Embryology

Fertilization

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

- Fertilization process occurs in the amullary 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).

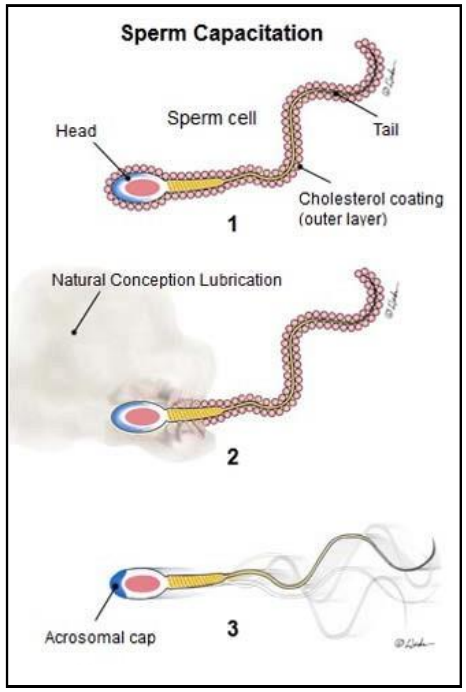


Figure-1: Sperm capacitation

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).

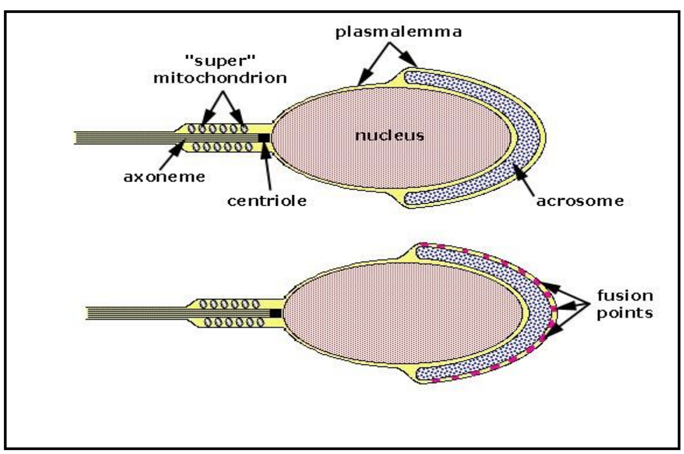


Figure-2: Acrosome reaction

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, fig.(3).

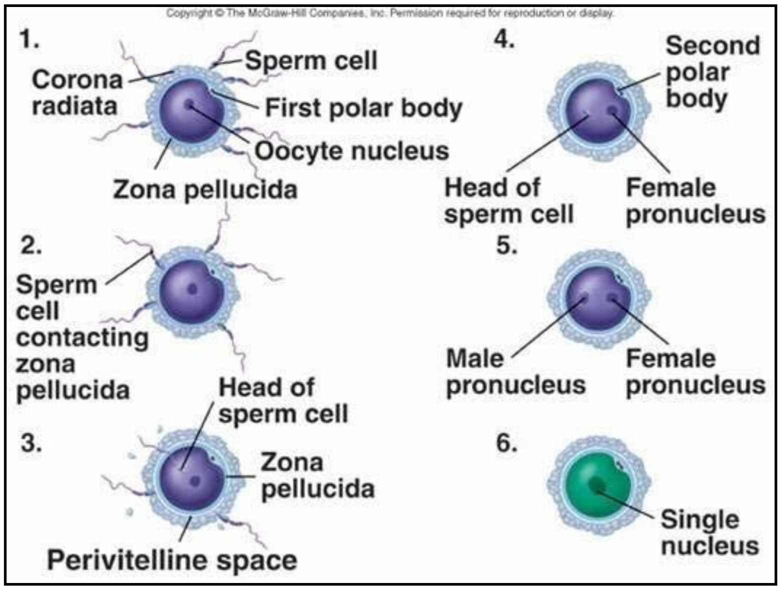


Figure-3: Activation of egg

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).

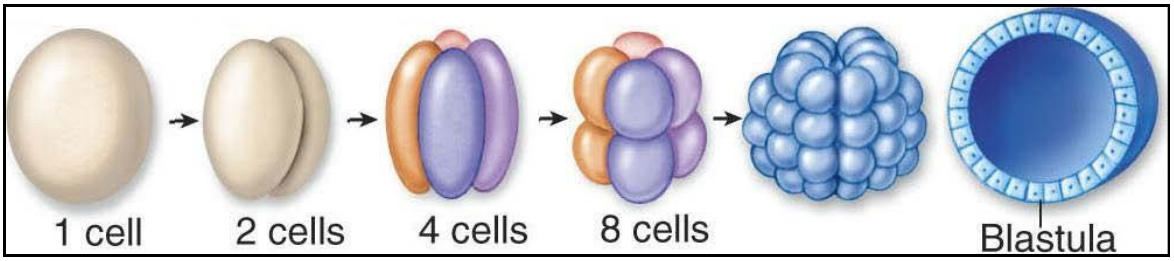


Figure-4: Stages of cleavage

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).

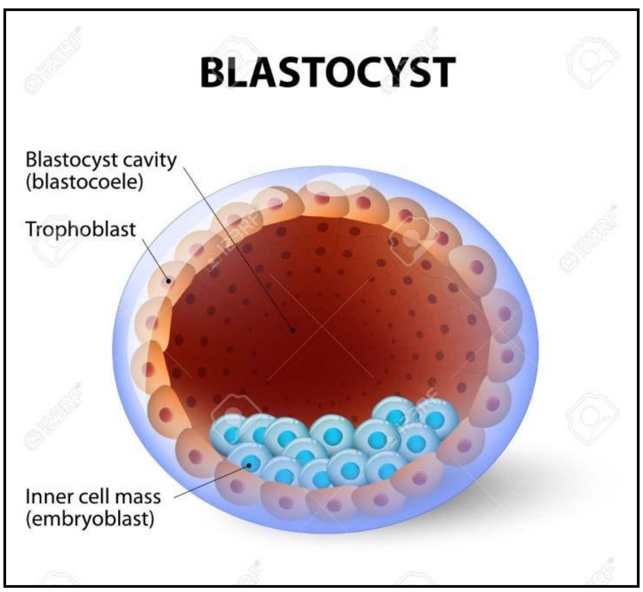


Figure-5: The blastocyst

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**.

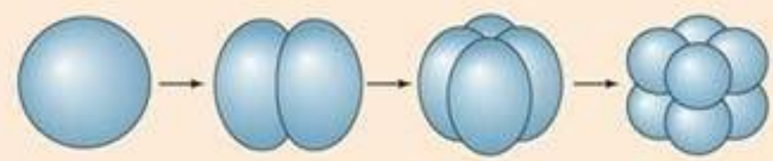
a- Equal holoblastic cleavage

-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*

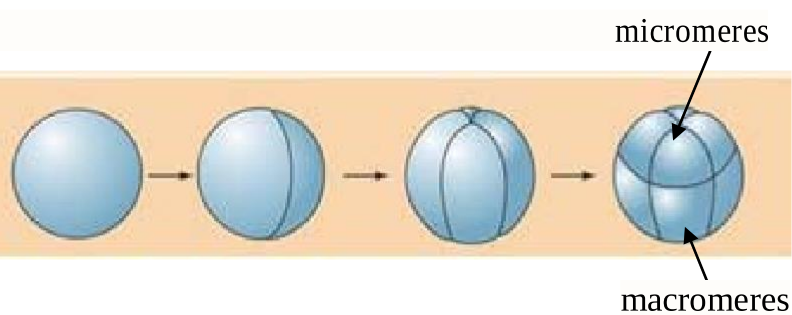


b- Unequal holoblastic cleavage

- 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.

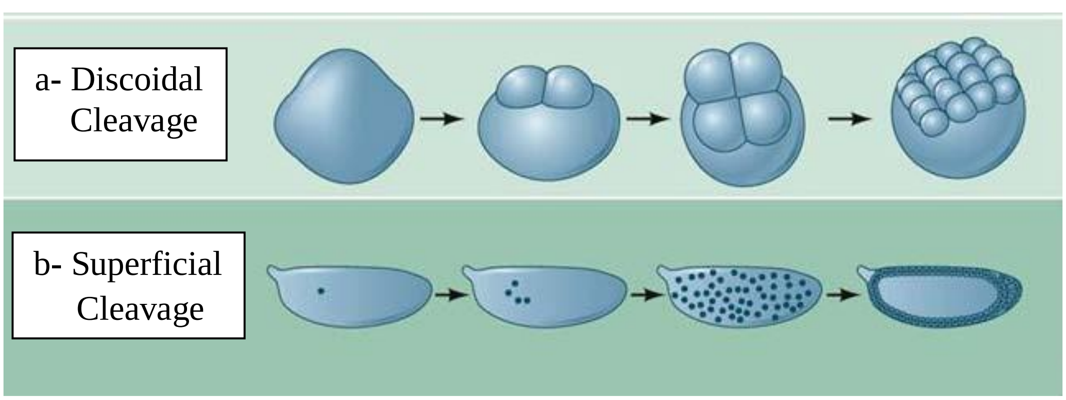


Figure-6: Meroblastic cleavage

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.

1. 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.