether all the sister chromatids are correctly attached to the spindle microtubules before the cell enters the irreversible anaphase stage.



Internal Checkpoints during the Cell Cycle

Role of chromosomes in cell division

The prokaryotic genome typically exists in the form of a circular chromosome located in the cytoplasm. In eukaryotes, however, genetic material is housed in the nucleus and tightly packaged into linear chromosomes. Chromosomes are made up of a DNA-protein complex called chromatin that is organized into subunits called nucleosomes. The way in which eukaryotes compact and arrange their chromatin not only allows a large amount of DNA to fit in a small space, but it also helps regulate gene expression. Cells package their DNA not only to protect it, but also to regulate which genes are accessed and when. Cellular genes are therefore similar to valuable files stored in a file cabinet — but in this case, the cabinet's drawers are constantly opening and closing; various files are continually being located, pulled, and copied; and the original files are always returned to the correct location. Of course, just as file drawers help conserve space in an office, DNA packaging helps conserve space in cells. Packaging is the reason why the approximately two meters of human DNA can fit into a cell that is only a few micrometers wide. But how, exactly, is DNA compacted to fit within eukaryotic and prokaryotic cells? And what mechanisms do cells use to access this highly compacted genetic material? Cellular DNA is never bare and unaccompanied by other proteins. Rather, it always forms a complex with various protein partners that help package it into such a tiny space. This DNA-protein complex is called **chromatin,** where in the mass of protein and nucleic acid is nearly equal. Within cells, chromatin usually folds into characteristic formations called **chromosomes**. Each chromosome contains a single double-stranded piece of DNA along with the aforementioned packaging proteins. Eukaryotes typically possess multiple pairs of linear chromosomes, all of which are contained in the cellular nucleus, and these chromosomes have characteristic and changeable forms. During cell division, for example, they become more tightly packed, and their condensed form can be visualized with a light microscope. This condensed form is approximately 10,000 times shorter than the linear DNA strand would be if it was

devoid of proteins and pulled taut. However, when eukaryotic cells are not dividing — a stage called **interphase** — the chromatin within their chromosomes is less tightly packed. This looser configuration is important because it permits transcription to take place.

In contrast to eukaryotes, the DNA in prokaryotic cells is generally present in a single circular chromosome that is located in the cytoplasm. (Recall that prokaryotic cells do not possess a nucleus.) Prokaryotic chromosomes are less condensed than their eukaryotic counterparts and don't have easily identified features when viewed under a light microscope.

Chromosomes are the thread-like structure found in the nuclei of both animal and plant cells. They are made of protein and one molecule of deoxyribonucleic acid (DNA). In most organisms, one chromosome is inherited from the mother and the other is inherited from the father; to ensure that offspring carry traits from both parents. It's crucial that certain cells, like reproductive cells, have the correct number of chromosomes in order to function properly. Organisms grow by undergoing cell division to produce new cells and replace older The fundamental importance of chromosomes is that they contain DNA, It is important that chromosomes replicate properly so that each resulting cell has the correct amount of DNA after division, All human cells except for egg cells and sperm cells have 46 chromosomes, the *diploid* human number. Gametes (sex cells) have 23 chromosomes, the *haploid* human number; everyone is the product of the fusion of an egg cell and a sperm cell, and when these combine, the result is the normal amount of chromosomes, 46 paternal and maternal chromosomes are known as *homologous chromosomes*

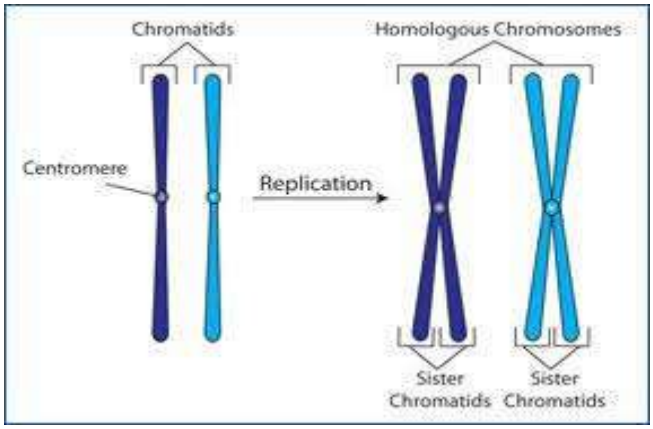
Types of chromosomes

The term chromosome comes from the Greek words for color (chroma) and body (soma). Scientists gave this name to chromosomes because they are cell structures,

or bodies, that are strongly stained by some colorful dyes used in research. Chromosomes are thread-like structures located inside the nucleus of animal and plant cells. Each chromosome is made of protein and a single molecule of deoxyribonucleic acid (DNA). Passed from parents to offspring, DNA contains the specific instructions that make each type of living creature unique.

Structure of chromosome

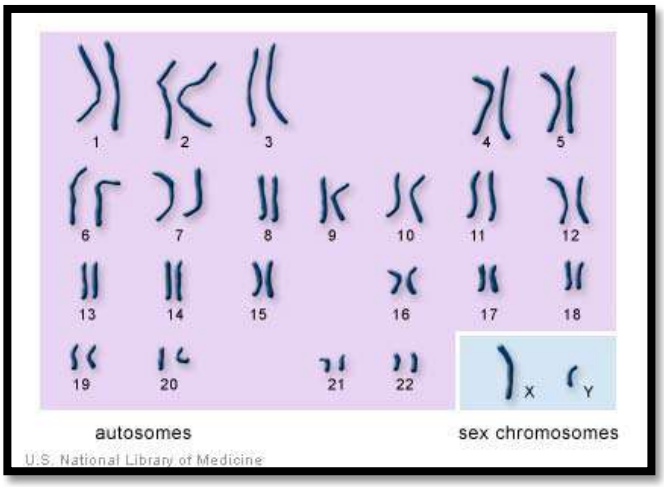
- In eukaryotic cells, chromosomes are composed of single molecule of DNA with many copies of five types of histones.
- Histones are proteins molecules and are rich in lysine and arginine residues, they are positively charged.
- During most of the cell's life cycle, chromosomes are elongated and cannot be observed under the microscope.
- During the S phase of the mitotic cell cycle the chromosomes are duplicated.
- At the beginning of mitosis the chromosomes are duplicated and they begin to condense into short structures which can be stained and observed easily under the light microscope.
- The attached, duplicated chromosomes are commonly called sister chromatids.
- The duplicated chromosomes are held together at the region of centromers.



Like all other eukaryotes, humans contain a fixed number of chromosomes within each of the nuclei in all their cells. There are essentially two types of chromosomes as characterized by karyotyping at the metaphase of cell division. These include:

Autosomes - There are 22 pairs of autosomes in humans.

Gonosomes or sex chromosomes - Humans contain two types of sex chromosomes including X and Y. While males have an X and a Y chromosome, females possess two X chromosomes.



Karyotype of the human genome

Each human cell thus contains 46 chromosomes in 23 pairs. The gametes or ovum produced by the female ovaries and the sperm produced by the male testicles, however, contain only 23 chromosomes. This ensures that when the egg and the sperm get fertilized to form a baby, it contains 23 pairs and restores the total chromosomal count to 46.

Males typically have two different kinds of **sex chromosomes** (XY), and are called the heterogametic **sex**. In humans, the presence of the Y **chromosome** is responsible for triggering male development; in the absence of the Y **chromosome**, the **fetus** will undergo female development. A human fetus does not develop its external sexual organs until seven weeks after fertilization. The fetus appears to be sexually indifferent, looking neither like a male or a female. Over the next five weeks, the fetus begins producing hormones that cause its **sex** organs to grow into either male or female organs so, Men

determine the sex of a baby depending on **whether** their sperm is carrying an X or Y chromosome. An X chromosome combines with the mother's X chromosome to make a baby **girl** (XX) and a Y chromosome will combine with the mother's to make a **boy** (XY).

Lec. 3

Cell Division

Division of vertebrates takes two forms, nuclear division (karyokinesis) and cytoplasmic division (cytokinesis).

The nuclear division in turn consists of two types: **mitosis** & **meiosis**, mitosis is associated with nuclear division of the somatic cells, while the meiosis occurs in the gametes. the random rearrangement of genetic material is associated with the production of offspring and therefore is called sexual reproduction, **unlike the asexual reproduction that is based exclusively on mitotic division, sexual reproduction involves three main characteristic events:**

1-fusion of two genetically different cells (gametes) contain half content of genetic material during fertilization.

2- meiosis allow to rearrangement of genetic material

Mitosis

Mitosis (*mitos*=fiber) is the standard form of cell division in somatic cells, begins at the end point of the interphase, it is important for growth, replacement of cells lost during normal development or under certain cases like wounds healing. The capacity of cells to inter mitosis is variables depends mainly on the function of this cell.

The mitosis is rapid during the early development but it slows down with age. In the embryo cells the mitosis is very rapid to allow the growth but later the DNA replication slows down to allow the cells to become differentiate. some cells lose the ability to divide after differentiate because stop the genes related to mitosis shut off as in the nerve cells and skeletal muscles, while some cells are functionally differentiated but never lose mitotic potential, like liver cells can resume the mitosis when they are isolated in nutrient culture medium or exposed to strong stimuli as wounds or some

cuts in the organ, also there are some cells like the bone marrow cells and epithelium cells in skin or in the digestive system remains mitotically active all life span of the organism.

There are 4 steps of mitosis:-

1- Prophase (*pro*= before)

- Appearance of chromosomes like the thin thread-like
- Cells become spherical
- Regress the nucleolus
- Appear the spindle fibers (mitotic apparatus)
- Regress the nuclear membrane

The chromosomes composed of 2 coiled filaments called the chromatids result from the replication of the DNA during the S phase in the cell cycle, bind together by the centromere (each chromosome have 4 thread-chromatids with one centromere) therefore they are called the sister chromatids, and the chromosomes called the daughter chromosomes, these chromatids become shorter and thicker. The cells have 2pairs of centrioles (duplicated in the interphase) migrate to the opposite site of the cell.

2- **Metaphase** (*meta*= between)

- The centromers occupy the middle plane of the cytoplasm (metaphase plate)
- the sister chromatids are still held together by connecting chromatin fibers at the centromere

3- **Anaphase** (*ana*= back)

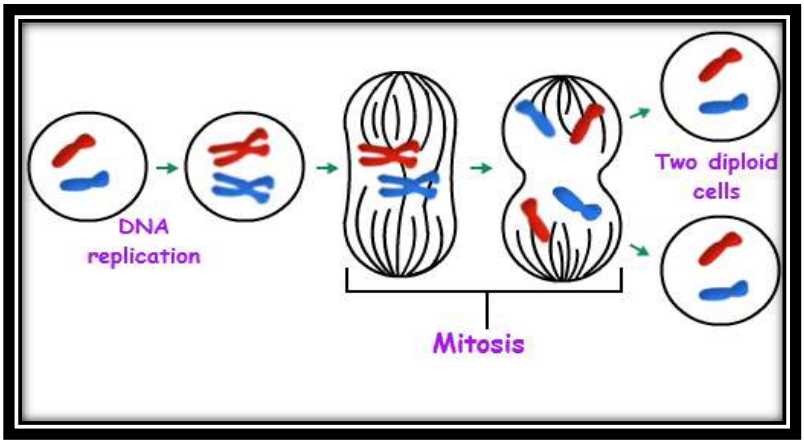
- The chromatids separate and migrate towards poles
- The centromere divide

4- **Telophase** (*telo*=end)

- The end of the daughter chromosomes migration marks the beginning of the Telophase and the Telophase is terminated after reorganization of the two new nuclei and their entry into G1
- The events here are reverse to the prophase
- New nuclear membrane are formed
- Reform the nucleoli
- Long, thick and slender chromosomes

Cytokinesis (cytoplasmic division)

- A furrow will appear in the surface of the cell
- Slowly cutting the cell into 2 daughter cells



Meiosis

Meiosis (*meioum*=to diminish) is a universal process restricted in sexual reproduction of animals, the numbers of the chromosomes is reduced by half, and one cell will give 4 haploid cells, so the meiosis consists of two divisions:

- Reduction division
- Equational division

The meiosis includes 3 minor processes:-

1- Reduction the number of chromosomes
2- Random arrangement of the homologous chromosomes
3- Crossing over or called recombination of some genes

Although the timing of meiosis is very different between male and female, the basic chromosomal events are the same in the two sexes. Therefore we can put a simple definition of it.

Meiosis: - is a specialized of cell division that occurs only in the germ cells (oogonia & spermatozoa) in which the chromosome number is reduced from diploid (2n) to haploid (n)

Mechanism of the meiosis

A meiocyte is any diploid cell that is undergoes meiosis. In animals the meiocyte such as spermatogonia in males and oogonia in females give rise to gametes, these cells undergo several mitosis to give another type of cells, primary spermatocytes and primary oocytes respectively, but then will shift from mitosis to meiosis during G2 phase

The meiocyte before inter the meiosis must have 4 times (4n) content of the amount of DNA thus the primary spermatocytes and primary oocytes are tetraploid (4n) amount of the DNA, after the meiosis1the amount of the DNA become diploid (2n), while after the meiosis2 only the haploid (n) amount of DNA is present. Thus the meiosis like the mitosis when the cell duplicates the amount of DNA during prophase, but contrast to the mitosis, this duplication is followed by two divisions.

Stages of meiosis

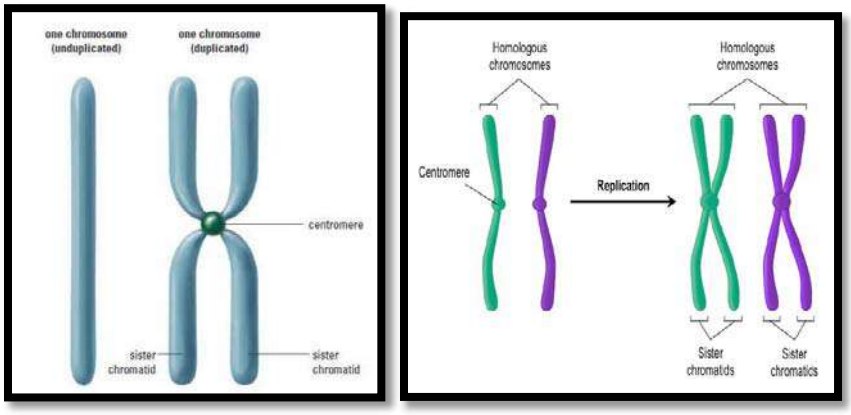
Meiosis requires two cell divisions:

1- **Meiosis I (reduction division)**
2- **Meiosis II (equatorial division)**

Meiosis I (reduction division)

At the following some important events that occur during this stage:-

- During early development the germ cell is a diploid chromosomes (46) with two copy of DNA (**diploid ,2n**)
- The DNA content is duplicated (2n ➔ 4n) while the chromosomes number (46) remain unchanged, so the cell is called **diploid with 4n**, once the DNA replicates, each chromosome consists of two parallel strands of chromatids joined together at a structure called **centromere**. Each chromatid contains a single DNA molecule (which itself double strand).



Replication of chromosome

The meiosis I consists of five phases like the mitosis.

A) Prophase I

This phase is longest phase of all meiosis, in human female it persists in each primary oocyte from a fetal age of 12-16 weeks until reach ovulation (12-16 years) if it reaches. The prophase I divided into five sub-stages:

(**leptotene, zygote, pachytene, Diakinesis ,and diplotene**)

1- Leptotene (*leptos*=thin)

- The nucleus enlarges
- The chromatin material condense
- The centrioles duplicate

2- Zygotene (*zygon*= joining)

Pair each of the homologous chromosomes nears each other and begin to pair (one comes from mother and the other from the father), this pair is called **the synapse**, this pairing or synapsis occurs between two homologous chromosomes the paired homologous chromosomes are called **bivalent** or **dyads**. This process stabilize the pairing of two homologous chromosomes and facilitate recombination by crossing over.

3- Pachytene (*pachus*= thick)

After the synapsis is complete each homologous chromosome of each bivalent or dyad splits longitudinally into two chromatids attached to the centromere, each bivalent now has four strands (4 chromatids) therefore called **tetrad**, and the two chromatids of each two homologous chromosomes is called **sister chromatids**.

During this phase two of the non-sister chromatids (one from paternal and other maternal) of the two homologous chromosomes exchange some genes or portions of chromosomes and fusion of these segments this cytogenetic activity called **crossing over or genetic recombination,** this process involves a varieties of molecules and enzymes such as endonuclease , R-protein and ß-DNA polymerase . This result in a genetic diversity of the future gametes and prevents the children from being clones of their parents. this phase may last for days,weeks or years whereas leptotene and Zygotene may last only few hours.

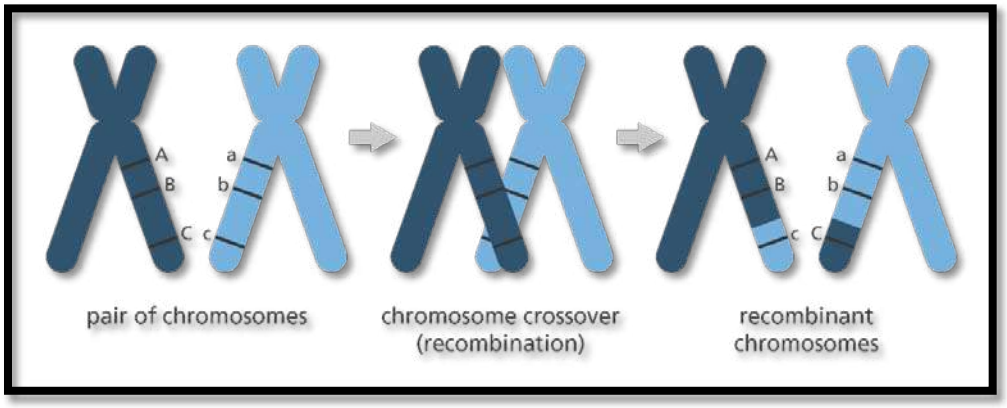
4- Diplotene (*diploos*=double)

- Beginning the separation of the paired chromosomes but not completely because the homologous chromosomes remain united by their points of will form a joint X- like structure called, **chiasmata (pl. chiasma)**

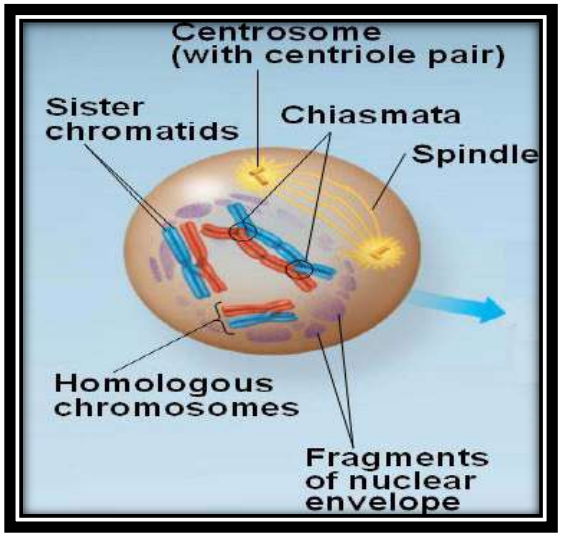
Chaismata represent the sites or points at which exchange of genes or chromosomal segments has occurred during crossing- over .

Diplotene is long lasting period, in human female its occur during fifth week of gestation the oocyte of the human embryo reach diploten stage and remain until many

years when ovulation occurs. In fish and amphibians and reptiles oocytes there is a marked uncoiling of chromosomes during this stage so that the nucleus become greatly enlarged such a nucleus is called germinal vesicle.



Synapse



Chiasmata

5- Diakinesis (*dia*=across)

- This is the final stage of the prophase1
- Chromosomes reach maximum contraction
- Chaismata gradually terminalize move toward the ends of chromosome arm
- Disappear of the nucleolus
- Degenerate the nuclear membrane
- Centrioles reach to opposite poles of the cell and start to forming spindle apparatus

B) Metaphase I

- Arrival the synapsed chromosome pairs at the equator of the cell begins the metaphase **I**
- The two sister chromatids still bind together therefore behave as a functional unit
- metaphase I can be distinguished by the fact that the homologous chromosomes are still attached by chiasmata at ends

C) Anaphase I

- In this stage the homologous chromosomes completely separate from each other move towards opposite poles of the cell
- the centromere that hold the chromatids do not divide as in mitosis, therefore each two chromatids of one chromosome will move together without separate

therefore the anaphase **I** is similar to anaphase in mitosis **except** that each chromosome consists of two chromatids that remain held together

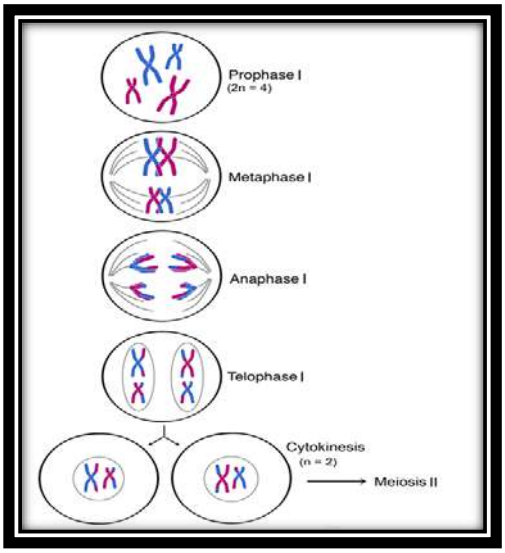
- homologous chromosomes migrate to opposite poles
- The daughter cells are haploid but 2n (1chromosomes with 2 sister chromatids), **and the important thing here**, **that these 2 sister chromatids are not genetically identical.** (This is unlike in the mitosis)

D) Telophase I

- The arrival of chromosomes at each poles signals the end of the anaphase **I** and beginning of the telophase **I**
- Formation of nuclear membrane and nucleolus
- The resultant cells are 2 daughter cells, each nucleus is haploid (double amount of DNA but one chromosome from each homologous chromosome.
- At each pole a nucleus is formed as in mitosis

E) Cytokinesis (division of the cytoplasm)

- The nuclear division is followed by cytokinesis the cytoplasm of the cells undergoes division to result 2 daughter cells which in animals male called two secondary spermatocytes and in females called secondary oocytes plus first polar body (polocyte)



Meiosis I

Meiosis II (equatorial division)

There is a very short time of interphase between meiosis **I** and meiosis **I I** there is no replication of chromosomes this differ from mitosis.

At the following some important events that occur during this stage:-

- Each haploid daughter cells resulting from the first meiosis now divides mitotically to give rise two haploid daughter cells
- No DNA replication will happen during short interphase
- The Meiosis II is similar to those in the mitosis and consists of 5 phases also. (**Prophase II, Metaphase II, Anaphase II, Telophase II, and Cytokinesis)**.

A) Prophase II

- Short stage and resembles mitosis prophase, except that sister chromatids of each chromosome are divergent

- The centrioles duplicate and migrate towards opposite poles
- The centromers replicate in the prophase II

B) Metaphase II

- In both daughter cells each double-stranded chromosome line up during the metaphase II.

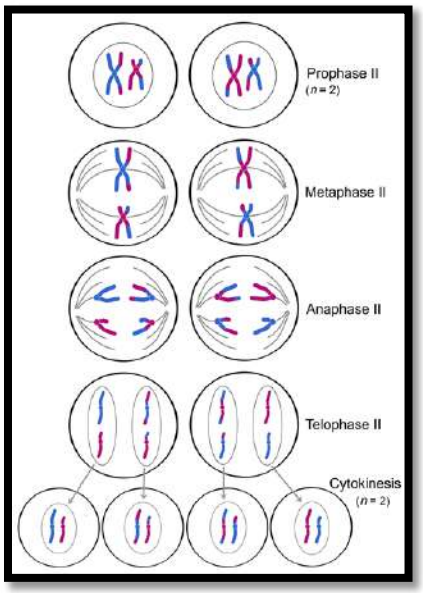
C) Anaphase II

- In the anaphase II the double-stranded chromosome pull a part into a side of the cell
- The centromere between two sister chromosomes will divide and move as daughter chromosomes similar to their movements in mitosis
- The arrival at the opposite poles marks the end of this phase

D) Telophase II

- Haploid sets of chromosomes at two poles uncoil
- Nucleolus reappears**,** nuclear envelope is formed
- Each four nuclei of telophase **II** has one chromatid of the tetrad
- Each nucleus has a haploid number of chromosomes

The telophase **II** is followed by cytokinesis thus the final result of one germ cell division give four daughter cells with half number of chromosomes and half copy of DNA molecule. So these 4 cells called (**haploid 1n**)

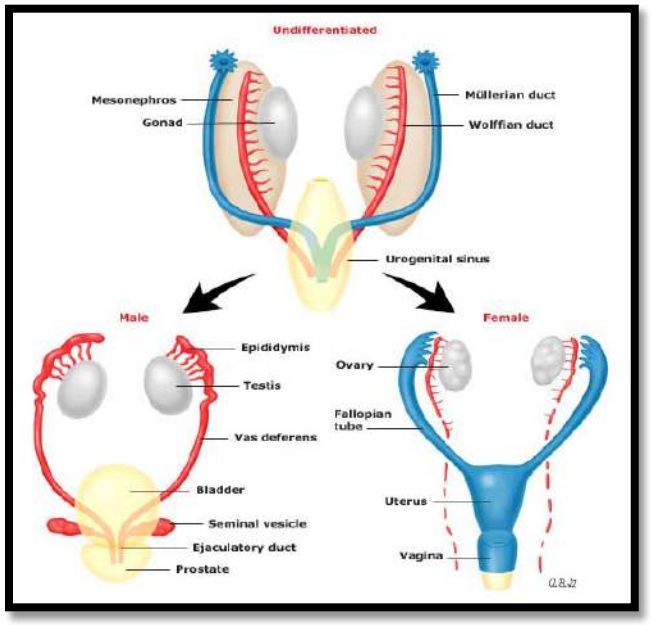


Meiosis II

Lec. 4

Male development

In early embryogenesis the gonads of XY and XX individuals do not have morphological differences. The gonads contain both male and female germ cells. Primordial germ cells colonize conadal cortex, where they can become oogonia, as well as the central medulla where they become spermatogenesis.



In XY embryos the gonads will develop to testis, the central medulla develops testis cords at puberty these cords will hollow to form the somniferous tubules in which the sperms are produce. the supporting cells differentiate to sertoli's cells these produce the hormonal anti-mullerian-duct factor (AMDF or called mullerian duct-inhibiting substance MIS), while the interstitial cells develop into leydig's cells that produce the male sex hormones (androgen) like testosterone.

Female development

The primordial germ cells in the cortex stop mitotic activity, become oocytes and inter meiosis. In contrast to male, where the meiosis in the spermatocytes is delayed until the puberty. In females meiosis begins in the ovaries at 12^{th}. Week of embryonic

development. The supporting cells assume the function of follicle cells and surround the oocytes. The interstitial cells become theca cells which produce female sexual hormone (estradiol) and estrogen. Any additional gonadal development depends on presence or not testosterone. This hormone is trigger factor to male development; its absence allows female development to take over.

Gametogenesis

At fertilization, the maternal and paternal gametes are united forming the zygote. The maternal gamete, the oocyte is the largest non-motile cell of the body, while the paternal gamete, the spermatozoon has ability for motion and penetration of the oocyte. The cells which produce the gametes during the embryological period are called **the Primordial germ cells** (**PGCs**)

The gametogenesis is the process by which the maternal and paternal gametes are produced from the primordial germ cells to form mature sex cells called the gametes.

Gametogenesis includes both mitosis and meiosis to allow for recombination of genetic material and for reduction of the number of chromosomes from diploid to haploid cells.

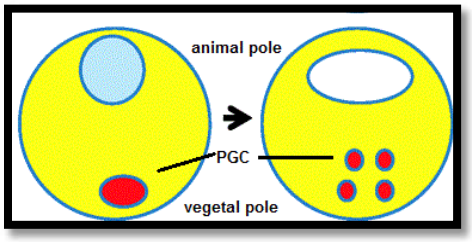
The gametogenesis includes two types of processes differs between male and female, in the male called, **Spermatogenesis**, and in the female called **Oogenesis**, and the two processes are also called **pre-embryonic development**.

Primordial Germ Cells (PGCs)

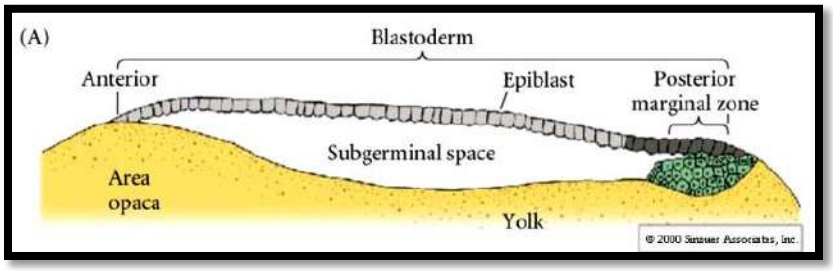
Although much of the early history of the germ cells is still unknown, the cells that give rise to the gametes are recognized at early stage in development.

PGC of birds, reptiles, and mammals arise in the epiblast of the embryo and then go temporary in extraembryonic tissues before return to the body of the embryo.

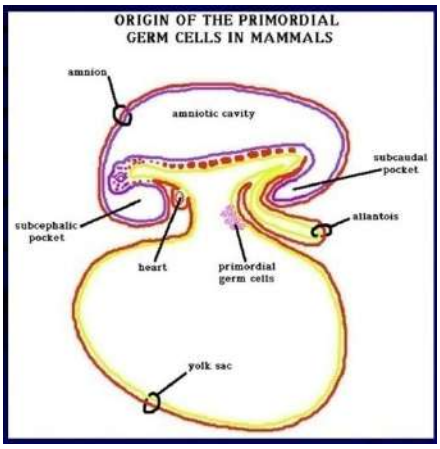
In frog and number of invertebrate species, germ cells can be recognized very early in the life of the animal around the vegetal pole cytoplasm of the zygote as specific cells during the cleavage stages. The PGCs of the birds are recognized in the germinal crescent which is located beyond the head region of the embryo, in the mammals the PGCs derived from yolk sac entoderm near caudal end of the body near the origin of the allantois. So many studies proved that the site of the PGCs in various reptiles, birds, and mammals is from **an extra-gonadal origin**.



PGC in frog



PGC in chick



PGC in human

In most vertebrates, mitosis in the PGC is arrested after their until reach the genital region, but this is differ in the mammals, there is no stop in the mitotic activity of the PGC during migration to the genital area.

Like all normal somatic cells (non-germ cells) the PGCs contain 23 pairs of chromosomes (46 chromosomes). One chromosome of each pair is obtained from the maternal gamete and the other from the paternal gamete, 22 pair consists of homologous chromosomes called **autosomes**, the remaining 2 chromosomes (1 pair) are called **sex chromosomes**.

In males, PGCs remain dormant in the testes from 6^{th}.Week of human embryonic development until puberty. At puberty, seminiferous tubules mature by the male hormones that stimulate the differentiation of the PGCs into **spermatogonia** by mitosis. In contrast in the female, the PGCs, undergo a few more mitotic divisions and invested by some somatic cells from the stroma of the ovaries before 5^{th}. Week of the human embryonic development the PGCs transform to the **oogonia**, and by the 5^{th} month of the fetal development all oogonia inter **meiosis** I, they are called **primary oocytes**, the primary oocytes still arrest in the ovaries until sexual maturity.

Spermatogenesis

The process in which an animal produces spermatozoa from spermatogonial stem cells by way of mitosis and meiosis. The initial cells in this pathway are called spermatogonia, which yield primary spermatocytes by mitosis. The development of the spermatozoa takes place in the male gonads, the testes, in all vertebrates the testes are mixed gland; exocrine organ, produce sperms and endocrine gland, producing male hormones.

The spermatogenesis takes place continuously from puberty until death, At birth, the germ cells in the infant male can be recognized in the sex cords of the testis, as large, pale cells surrounded by supporting cells. The supporting cells called the **sertoli cells**;

originate from the surface of epithelium of the seminiferous tubules, the sertoli cells have physical and chemical support to the spermatocytes.

At puberty, the testes begin to secret greatly increased amounts of the steroid hormones, testosterone, among effects of this hormone; the PGCs will resume the development and divide several times by mitosis, and then differentiate into **Spermatogonia**. Spermatogonia locate under the basement membrane of the seminiferous tubule.

The spermatogenesis is a continuous process; it can be divided into two stages:

1- Spermatocytogenesis **2- Spermiogenesis**

1- Spermatocytogenesis: - the process which the primordial germ cells (PGCs) produce the spermatozoa during several stages of mitosis.
2- Spermiogenesis: - the process which includes the re-structuring of the spermatids to spermatozoa (sperms) without any cell division only morphological changes. Because a sperm or spermatozoon is very active and motile, therefore it requires a degree of specialization, head and tail of the sperm are formed in this process.

1- Spermatocytogenesis

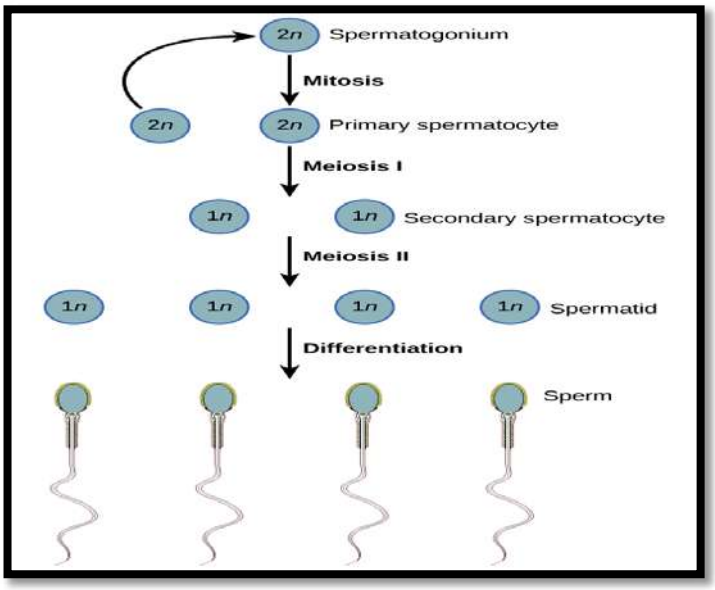
PGCs (**46,2n**) move from the wall of the yolk sac arrive in the testes and remain dormant until birth, **at puberty** the testes differentiate during mitosis into Spermatogonia (**46,2n**) which are located peripherally in the seminiferous tubules, these cells are active mitotically all the life. The DNA replication is occur in mitosis convert the Spermatogonia from **2n** to **4n** the resultant cells called the Primary spermatocytes (**46, 4n**)

Primary spermatocytes (**46, 4n**) inter the **meiosis I** and divided into two daughter cells called **secondary spermatocytes** (**23, 2c**), each of the secondary spermatocytes inter the **meiosisII** to form **four haploid spermatids** (**23,1c**). Commonly in the human

the **meiosis I** last for several weeks, whereas the **meiosis II** is completed in about 8 hours.

Through this series of division, cytokinesis is incomplete; leaving all cells still connected through thin cytoplasmic bridges, and connects with **sertoli cells**, which support them physically and metabolically.

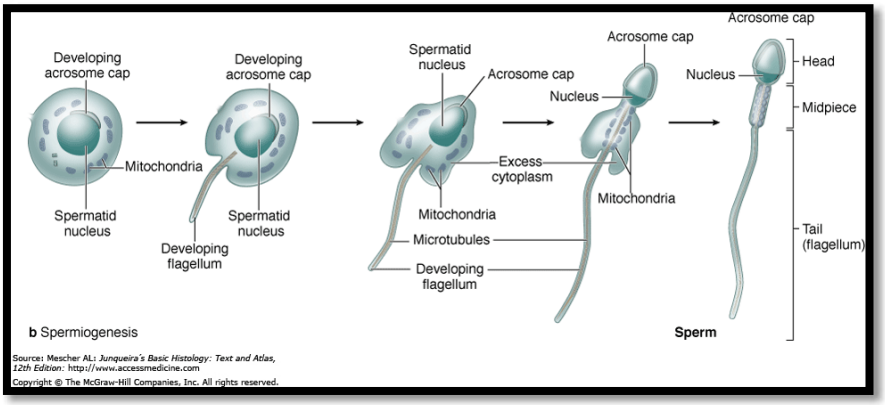
Although the spermatids no longer divide, they undergo a transformation to specialized spermatozoa; this is done by the spermiogenesis process.



2- <u>Spermeiogenesis</u>

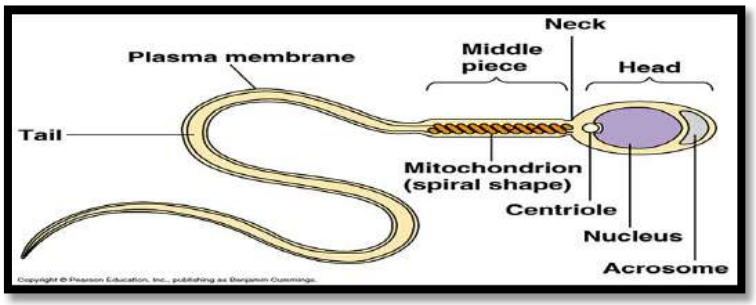
The Spermeiogenesis is the second process of the spermatogenesis mechanisms, it consists of series of morphological changes that responsible of transformation the spermatids into mature spermatozoa (sperms) (**23,1n**). Because the sperm or spermatozoon is very active and mobile cells, so it must be supported with great amount of energy and activation, therefore there is need to a high degree of specialization must occur in the sperm cells before release from the testes.

After the end of the meiosis II, the nucleus begins to lose fluid, decrease its size The nucleus loses its RNA molecules, nucleolus and most proteins, only the haploid copy of the DNA will remain, and the chromatin compress until forming the head of the sperm, at the apical end of the developing sperm head, there is a Golgi complex form the pro-acrosomal granules, contains hydrolytic enzymes that are released during fertilization. The centriole develop to be a point of the flagellum, after the meiosis II, the two centrioles move through the cytoplasm of the spermatid just behind the nucleus, these centrioles give rise to the axial filament of the flagellum of the sperms, which later differentiate into tail. mitochondria begin to form a spiral form called the mitochondria helix as a source of energy, during development the rest of the cytoplasm will sloughed off and phagocytized by the sertoli cells, all these events make the mature spermatozoa leaves all the non-essential parts,



at the end the mature spermatozoa will consists of :-

1- Head; containing nucleus and acrosome
2- A neck; containing the centriole
3- A middle piece; containing the proximal part of the flagellum and mitochondria helix
4- The tail, highly specialized flagellum



Lec. 5

Oogenesis

The **oogenesis** is a period of growth and maturation of the egg occurring in the female gonads (ovaries).

The female gametes is larger than most somatic cells and non-motile, because in all animal egg have many vital roles like; it has a nucleus containing half of the chromosomal content (haploid number of the chromosomes), it has to supply all cytoplasm to the embryo after fertilization, also it has supply food store to the embryo to develop. Primordial germ cells migrate into the developing gonad early in embryogenesis, and differentiate into oogonia. These oogonia proliferate by mitosis

It is divisible into following three phases:

1. Multiplication Phase:

The primary germinal cells of the ovary with diploid number of chromosomes (46,2n, 2c) divide several times mitotically so as to form a large number of daughter cells known as oogonia found in the cortex of ovary

2. Growth Phase:

The oogonium will differentiate to increases in size to form a primary oocyte, diploid number of chromosomes This process is called oocytogenesis (46,2n,4c) The growth is associated with both nuclear and cytoplasmic growth. The nuclear growth is due to accumulation of large amount of nuclear materials and is termed as germinal vesicle. The cytoplasmic growth is associated with increase in number of mitochondria, endoplasmic reticulum and Golgi complex and accumulation of reserve food material called yolk, Oocytogenesis is complete either before or shortly after birth. When oocytogenesis is complete, no additional primary oocytes are created, in contrast to the male process of spermatogenesis, where gametocytes are continuously created. In other

words, primary oocytes reach their maximum development at ~20 weeks of gestational age, when approximately seven million primary oocytes have been created; however, at birth, this number has already been reduced to approximately 1-2 million.

3. Maturation phase:

The primary oocyte undergoes two successive divisions by meiosis. The first division is meiosis-I and two unequal daughter cells are produced during embryonic period, the large cell is called secondary oocyte containing haploid (n) set of chromosomes (due to reduction division) and entire amount of cytoplasm. Haploid (23,1n, 2c) The smaller cell is called first polar body or polocyte containing 'n' number of chromosomes and practically no cytoplasm.

it stops at diplotene stage of prophase I until puberty. In late fetal life, all oocytes, still primary oocytes, have arrested at this stage of development. **This called the first stop point.** These cells then continue to develop, only a few do so every menstrual cycle. synapses occurs and tetrads form, enabling chromosomal crossover to occur. As a result of meiosis I, the primary oocyte has now developed into the secondary oocyte and the first polar body.

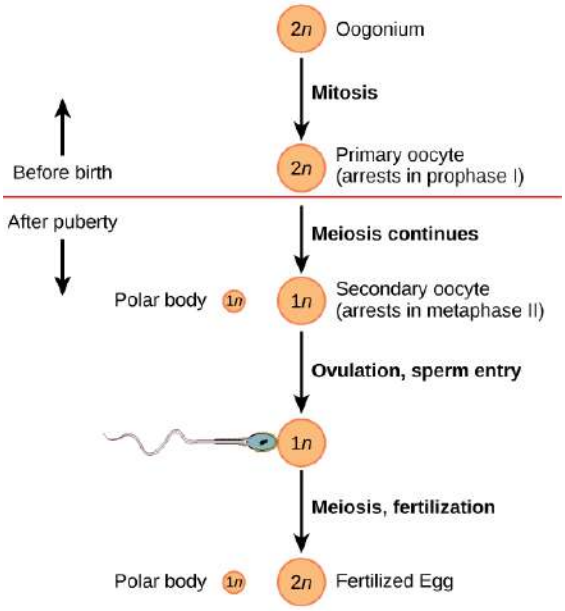
- At the ovulation during puberty :

immediately after meiosis I, the haploid secondary oocyte initiates meiosis II. However, this process is also stop again at the metaphase II stage until fertilization,**This called the second stop point**.

When fertilization is occur meiosis II has completed to form mature ovum and another polar body have now been created.

the first polar body may divide into two polar bodies or may not divide at all. Thus only one functional ovum is formed and the two or three polar bodies soon degenerate. In vertebrates the first polar body is formed after the primary oocyte is released from ovary

and has entered into the oviduct. The second polar body is formed only when the sperm enters into ovum during fertilization.



Development of the ovarian follicles

1- Primordial follicle

Primordial germ cells migrate into the developing gonad early in embryogenesis, and differentiate into oogonia. These oogonia proliferate by mitosis. Some of these enlarge and develop into larger cells called primary oocytes and enter the first meiotic division on the pathway to making gametes by meiosis. This happens between 3 and 8 months of gestation in the human embryo.

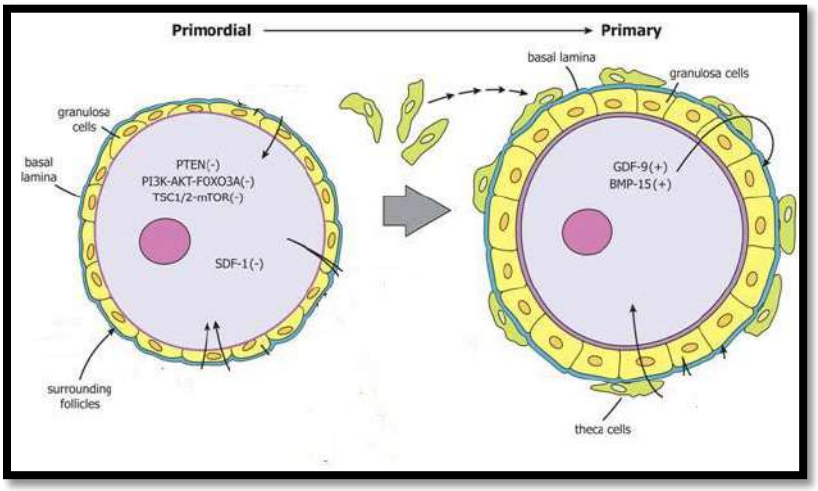
These 'primary' oocytes become arrested in prophase of the first meiotic division until the female becomes sexually mature. At sexual maturity, a small number of primary oocytes (20-50) mature each month and complete the fist meiotic division to become secondary oocytes, under the influence of **follicle stimulating hormone**. The oocytes synthesize a coat and cortical granules - this glycoprotein coat is called the 'zona pellucida'. They also accumulate ribosome, yolk, glycogen, lipid and the mRNA that will be used later on after fertilization to direct early development of the embryo.

After a second mitotic division, ova are formed.

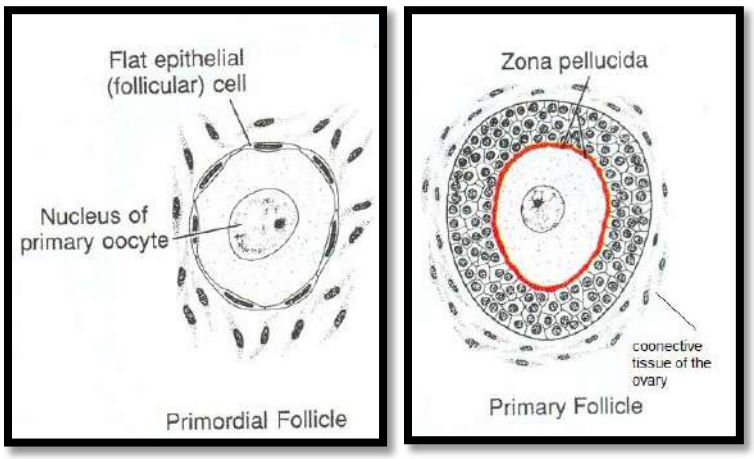
In primordial follicles, the oocyte is arrested in the last stage of prophase at this stage, it is surrounded by a single layer of flattened **ovarian follicular epithelial cells**. (These cells are also known as granulosa cells).
They are small, and usually found close to the outer edge of the cortex.

2- Primary follicle

When the primordial follicle is stimulated, it becomes a **primary follicle**. The oocyte enlarges, and the **follicular cells** divide called the granulose cells with two layers of granulose cells is called a primary follicle. These cells continue to hypertrophy and proliferate to form many layers surrounding the oocyte. Eventually these cells become known as 'granulosa' cells. The granulosa cells will secrete progesterone after ovulation. A thick glycoprotein layer develops between the oocyte and the zona granulosa, called the **zona pellucida**.Finally, the **stroma** around the follicle develops to form a capsule like 'theca'. (Theca is greek for 'box'). Only one of the maturing follicles completes the maturation process each month. The rest degenerate into **atretic** follicles. Follicular maturation takes about 3 months.



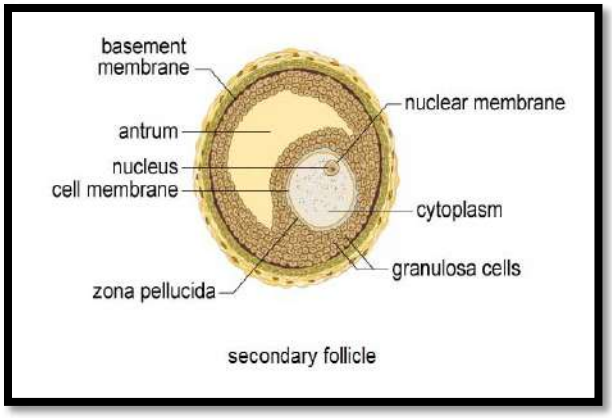
Development of the primordial follicle to primary follicle in the ovary of the female embryo



3- Secondary Follicle

The primary follicle develops into a **secondary follicle**. The secondary follicles look very similar to primary follicles, except that they are larger, there are more follicular cells, and there are small accumulations of fluid in the intracellular spaces called **follicular fluid** (nutritive fluid for the oocyte) to form an **antrum**. The surrounding granulosa cells is called the **cumulus oophorus** (greek for 'egg bearing heap').

The surrounding theca differentiates into two layers: the **Theca interna** (rounded cells that secrete androgens and follicular fluid) and a more fibrous **Theca externa** - spindle shaped cells. The androgens are converted into oestrogen by the granulosa cells.



4- Graffian follicle

The secondary follicle develops into a **Graffian follicle**.

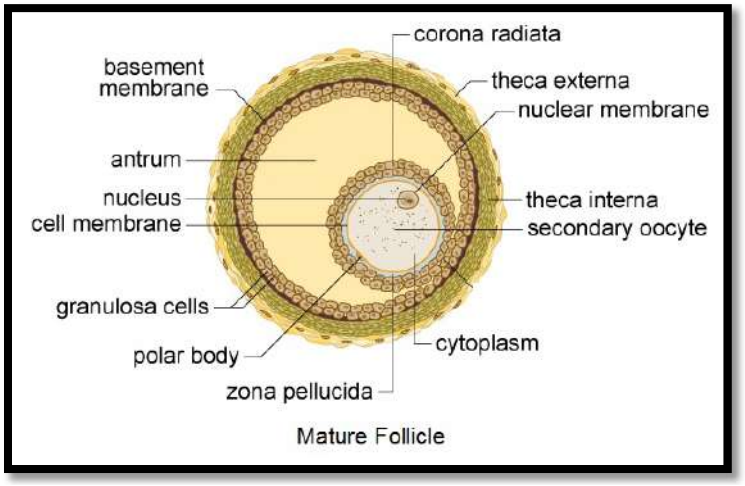
The first meiotic division is now completed, and the oocyte is now a secondary oocyte, and starts its second meiotic division. After the first meiotic division, most of the

cytoplasm goes into one of the two daughter cells. The other becomes the polar body (hard to see).

The folicular fluid fills a single space, called the **antrum**, which is surrounded by the follicular cells - called the **membrana granulosa**. The granulosa cells that surround the oocyte, and project into the antrum are called as the **cumulus oophorus**. There is a basement membrane between the granulosa cells and the **theca interna**. The fibrous **theca externa** merges with the surrounding stroma.

The **oocyte**, **zona pellucida** and the follicular cells surrounding the ooctye (known as the **corona radiata**) are all expelled at ovulation, and enter the fallopian tube.

Once released, the oocyte begins its second meiotic division, as far as metaphase II. Division only carries on if the ovum is fertilized.



Lec. 6

Fate of the degenerated follicles

Corpus Luteum

After ovulation, the ruptured follicle collapses and fills with a blood clot (corpus haemorrhagicum) which then forms the corpus luteum. The **granulosa cells** enlarge, and become vesicular, and are now called the **granulosa lutein** cells. these become folded, as you can see here.

The spaces between the folds are filled with **theca interna** cells, which also enlarge and become **glandular**, and are now known as the **theca lutein** cells.

The **zona granulosa** cells begin to secrete progesterone (granulosa lutein cells). The corpus luteum also secretes estrogen (which inhibits FSH) and relaxin (which relaxed the fibro cartilage of the pubic symphysis).

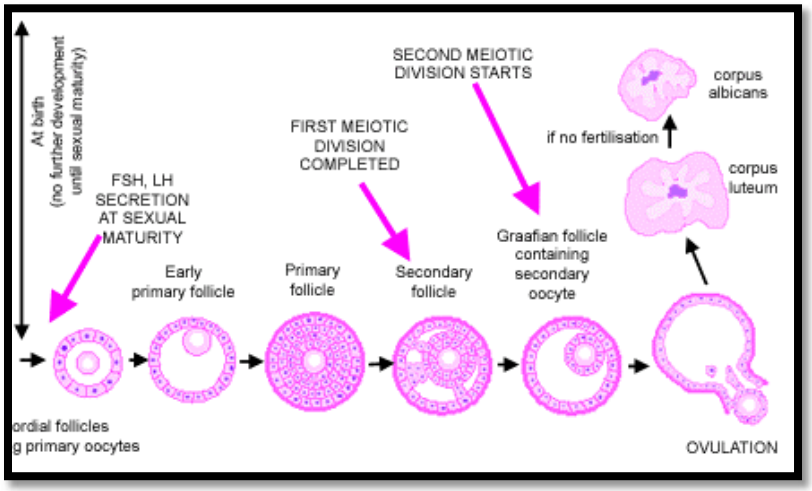
If pregnancy does not occur, then the corpus luteum degenerates into the **corpus albicans**, and levels of estrogen and progesterone fall, allowing release of FSH and LH.

If pregnancy does occur, then the syncytiotrophoblasts of the placenta release **human chorionic gonadotrophin**, and the corpus luteum persists.

About 20 primordial follicles start developing in each cycle, but only ONE makes it!

Corpus albicans

This image shows an atretic corpus luteum or corpus albicans. The cellular elements have degenerated, and macrophages phagocytose the dead cells. Fibrous tissue is left behind. The corpus albicans looks pale. It will continue to shrink, eventually forming a small scar on the side of the ovary.



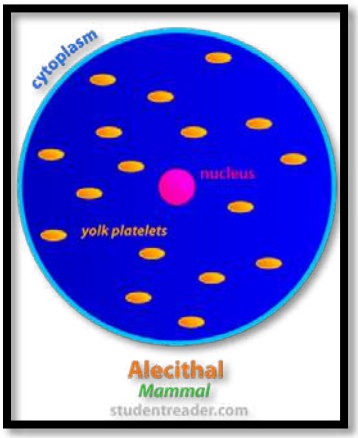
Classification of eggs

Yolk, the major nutritional reserve of the oocytes during the growth and development and after the fertilization to provide the embryo with nutrition, the yolk varies greatly in amount and distribution in different animals groups.

❖ **Based on the amount of the yolk, the eggs can be classified into the following:-**

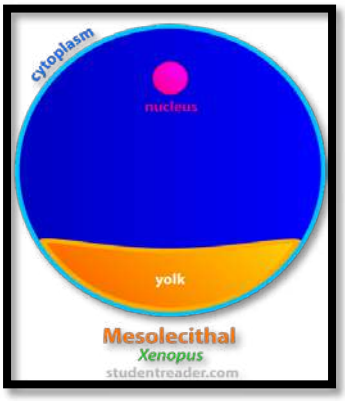
1- Microlecithal (oligolecital) eggs

These are small-sized eggs which contain a very small amount of yolk distributed in the cytoplasm (ooplasm), this type found in certain marine invertebrates, ex: *Hydra*, and some chordates like *Amphioxus*, cephalochordates, tunicates, and the eutherian mammals, in the mammals this type of egg called also **Alecithal egg.**



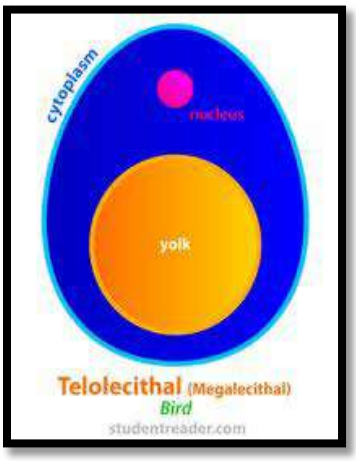
2- Mesolecithal eggs

This type of eggs contain moderate amount of yolk, found in annelid worms, molluscus, *Petromyzon*, lung fish and amphibian.



3- Macrolecithal (megalecithal) eggs

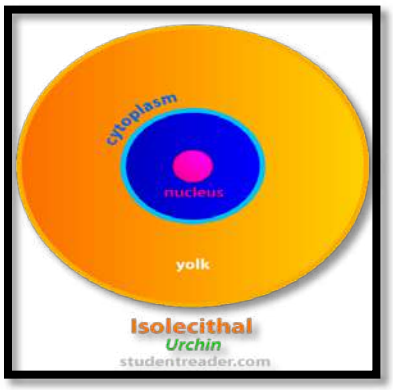
These eggs contain enormous amount of yolk, found in insects, chondrichthyes, reptiles, birds and monotrems.



❖ Based on the distribution of the yolk

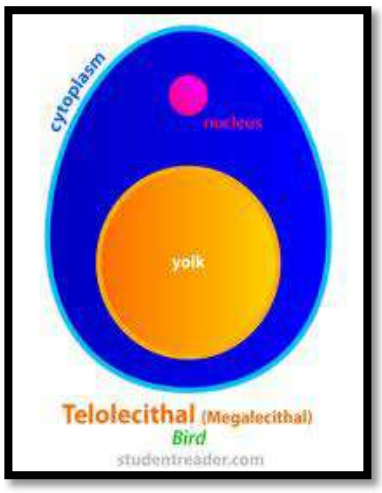
1- Homoelcithal or isolecithal eggs

In Microlecithal eggs, the amount of yolk is little, therefore it is found almost scattered through all the cytoplasm of the egg.



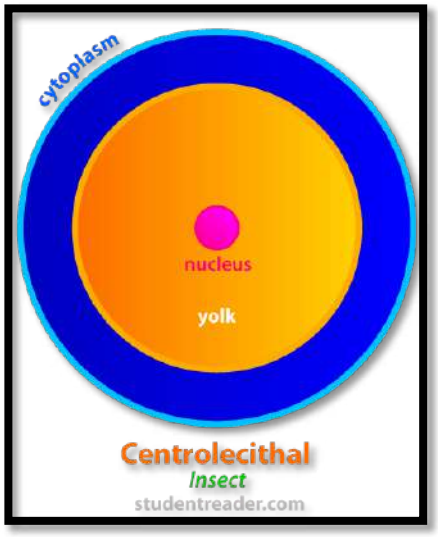
2- Telolecithal eggs

This type of egg has a **polarized** distribution of yolk in the ooplasm due to the gravity of the yolk; it concentrated more in one side than in the other. The side that contain no or very small amounts of yolk is called the **animal pole**, while the side where the yolk concentrated more called the **vegetal pole**. This type found in the amphibian, *Petromyzon*, cartilaginous and bony fishes, reptiles, and birds.



3- Centrolecithal eggs

In insects and some hydrozoa, the yolk is concentrated in the center of the egg and the active ooplasm and nucleus form a thin peripheral layer around the yolk.



Formation of egg membranes

In most animals, except the sponges and coelenterates, oocyte maturation is not completed until additional structures, called egg membranes, egg membranes are added outside the plasma membranes of egg and vary in different animal groups and sometimes reflect the adaptations by the animals, protect eggs from predators, disease, and many environmental effects like PH , There are several ways of classifying the egg membranes, but the simplest way is according to their origin as follow:-

1- Primary egg membranes

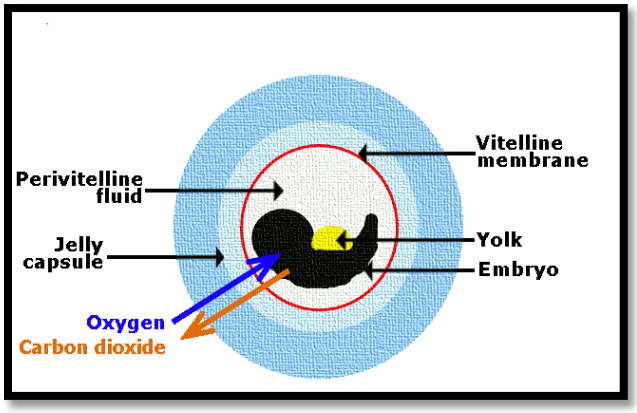
These membranes are formed in the ovary between the egg plasma membrane and follicle cells, they are formed either by ovum and follicle cells, this type of egg membranes includes:-

a- Vitelline membrane

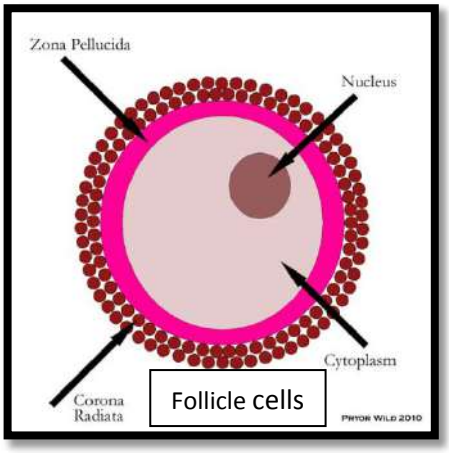
In fact it is not a membrane, but a non-cellular transparent layer of mucoprotein out of egg give the physical support and elasticity.

The Vitelline membrane is a structure directly adjacent to the outer surface of the plasma membrane of an ovum

Vitelline membrane has different names for example, in birds it contact to the ooplasm until the fertilization then will separate therefore it's called the fertilized membrane, in fish called the chorion, and in the reptiles and mammals called zona pellucida.



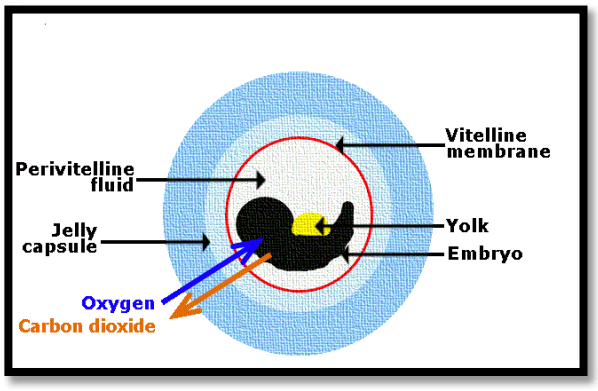
Vitelline membrane in amphibians



Zona pellucida

b- Jelly envelope

In echinoderms and many eggs of the marine invertebrates, the primary egg envelope is much thicker structure like jelly coat.



2- Secondary egg membrane

The secondary egg membrane is secreted outside the primary egg membrane by the follicle cells. It occurs in the form of chitinous shell around egg in insects and cyclostomes and called the chorion, this chorion is different from the chorion in fish that is formed by the oocyte and contains proteins and polysaccharides.

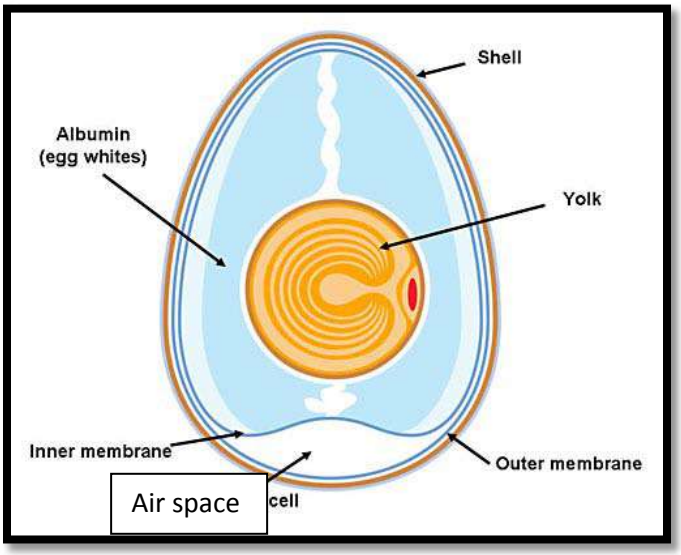
No secondary membranes are found in the amphibians, reptiles, birds and even mammals eggs.

3- Tertiary egg membrane

The tertiary membrane secreted through passage the egg in the oviduct or during the presence of the egg in the uterus secreted by the cells of the oviduct itself.

This membrane is found in:

- In oviparous sharks the eggs are surrounded by albumin and hard capsule secreted by shell glands of the oviduct.
- In amphibians, three layers of albumin (jelly) are deposited around egg, during the amphibian's eggs down in water; the jelly membranes absorbed the water and swells. These jelly membrane protect the eggs from infection and predators.
- In reptiles, bird's five tertiary membranes make up the envelopes of the egg out of the vitelline membrane.



Anatomy of chick egg

Lec.7

The ovarian cycle

The ovary

- An ovary contains many follicles, and each one contains an immature egg, called an oocyte.
- A female is born with as many as two million follicles, but the number is reduced to 300.000-400.000 by the time of puberty.

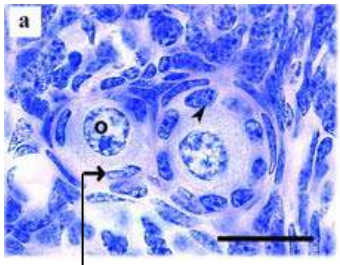
- During the lifetime of a female, only 400 follicles mature.

- As the follicle matures during the **ovarian cycle**, it changes from a primary to a secondary to a vesicular (graafian) follicle, **Figure (1)**.

- ***Primary follicle***: epithelial cells of a primary follicle surround a primary oocyte.
A primary oocyte undergoes **meiosis I**, and the resulting cells are haploid with **23 chromosomes** one of these cells is called a polar body. Primary follicle produces estrogen.

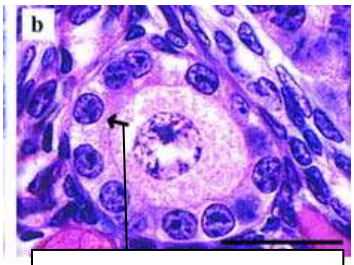
- ***Secondary follicle***: pools of follicular fluid bathe the secondary oocyte in a secondary follicle. A secondary oocyte undergoes **meiosis II**, but only if it is fertilized by a sperm. Secondary follicle produces estrogen and some progesterone, **Figure (2)**.
If the secondary oocyte remains unfertilized, it never completes meiosis and will die after being released from the ovary.

- ***Vesicular (graafian) follicle***: the fluid-filled cavity increases to the point that the follicle wall balloons out on the surface of the ovary. Eventually, the vesicular follicle ruptures, and the secondary oocyte (often called egg) is released. The follicle then becomes the corpus luteum, which produces progesterone and some estrogen.



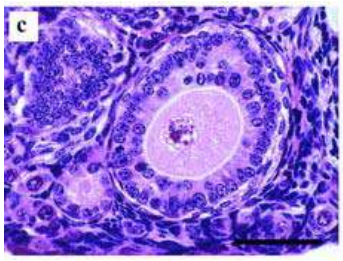
(a)- Primordial follicles were defined as an oocyte (o) surrounded by a layer of squamous (flattened) granulosa cells (arrow).

Squamous granulosa cells

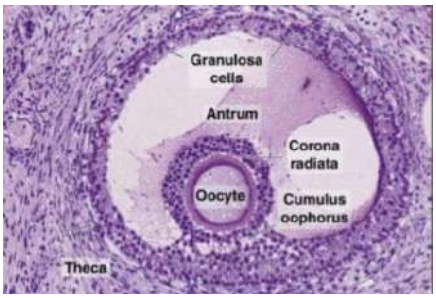


(b)- Primary follicles possessed an oocyte surrounded by a single layer of cuboidal **granulosa cells (arrow).**

cuboidal granulosa



(c)- Secondary follicles were surrounded by more than one layer of cuboidal granulosa cells, with no visible antrum.



(d)- Graafian follicles were the largest of the follicular types, possessed a clearly antral space and a cumulus granulosa cell layer

Figure- 1 Maturation of a follicle

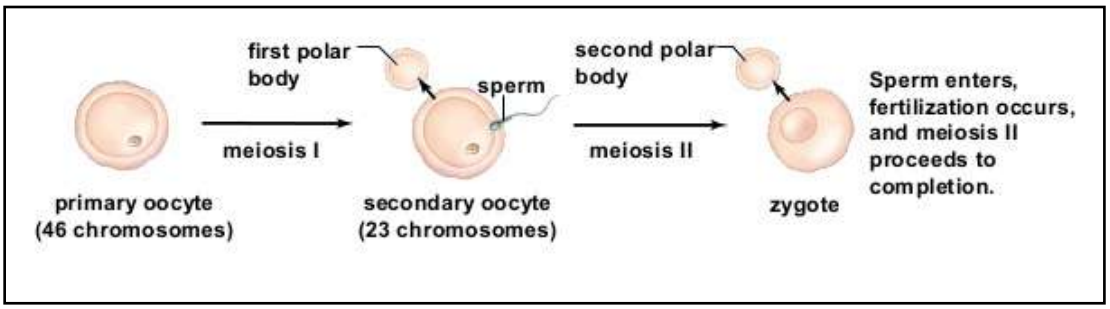


Figure -2: Oocyte development

At puberty, the female begins to undergo regular monthly cycles. These sexual cycles are controlled by the hypothalamus. Gonadotropin-releasing hormone (GnRH), produced by the hypothalamus, acts on cells of the anterior lobe (adenohypophysis) of the pituitary gland, which in turn secrete gonadotropins, which include :

- Follicle-stimulating hormone (FSH)

- Luteinizing hormone (LH)

These hormones stimulate and control cyclic changes in the ovary, fig. (3).

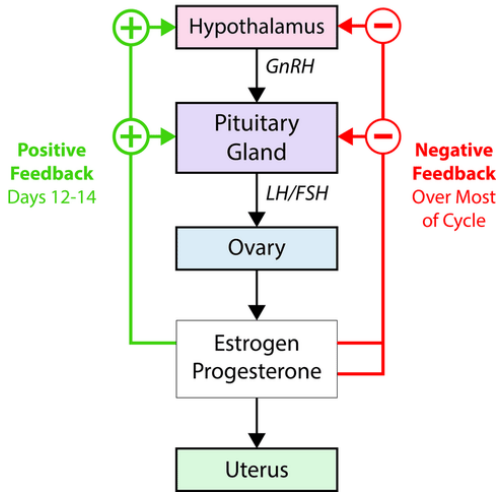


Figure- 3: Hormonal control of ovarian cycle

Phases of the ovarian cycle

- Follicular phase

- FSH promotes the development of follicles that primarily secrete estrogen.

- Due to a positive feedback effect, an estrogen spike causes a sudden secretion of a large amount of GnRH from the hypothalamus. This leads to a surge of LH production by the anterior pituitary and to ovulation at about the 14^{th} day of a 28-day cycle.

- Luteal phase

- During the luteal phase of the ovarian cycle, LH promotes the development of the corpus luteum, which secretes primarily progesterone.
- When pregnancy does not occur, the corpus luteum regresses, and a new cycle begins with menstruation.

Beginning of ovarian cycle

- 15-20 primary follicles are stimulated to grow under the influence of FSH.

- Under normal conditions, only one of these follicles reaches full maturity, and only one oocyte is discharged at ovulation; the others degenerate and become atretic.

- FSH stimulates maturation of follicular (granulosa) cells surrounding the oocyte.

- Proliferation of follicular cells is mediated by growth differentiation factor 9 (GDF-9), a member of the transforming growth factor-β (TGF-β) family.

- Theca interna and granulosa cells produce estrogens

[Theca interna cells produce androstenedione and testosterone, and granulosa cells convert these hormones to estrone and 17 β- estradiol].

Effects of estrogen production

- The uterine endometrium enters the follicular or proliferative phase.

- Thinning of the cervical mucus occurs to allow passage of sperm.

- Stimulate the anterior lobe of the pituitary gland to secrete LH.

At mid ovarian cycle

There is an LH surge that:

- Elevates concentrations of maturation promoting factor, causing oocyte to complete meiosis I and initiate meiosis II.

- Stimulates production of progesterone by follicular stromal cells (luteinization)

(Luteinization: is the process of transformation of follicular granulosa cells into lutein cells).

- Causes follicular rupture and ovulation.

After ovulation and during the luteal phase of the ovarian cycle

- LH promotes the development of the corpus luteum

- Progesterone in particular causes the endometrial lining to become secretory

When progesterone production declines to a low level; menses occur.

[Menses due to the breakdown of the endometrium].

Embryology: Study of development of the embryo**.**

- Embryo: implantation to 8 weeks

- Fetus: after 8 weeks

- Gestation: carrying of an embryo/fetus inside a female

Embryonic development

In animal, embryonic development includes five essential stages:

1) Gametogenesis: gamete production

2) Fertilization: gamete ⟶ zygote

3) Cleavage: zygote ⟶ blastula

4) Gastrulation: blastula ⟶ gastrula

5) Organogenesis: organ formation

i.e. Neurulation: gastrula ⟶ Neurula

First week of human embryonic development: Ovulation to implantation

Ovulation

- In the days immediately preceding ovulation, under the influence of FSH and LH, the follicle grows rapidly to a diameter of **25 mm** to become a mature vesicular (graafian) follicle.

- With final development of the vesicular follicle, estrogens, produced by follicular and thecal cells, stimulate increased production of LH that causes the follicle to enter the mature vesicular (graafian) stage.

- Primary oocyte complete meiosis I and enter meiosis II, but the oocyte is arrested in metaphase approximately 3 hours before ovulation.

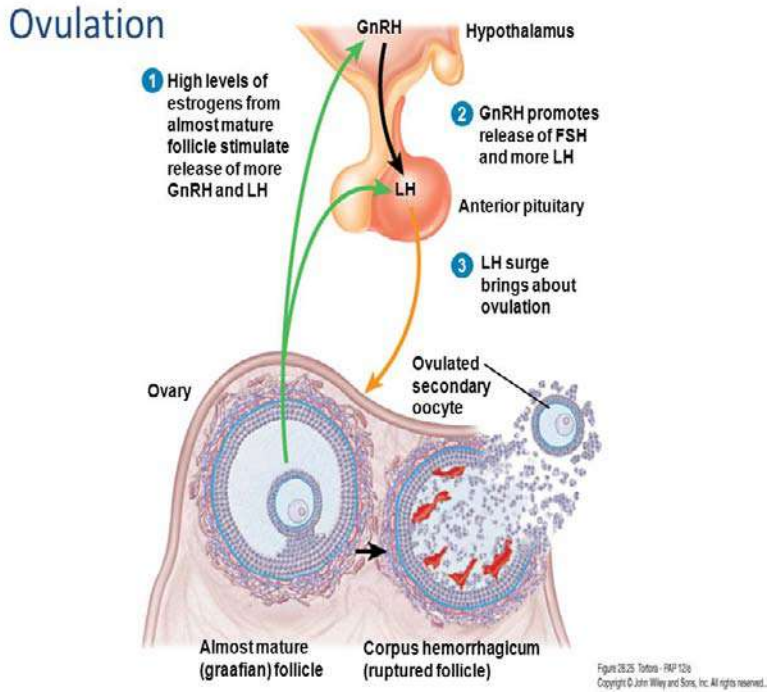
- In the meantime, the surface of the ovary begins to bulge locally, and stigma appears

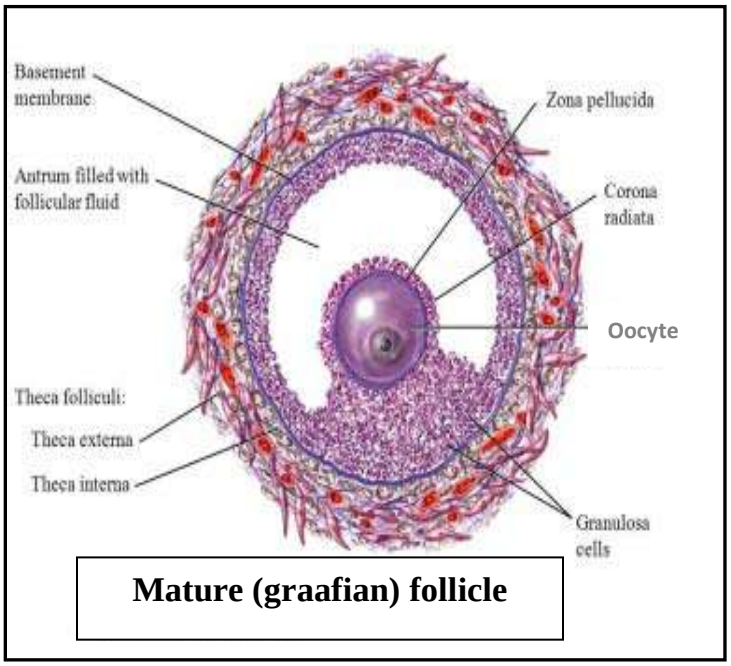
- High concentration of LH increases collagenase activity, resulting in digestion of collagen fibers surrounding the follicle.

- Prostaglandin levels also increase in response to the LH surge and cause local muscular contractions in the ovarian wall.

- Those contractions extrude the oocyte together with its surrounding granulosa cells from the region of the cumulus oophorus and floats out of the ovary.

- Then some of the cumulus oophorus cells rearrange themselves around the zona pellucid to form the corona radiate.





Mature (graafian) follicle

Corpus luteum

After ovulation, granulosa cells remaining in the wall of the ruptured follicle, together with cells from the theca interna, are vascularized by surrounding vessels. Under the influence of LH, these cells change into lutein cells, which form the corpus luteum and secrete **estrogen** and **progesterone.** Progesterone, together with some estrogen, causes the uterine mucosa to enter the **progestational or secretory stage** in preparation for implantation.

If the oocyte is fertilized, degeneration of the corpus luteum is prevented by **human chorionic gonadotropin** (is a hormone secreted by the syncytiotrophoblast of the developing embryo).

- Yellowish luteal cells continue to secret progesterone until the end of the fourth month.

- Thereafter, luteal cells regress slowly.

- Secretion of progesterone by the trophoblastic component of the placenta becomes adequate for maintenance of pregnancy.

- Removal of the corpus luteum before the fourth month leads to abortion.

Corpus albicans

If fertilization does not occur:

- The corpus luteum reachs maximum development approximately **9 days** after ovulation.

- Then, the corpus luteum shrinks because of degeneration of lutein cells **(luteolysis**) and forms the corpus albicans.

- Progesterone production decreases therefore menstruation occurs.

Oocyte transport

- Before ovulation, fimbriae of the uterine tube (fallopian tube) sweep over the surface of the ovary and the tube begins to contract rhythmically.

- The oocyte surrounded by some granulosa cell is passed into the tube by these sweeping movements of the fimbriae and by movement of cilia on the epithelial lining.

- In the tube, granulosa cells remove from the zona pellucid and lose contact with the oocyte.

- In the uterine tube, oocyte pushes by muscular contractions and by cilia in the tubal mucosa with endocrine regulation.

- The fertilized oocyte reaches the uterine lumen in approximately 3-4 days, fig. (5).

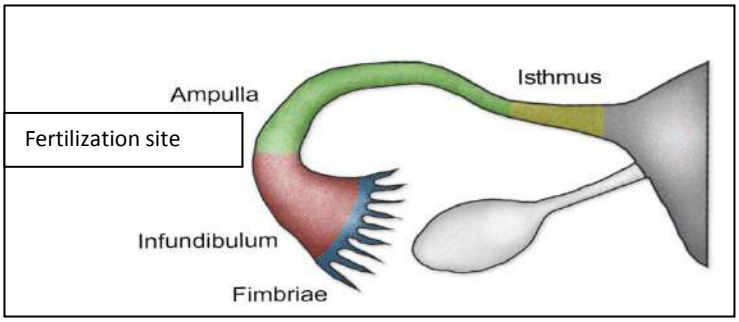


Figure-5: The fallopian tube

Lec. 8

Fertilization

- Fertilization is the fusion of haploid gametes (egg and sperm), to form the diploid zygote.

- Fertilization process occurs in the ampullary region of the uterine tube.

- Spermatozoa remain viable in the female reproductive tract for several days.

-only 1% of sperm deposited in the vagina enter the cervix.

- Movement of sperm from the cervix to the uterine tube occurs by muscular contractions of the uterus and uterine tube and very little by their own propulsion.

- After reaching the isthmus, sperm become less motile and cease their migration.

- At ovulation, sperm again become motile and swim to the ampulla where fertilization occurs.

- Without fertilization, the oocyte degenerates 24 hours after ovulation.

Spermatozoa are not able to fertilize the oocyte immediately upon arrival in the female genital tract but must undergo two processes:

1- Capacitation and 2- Acrosome reaction

Capacitation

Occurs in the uterine tube and involves epithelial interactions between the sperm and the mucosal surface of the tube. During this time, a glycoprotein coat, cholesterol, and seminal plasma proteins are removed from the plasma membrane of the spermatozoon head. Only capacitated sperm can pass through the corona cells, contact the zona pellucida and undergo the acrosome reaction, fig. (1).

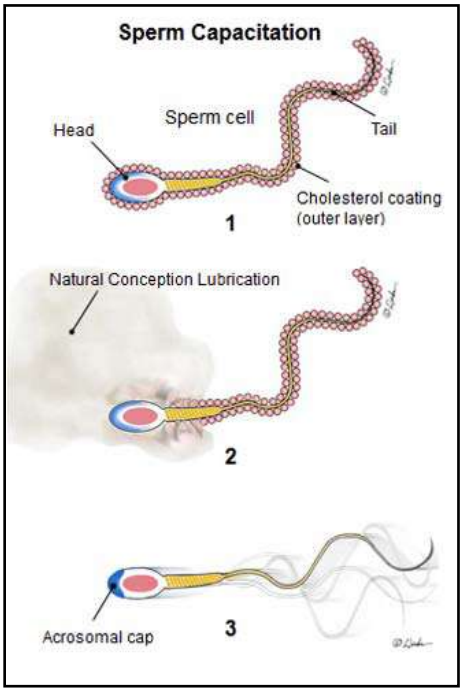


Figure-1: Sperm capacitation

Acrosome reaction

This occurs after binding to the zona pellucida, during which zona pellucida released enzymes including acrosin and trypsin-like substances that aid penetration of the zona pellucida fig.(2).

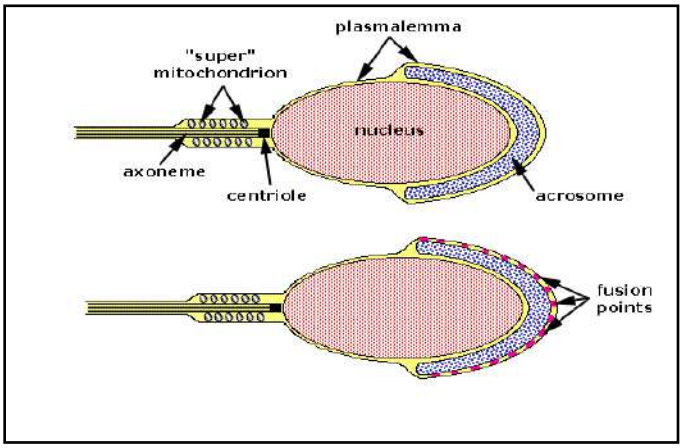


Figure-2: Acrosome reaction

The phases of fertilization

During fertilization, the spermatozoon must penetrate

1- Penetration of the corona radiata

2- Penetration of the zona pellucida

3- Fusion of the oocyte and sperm cell membranes

Penetration of the corona radiata

- 200-300 million spermatozoa normally deposited in the female genital tract.
- Only 300-500 reach the site of fertilization.
- Only one of these fertilizes the egg.
- Capacitated sperm pass freely through corona cells.

Penetration of the zona pellucida

- Zona pellucida is a glycoprotein shell surrounding the egg that facilitates and maintains sperm binding and induces the acrosome reaction.
- Both binding and the acrosome reaction are mediated by the **ligand ZP3 (a zona protein).**
- Release of acrosomal enzymes (acrosin) allows sperms to penetrate the zona, and become contact with the plasma membrane of the oocyte.
- This contact results in release of lysosomal enzymes from **cortical granules (lining the plasma membrane of the oocyte).**
- These enzymes alter properties of the zona pellucida to prevent sperm penetration and inactivate receptor sites for spermatozoa on the zona surface.

Fusion of the oocyte and sperm cell membranes

- Adhesion of sperm to the oocyte is mediated by the interaction of integrins (on the oocyte) and disintegrins (on sperm).
- After adhesion, the plasma membranes of the sperm and egg fuse.
- In human, both head and tail of the spermatozoon enter the cytoplasm of the oocyte, but the plasma membrane is left behind on the oocyte surface.

When the spermatozoon has entered the oocyte, the egg responds in three ways:

1- Cortical and zona reaction

- As a result of the release of lysosomal enzymes from the cortical granules, zona pellucida alters its structure and composition to prevent sperm binding and penetration, these reactions prevent **polyspermy** (penetration of more than one spermatozoon into the oocyte).

2- Resumption of the second meiotic division

- The oocyte finishes its second meiotic division immediately after entry of the spermatozoon.
- One of the daughter cells, is known as the **second polar body**
- The other daughter cell is the **definitive oocyte, its chromosomes (22 plus X)** arrange themselves in a vesicular nucleus known as the **female pronucleus.**

3- Metabolic activation of the egg

- Activation involves the cellular and molecular events associated with early embryogenesis.
- The spermatozoon moves forward and become lies close to the female pronucleus
- Then the nucleus of the spermatozoon becomes swollen and forms the **male pronucleus;** the tail separates and degenerates.

Finally, female pronucleus and male pronucleus (both haploid) become contact and lose their nuclear envelopes, each pronucleus must replicate its DNA, the 23 maternal and 23 paternal (double) chromosomes split at the centromere, and undergo a mitotic division and sister chromatids move to opposite poles, gradually dividing the cytoplasm, and giving rise to the two-cell stage.

Results of fertilization

1- Restoration of the diploid number of chromosomes, half from the mother and half from the father.

2- Determination of the sex of the embryo

If X-carrying sperm produces a **female (XX)**

If Y-carrying sperm produces a **male (XY)**

3- Initiation of cleavage

Without fertilization, the oocyte usually degenerates 24 hours after ovulation.

Cleavage

Is a series of mitotic divisions that results in an increasing the numbers of cells, are known as **blastomeres,** which become smaller with each division. During cleavage there is no growth in the blastomeres. The total size and volume of the embryo remains the same. The cleavages result in a compact mass of blastomeres called **morula** (solid ball of cells). It gets transformed into **blastula** (hollow ball of cells). While the wall of the blastula is called the **blastoderm**, the cavity is called the **blastocoel,** Fig. (4).

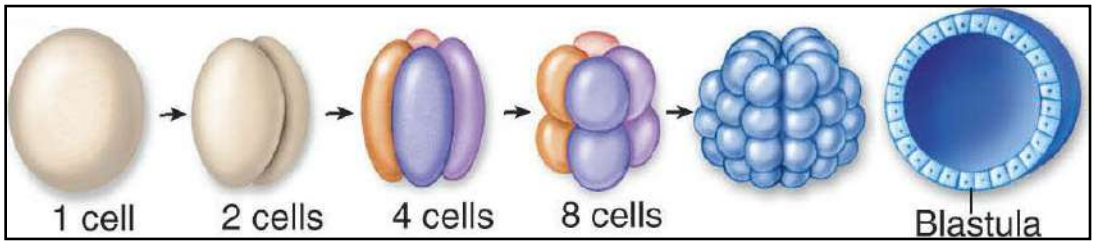


Figure-4: Stages of cleavage

In human, **First cleavage** takes place about 30 hours after fertilization, resulting in two blastomeres. **Second cleavage** occurs within 40 hours after fertilization, resulting in four blastomeres. **Third cleavage** takes place about 72 hours after fertilization, resulting in eight blastomeres, and then these blastomeres divide to form a 16-cell morula (solid ball of cells). During these early cleavages, the young embryo moves slowly down the fallopian tube towards the uterus. As the morula enters the uterus on the third or fourth day after fertilization, a cavity begins to appear called the blastocoel, and the blastocyst (hollow ball of cells) forms. 32-cell blastocyst consisting of:

1 - **The inner cell mass**, which is developed into the tissues of the embryo proper.

2 - **The outer cell mass** forms the trophoblast, which later form the placenta, Fig. (5).

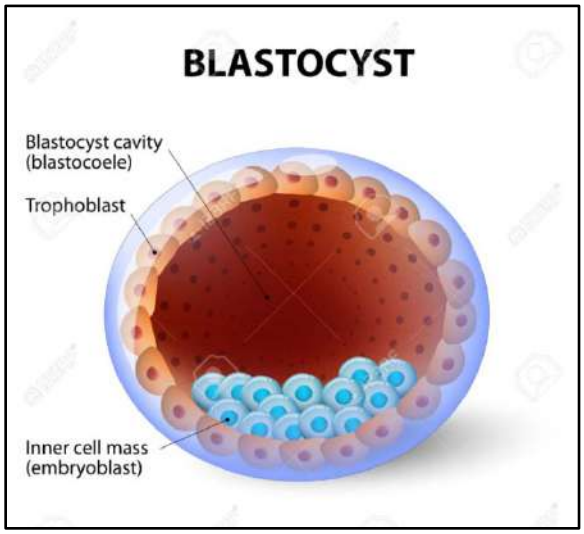


Figure-5: The blastocyst

Morula versus Blastula	
Morula	**Blastula**
1-morula is a solid ball consists of small, spherical cells formed by the rapid cleavage of the zygote.	1-blastula is a hollow structure consists of a spherical cell layer of blastomeres and a fluid-filled cavity called blastocoel.
2- form 4-5 days after fertilization	2- form 5-10 days after fertilization
3-develops into the blastula in a process called blastulation.	3-develops into the gastrula in a process called gastrulation.

Blastula versus Blastocyst	
Blastula	**blastocyst**
1- occurs in animals	1- occurs in mammals
2- the outer cell layer: blastoderm	2- the outer cell layer: trophoblast
3- dose not contain an inner cell mass	3- contain an inner cell mass
4- blastomeres or blastoderm is pluripotent	4- the inner cell mass is pluripotent

Stages of development of a human embryo

1-Gamete formation
Egg and sperm

2- Fertilization
The union of egg and sperm

- Occurs in fallopian tubes

- Fusion of egg + sperm: a new diploid zygote (2n)

3- Cleavage

Mitotic cell divisions begins, converting the zygote to a multicellular organism

Day 1: first cleavage- 1 cell becomes 2

Day 2: second cleavage- 4-cell stage

Day 3: 6-12 cell stage

Day 4: 16-32 cell stage (morula: solid ball of cells)

Day 5: solid ball develops into hollow, fluid filled blastula.

The embryo will develop from the inner cell mass or embryonic disc.

Day 6-7: blastocyst attaches to uterus (implantation)

- The blastocyst secretes human chorionic Gonadotropin (HCG).

- Pregnancy test measures this hormone.

Types of cleavage according to the amount of yolk and its distribution

1- Holoblastic cleavage

- It divides the zygote and blastomeres completely into daughter cells

Holoblastic cleavage may be either **equal** or **unequal**.

a- Equal holoblastic cleavage

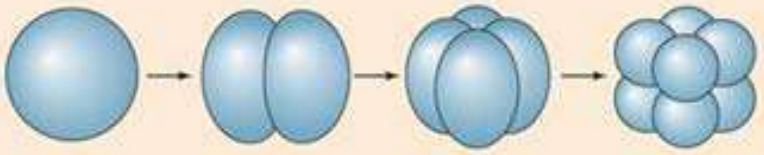
-In microlecithal and isolecithal (very little yolk, even distribution) eggs

- It forms equal blastomeres

- Occurs in *Amphioxus* and placental mammals

Equal holoblastic

Cleavage in *Amphioxus*



b- Unequal holoblastic cleavage

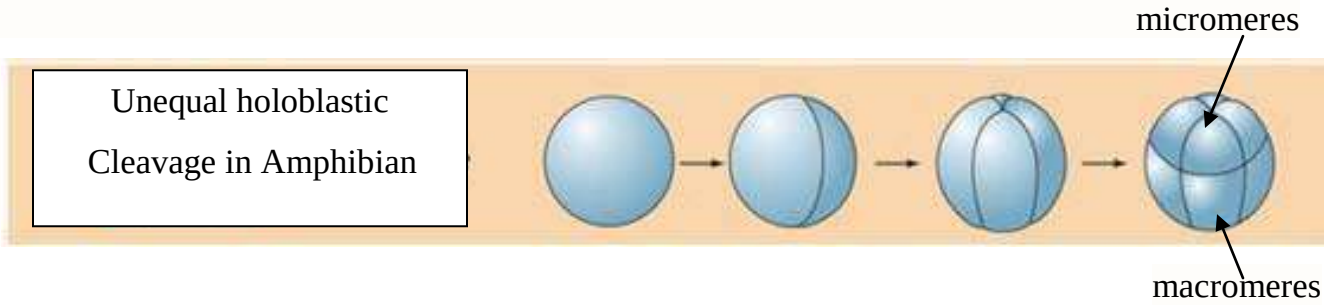
- In mesolecithal egg (moderate amount of yolk concentrated at vegetal pole) and telolecithal egg (lots of yolk at vegetal pole)

- It forms unequal blastomeres, small sized micromeres and large sized macromeres.

- Occurs in Amphibian.

Unequal holoblastic

Cleavage in Amphibian



2- Meroblastic cleavage

- Partial cleavage

- The cleavage furrows are restricted to the active cytoplasm found either in the animal pole (macrolecithal egg) or peripheral region of egg (centrolecithal egg) the yolk remains undivided. Meroblastic cleavage may be of two types: **Discoidal and Superficial cleavage,** fig. (6).

a- **Discoidal cleavage**

- In macrolecithal eggs, which contain abundance of yolk, the cytoplasm is restricted to the narrow region in the animal pole.

- Divisions are confined to the cytoplasmic disc (called germinal disc or blastodisc) at the animal pole

- Occurs in birds and reptiles.

b- **Superficial cleavage**

- In centrolecithal eggs

- The cleavage remains restricted to the peripheral cytoplasm of the egg

- Occurs in arthropods especially insects.

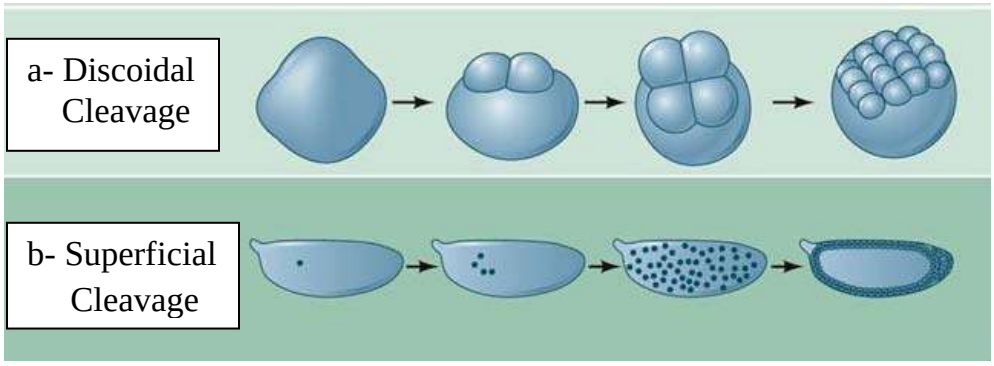


Figure-6: Meroblastic cleavage

Planes of Cleavage:

1- Meridional plane: The plane of cleavage lies on the animal vegetal axis. It bisects both the poles of the egg. Thus the egg is divided into two equal halves.

2- Vertical plane: The cleavage furrows passes in any direction (does not pass through the median axis) from the animal pole towards the opposite pole.

3- Equatorial plane: This cleavage plane divides the egg halfway between the animal and vegetal poles. It lies on the equatorial plane. It divides the egg into two halves.

4. **Latitudinal plane**: It is similar to the equatorial plane, but it lies on either side of the equator. It is also called as **transverse** or **horizontal cleavage**.

Types of Blastulae

1- Coeloblastula

- It is hollow sphere and blastocoels is filled with mucopolysaccharides and blastoderm is of single layer of cells
- Ex. Echinoderms and Amphioxus

2- Stereoblastula

-It is solid blastula because there is no blastocoels cavity
- Ex. Mollusca

3- Periblastula or Superficial blastula

- Is formed in insect eggs and there is no blastocoel in it
- The nuclei collect in the peripheral layer
- Actually cavity is present but filled with yolk from beginning of cleavage

4- Discoblastula

- Is formed in eggs of fish, reptiles and birds
- It is called discoblastula because it appears at the animal pole in the form of small multilayered flat disc separated from yolk by narrow subgerminal cavity

5- Blastocyst

- Is formed in mammals
- The small cavity called blastocoels
- The cluster of cells differentiates into two groups called trophoblast cells and embryoblast cells.

Lec. 9

Blastocyst formation

- The morula enters the uterine cavity

- Fluid begins to penetrate through the zona pellucida into the intercellular spaces of the inner cell mass.

- A single cavity (blastocoel) forms

- At this time, the embryo is a blastocyst

- Cells of the inner cell mass, now called the embryoblast, are at one pole

- Cells of the outer cell mass, called trophoblast, flatten and form the epithelial wall of the blastocyst

- Zona pellucida has disappeared, allowing implantation to begin.

- Trophoblastic cells begin to penetrate between the epithelial cells of the endometrium on about the sixth day, Fig. (3).

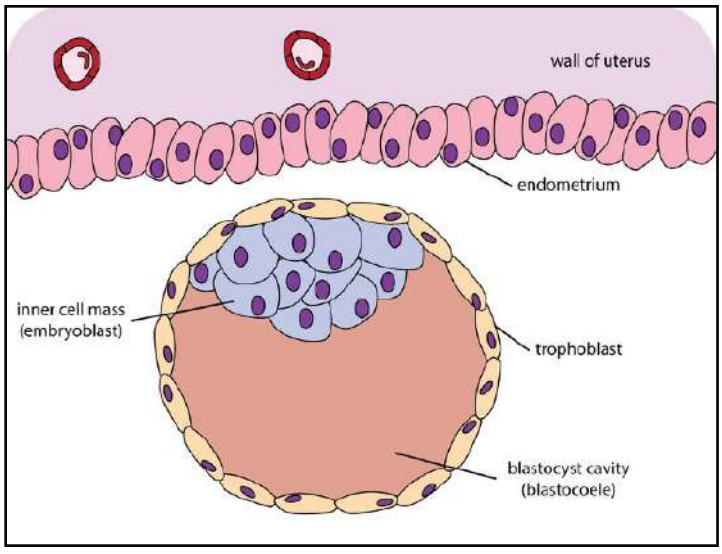


Figure-3: Human Blastocyst

Uterus at time of implantation

In human, the wall of the uterus consists of three layers:

1- Endometrium or mucosa lining inside wall

2- Myometrium, a thick layer of smooth muscle

3- Perimetrium, the peritoneal covering lining the outside wall.

From puberty (11-13 years) until menopause (45-50 years), the endometrium undergoes changes in a cycle of approximately 28 days under hormonal control by the ovaries. During this menstrual cycle, the uterine endometrium passes through three stages:

1- Follicular or proliferative phase

2- Secretory or progestational phase

3- Menstrual phase

The uterus at time of implantation is in the secretory phase, and the blastocyst implants in the endometrium. If fertilization does not occur, then the menstrual phase begins.

Second week of human embryonic development: Bilaminar germ disc

The second week of development is known as the week of 2's because:

1- The trophoblast differentiates into <u>two</u> layers:

a- Cytotrophoblast (inner layer of mononucleated cells)

b- Syncytiotrophoblast (outer multinucleated zone without distinct cell boundaries)

- Mitotic figure found in the Cytotrophoblast but not in the Syncytiotrophoblast.
- By day 9, lacunae develop in the Syncytiotrophoblast.
- Subsequently, cells of the Syncytiotrophoblast penetrate deeper into the stroma and erode the endothelial lining of the maternal capillaries. These capillaries are known as sinusoids.
- The syncytial lacunae become continuous with the sinusoids, maternal blood enters the lacunar network, and by the end of the second week, a primitive uteroplacental circulation begins.

- The cytotrophoblast, forms cellular columns penetrating into and surrounded by the syncytium, these columns are primary villi.
- By the end of the second week, the blastocyst is completely embedded, fig. (5).

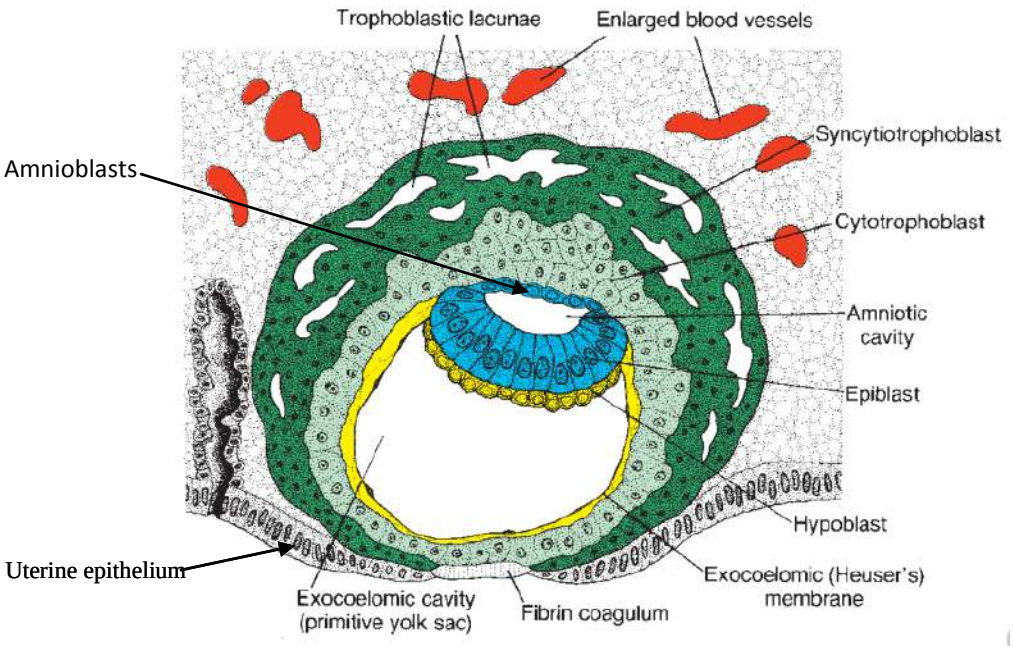


Figure-5: 9-day human blastocyst

2- The embryoblast forms <u>two</u> layers:

a- Epiblast (a layer of high columnar cells)

b- Hypoblast (a layer of small cuboidal cells)

- Together forming a bilaminar disc.
- A small cavity appears within the Epiblast, this cavity enlarges to become the amniotic cavity.
- Flattened cells originated from the hypoblast form a thin membrane called exocoelomic membrane that lines the inner surface of the cytotrophoblast.
- Exocoelomic membrane together with the hypoblast forms the lining of the exocoelomic cavity or (primitive yolk sac), fig. (5).

3- The extraembryonic mesoderm splits into <u>two</u> layers

a- Extraembryonic somatic mesoderm (lining the cytotrophoblast and amnion)

b- Extraembryonic splanchnic mesoderm (covering the yolk sac), fig. (6).

Extraembryonic mesoderm fills the space between:
- The <u>trophoblast</u> externally and - The <u>amnion</u> and <u>exocoelomic membrane</u> internally.

A cavity develops in the extraembryonic mesoderm called **extraembryonic cavity**

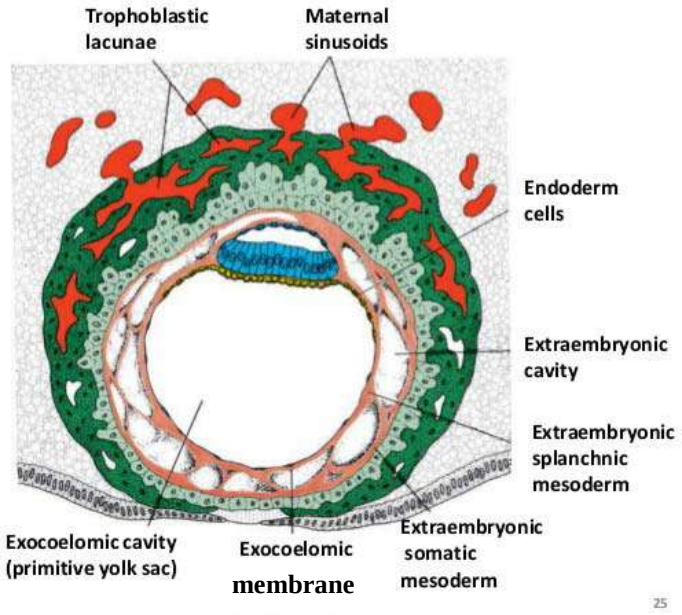


Figure-6: Human blastocyst of approximately 12 days

4- <u>Two</u> cavities form:

a- Amniotic cavity: a small cavity appears within the Epiblast. Epiblast cells adjacent to the cytotrophoblast are called amnioblasts; together with the rest of the epiblast, they line the amniotic cavity.

b- Yolk sac cavity: the hypoblast produces additional cells that migrate along the inside of the exocoelomic membrane. These cells form a new cavity called definitive yolk sac within the exocoelomic cavity, fig. (7).

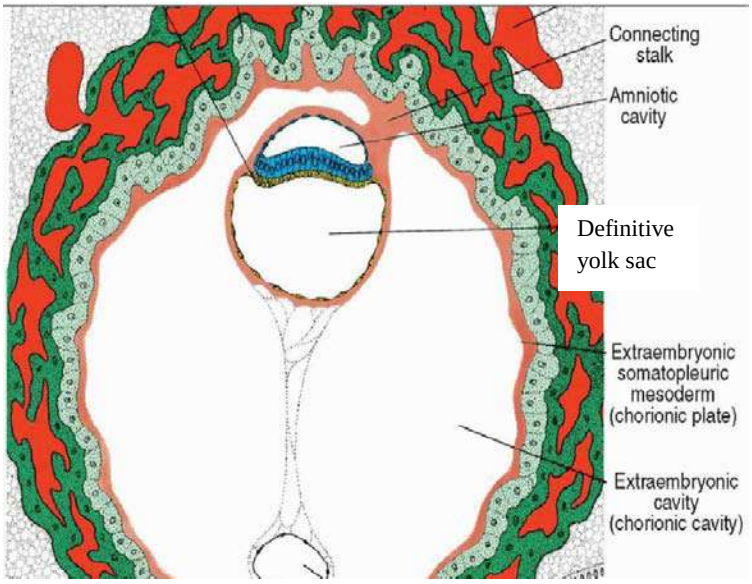


Figure-7: Human blastocyst of approximately 13 days

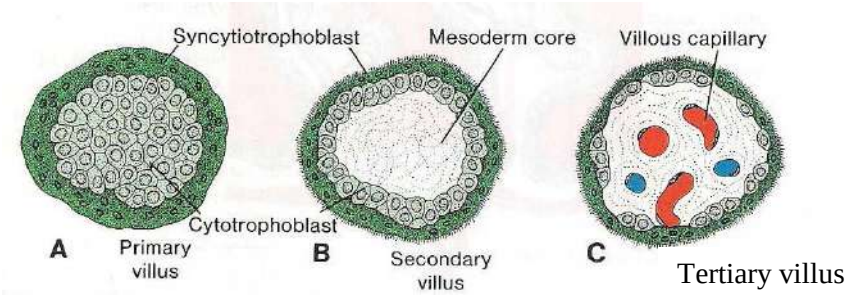
Development of the trophoblast

By the beginning of the third week, the trophoblast is characterized by:

A- Primary villi: consist of a cytotrophoblastic core covered by a syncytial layer

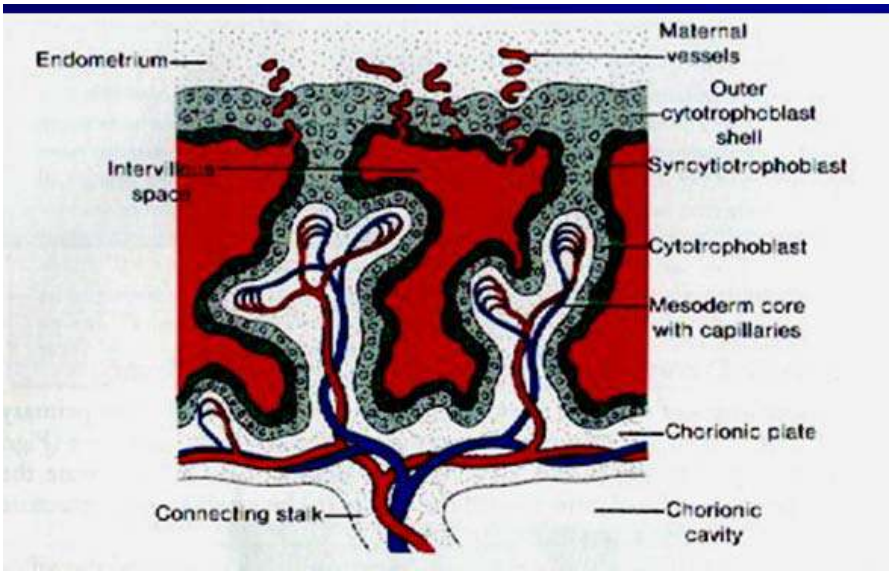
B- Secondary villi: consist of a mesoderm core covered by a single layer of cytotrophoblastic cells, which in turn is covered by syncytium.

C- Tertiary villi: by the end of the third week, mesodermal cells in core of the villus begin to differentiate into a number of capillaries and venules.



Capillaries in tertiary villi make contact with capillaries of the chorionic plate and connecting stalk. These vessels, in turn, connecting the placenta and the embryo, (see the figure below).

In human, when the heart begins to beat in the 4th week of development the villous system is ready to supply the embryo with essential nutrients and oxygen.



Gastrulation

During gastrulation, cell movements result in a massive reorganization of the embryo from the blastula into a multi-layered organism. Although the details of gastrulation differ between various groups of animals, the cellular mechanisms involved in gastrulation are common to all animals. Gastrulation involves changes in cell motility, cell shape, and cell adhesion. Gastrulation has been studied in a large variety of animal models, during gastrulation; cells undergo two types of movements, **called morphogenetic movements.** Some cells that are located on the surface of a hollow ball (in amphibians) or a flattened disc (fishes, amniotes) move through an opening to enter the embryo. In some classes of vertebrate embryos (e.g. amphibians), this movement occurs through a blastopore. In others (most amniotes), cells enter through a primitive streak, fig. (8).

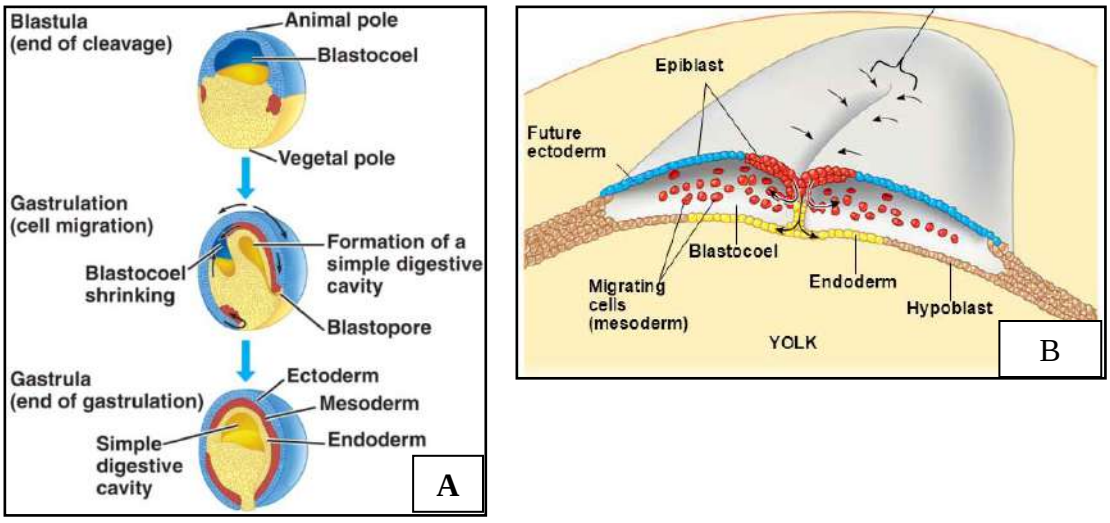


Figure- 8: (A) Gastrulation in amphibians, (B) Gastrulation in amniotes

[**The amniote** a group that includes reptiles, birds, and mammals, in which the egg is protected by amniotic membranes].

Types of morphogenetic movements that occur during gastrulation:

1- Epiboly:

- It occurs only in the ectodermal blastomeres.

- Involves the spreading of a sheet of cells (an epithelial sheet) on the surface of an embryo.

- Ex. Amphibian and Sea urchins.

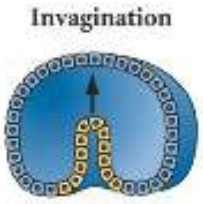
2- Emboly:

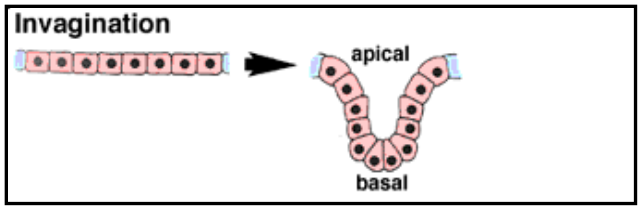
- It occurs in mesodermal and endodermal blastomeres.
- Involves the movement of individual cells or sheets of cells into the interior of an embryo
- Is classified into different types depending on the behavior of migrating cells, **these are:**

a- Invagination:

- Infolding of sheet of cells into the embryo to form a cavity.

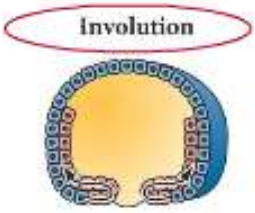
- For example: the gastrulation of Amphioxus and frog, the wall of the blastoderm is invaginated inside the blastocoel. This creates a new cavity called the archenteron (or primitive gut) which opens to the exterior by a blastopore.

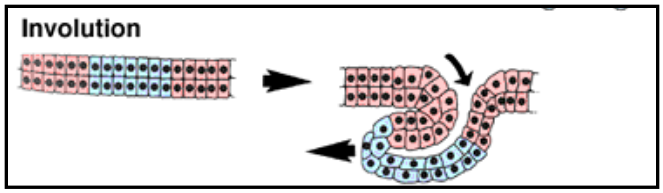




b-*Involution:*

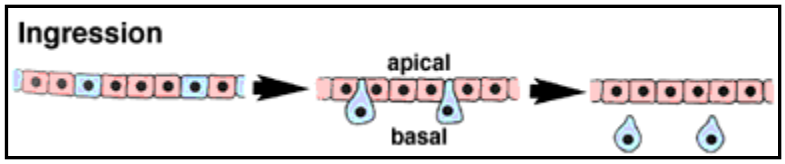
- Inward movement of an expanding outer layer (epithelial layer) to form an underlying layer.
- For example: the gastrulation of amphibian and avian eggs; from one end near the edge of the blastoderm, the cells begin to move inwards to form the inner lining of the blastoderm.





c-Ingression:

- Individual cells leave an epithelial sheet and become freely migrating mesenchyme cell.
- For example: sea urchin mesoderm.



Animals can be divided into two main groups based on the type of symmetry of their body plan:

1- Radially symmetric animals are Diploblastic

During gastrulation, diploblastic organisms form a gastrula which consists of:

1- Two germ layers (ectoderm and endoderm) but not mesoderm.

2- Coelom is absent

3- Ex. Hydra (coelenterates), Sponges (Porifera).

2- Bilaterally symmetric animals are Triploblastic

During gastrulation, triploblastic organisms form a gastrula which consists of:

1- Three germ layers (ectoderm, endoderm and mesoderm)

2- Coelom is present

3- Ex. Annelids, Arthropods, Mollusca, Echinoderms, and Chordates (common examples are Mammals, birds, reptiles, and amphibian).

Lec. 10

Third week of human development: Trilaminar germ disc

The most event occurring during the third week of gestation is gastrulation. In human, similar mechanisms regulate gastrulation to those found in other vertebrates.

By the process of gastrulation:

- Bilaminar germ disc converts into trilaminar germ disc, and embryo is referred as gastrula.
- The embryo differentiates into three germ layers: (ectoderm, mesoderm, and endoderm) and axial orientation is established in embryo.
- Gastrulation begins with formation of the primitive streak on the surface of the Epiblast
- Primitive streak visible as a narrow groove with slightly bulging regions on either side, primitive streak has at its cephalic end the primitive node.
- In the region of the node and streak, epiblast cells move inward (invaginate) to form new cell layers (endoderm and mesoderm). Cells that do not migrate through the streak but remain in the epiblast form ectoderm.
- Hence, epiblast gives rise to all three germ layers in the embryo (ectoderm, mesoderm, and endoderm), and these layers form all of the tissues and organs, fig. (1).

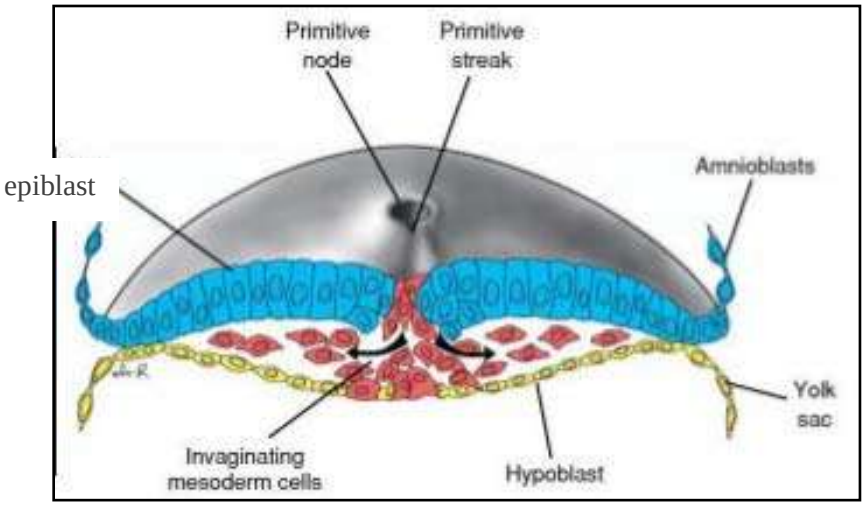


Figure-1: Cross section through the primitive streak showing invagination of epiblast cells

End product during gastrulation in vertebrate:

Ectoderm gives rise to: brain, spinal cord, eyes, peripheral nervous system, epidermis of skin and associated structures, melanocytes, and connective tissues (dermis).

Mesoderm gives rise to: notochord, muscles, skeletal system, connective tissue of skin, urogenital system, and circulatory system.

Endoderm gives rise to: epithelial linings of gastrointestinal and respiratory tracts.

Fate map established during gastrulation

Fate map of regions is established by cell migration and ingression from epiblast.

- The cells that enter in through the cranial region of the node will form the **notochord**.

- Cells migrating through the lateral edges of the node and from the cranial end of the streak will form **paraxial mesoderm**.

- Cells migrating through the midstreak region will form **intermediate mesoderm**.

- Cells migrating through the more caudal part of the streak will form **lateral plate mesoderm**.

- Cells migrating through the most caudal part will contribute to **extraembryonic mesoderm**.

Establishment of the body axis

Embryos must develop three very important axes that are the foundations of the body:

1- The anterior-posterior axis (or anteroposterior axis**)**: is the line extending from head to tail (or mouth to anus in those organisms that lack heads and tails).

2- The dorsal-ventral axis (or dorsoventral axis): is the line extending from back to belly.

3- The right-left axis: is a line between the two lateral sides of the body.

Formation of the notochord

- The notochord found in embryos of all chordates, derived from the mesoderm.

- Formation of notochord starts by appearance of prechordal plate.

- Prechordal plate is derived from some of the first cells that migrate through the node in the midline and move in a cephalic direction.

- In the prechordal plate there is a contact between the ectoderm and endoderm without mesoderm between.

- Prenotochordal cells invaginating in the primitive node move forward cranially in the midline until they reach the prechordal plate. They intercalated in the endoderm as the notochordal plate.

- With further development, the plate detaches from the endoderm, and the notochord (solid cord) is formed.

- Notochord induces the overlying ectoderm to thicken and form the neural plate.

- Notochord underlies the neural tube and serves as the basis of the axial skeleton.

Derivatives of the ectodermal germ layer

The ectodermal germ layer gives rise to the organs and structures that maintain contact with the outside world:

1- Central nervous system

2- Peripheral nervous system

3- Sensory epithelium of ear, nose, and eye

4- Epidermis of skin, including hair and nails

5- Pituitary, mammary, and sweat glands and enamel of the teeth.

At the beginning of the embryonic development, the ectodermal germ layer has the shape of a disc that is broader in the cephalic than in the caudal region. Appearance of the notochord induces the overlying ectoderm to thicken and form the neural plate, which forms the neural tube in a process called **neurulation**.

Neurulation

Neurulation is a process of neural tube formation, which is the precursor of the brain and spinal cord. Neurulation begins with the formation of a **neural plate**, a thickening of the ectoderm caused when cuboidal epithelial cells become columnar; the lateral edges of the neural plate become elevated to form **neural folds**, and the mid region forms the **neural groove**. Gradually, the neural folds meet in the midline to form a **neural tube**. As the neural folds fuse, cells at the lateral border of the neuroectoderm begin to dissociate from their neighbors, this cells called **neural crest** and will migrate to enter the underlying mesoderm. Failure of neurulation results in neural tube defects, major anomalies associated with morbidity and mortality, fig. 2.

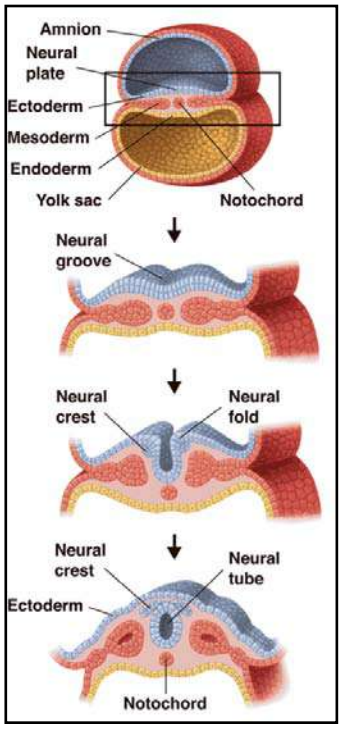


Figure-2: Neurulation process

In vertebrate embryos, neurulation occurs in two phases:

- Primary neurulation and -Secondary neurulation.

Primary neurulation, the formation of the neural plate and subsequent morphogenetic movements that transform it into a neural tube, forms the entire neural tube in amphibians and reptiles.

Secondary neurulation, the formation of an epithelial cord and neural tube, forms the entire neural tube in fishes.

Both primary and secondary neurulations occur in birds and mammals. The brain and trunk level of the spinal cord form by primary neurulation, whereas the tail spinal cord forms by secondary neurulation.

Neural crest derivatives in vertebrate

- Cranial nerve ganglia
- Septum in the heart
- Odontoblast
- Dermis in face and neck
- Spinal ganglia
- Sympathetic ganglia
- Parasympathetic ganglia of the gastrointestinal tract
- Connective tissue and bones of the face and skull
- Smooth muscles to blood vessels of the face and forebrain.
- Adrenal medulla
- Schwann cells
- Glial cells
- Meninges
- Melanocytes

Derivatives of the mesodermal germ layer

Important components of the mesodermal germ layer are:

1- Paraxial mesoderm **2-** Intermediate mesoderm **3-** Lateral plate mesoderm

Paraxial mesoderm begins to be organized into segments, known as somitomeres.

Somitomeres further organize into somites. Somites give rise to:

- Sclerotome which forms (tendon, cartilage, and bone)

- Myotome which providing the muscle component

- Dermatome which forms the dermis

Intermediate mesoderm

Intermediate mesoderm differentiates into:

- Reproductive system
- Collecting duct and tubules of the kidney
- Nephrons of the kidney

Lateral plate mesoderm

Lateral plate mesoderm splits into:

a- Somatic or (parietal) mesoderm layer **b-** Splanchnic or (visceral) mesoderm layer

Intraembryonic cavity found between these two layers.

The somatic mesoderm, which is

- Adjacent to the ectoderm
- Gives rise to: • Connective tissue and lining of the body wall
  • Bones, ligaments and dermis of the limbs

The splanchnic mesoderm, which is

- Adjacent to the endoderm
- Gives rise to: • Cardiac mesoderm
  • Blood vessels
  • Smooth muscle and connective tissues of the respiratory and digestive organs.

Intraembryonic cavity gives rise to three cavities:

- Pericardial
- Pleural
- Peritoneal

Organogenesis

Organogenesis is the process by which the three germ tissue layers of the embryo, which are the ectoderm, endoderm, and mesoderm, develop into the internal organs of the organism. Organs form from the germ layers through the differentiation: the process by which a less-specialized cell becomes a more-specialized cell type. This must occur many times as a zygote becomes a fully-developed organism. During differentiation, the embryonic stem cells express specific genes which will determine their definitive cell type. For example, some cells in the ectoderm will express the genes specific to skin cells. As a result, these cells will differentiate into epidermal cells. Therefore, the process of differentiation is regulated by cellular signaling cascades.