Fertilization

Fertilization is formation of the Zygote.

Fertilization happens in the ampulla of the fallopian tube (oviduct) or ovarian tube.

The Zygote then moves through the fallopian tube to the cavity of the uterus.

- Zero Time is an indication of Fertilization. We use time of fertilization as a way to know how far did the zygote develop until we get the implantation in the posterior wall of the uterus.



The mature ovum as it appears after ovulation (in the 14th day of the menstrual cycle) is surrounded by zona pellucida and corona radiata cells and cumulus oophorus and it is a secondary oocyte in the diplotene stage (resting stage in metaphase of second meiotic division).

Sperms "attack" the mature ovum and only one sperm penetrates the zona pellucida to enter the oocyte.

Sperms have a long journey form the vagina to the ampulla of fallopian tube in females.

In the oocyte, the corona radiata and the zona pellucida have a role in the facilitation of the penetration of the sperm; they have receptors and protein secretion that attract the sperm and facilitate its penetration. Along with other factors that facilitate the motility of the sperm and attract it to the ampulla.

Eventually, the two nuclei of the male and female (pronuclei) fuse, then they immediately perform mitosis to produce two cells with the same number of chromosomes.

So, the zygote will be a single cell with 46 chromosomes.

From this very moment, the sex will be determined.

The number of sperms in the vagina after ejaculation is large (more than 100 million and can reach 300 million), this large number of sperms allows them to push each other towards the ampulla. If their number was less than 20 million, the male would be infertile (sterile). Also, an abnormality in sperms would also affect fertility. Other factors that affect the sperm fertility are the motility and viability.

Only 1% of the sperms will reach the cervix and enter the cavity of the uterus to go through the isthmus of the fallopian tube and reach the ampulla. This trip of sperms (a.k.a: long journey) from the cervix to the oviduct requires 2 hours minimum and 7 hours maximum.



As you see in the picture above of a sperm and a mature ovum, the sperm initially passes between the corona radiata cells and then pierces the zona pellucida.

Capacitation: is considered to be a period of conditioning and care in the female reproductive tract (uterine tube) that lasts about 7 hours in the human being. And includes changes that increase the power of the sperm to penetrate the zona pellucida, and is gained from the wall of uterine tube or the mature ovum itself.

Changes in capacitation include:

- 1- Changes in the epithelial cells and mucosa of the uterine tube;
- 2- Glycoprotein coat and seminal plasma protein are removed (Dissolved) from the plasma membrane overlying the Acrosomal region.
- The acrosome is a type of glycoprotein wrapping the head of the sperm.

<u>The capacitated sperm is the only sperm able to go through the corona radiata cells and penetrate the zona pellucida</u>



The zona pellucida has zona protein receptors that provide attraction to the capacitated sperm only, then activates penetration.

Acrosomal reaction, which occurs after binding to the zona pellucida, also helps to increase the capability of the sperm to penetrate the zona pellucida.

Sometimes, the reason for infertility is that the sperm has no capacity nor capability to perform the Acrosomal reaction to penetrate the zona pellucida. In such cases, certain medications will be given which will encourage penetration.

*This is why we should go back to the roots of the problem in order to solve it! (إذا عرف السبب بطل) العجب)

Phases of Fertilization

We can put the fertilization or penetration into three phases:

Phase 1: Penetration of corona radiata;

Phase 2: penetration of zona pellucida;

Phase 3: Fusion of Oocyte and sperm cell membrane.

We have about 200 million or 300 million spermatozoa deposited in the female gentile tract (Fornix of the vagina), but only 200 to 300 reach the site of fertilization (ampulla), and amazingly only one of these sperms fertilizes the egg.

Why? The protein receptors that attract sperms on the zona pellucida stop their action once one of the sperms penetrates, also to prevent any other sperm from entering to the ovum (polyspermy), the zona pellucida changes its structure.

A student asks: What about Twins Case?!

Professor Mohtasib: What we're talking about stands very far from twins. Identical twin case originates from the Zygote's division (One Zygote divides into 2 cells where each cell grows into an embryo identical to the other) here we're considering the development of 1 embryo only [Which is considered more healthy]

A note from the writer of the sheet: "According to what I think you have on mind, if more than one sperm fertilizes the egg we will have a triploid nucleus (1.5 times more DNA than a normal Zygote nucleus= 69 chromosomes)" which is abnormal so the mother will undergo (Abortion) إجهاص مبكر

Phase 1: Penetration of corona radiata:

The capacitated sperm tries to make its way between the corona radiata cells and passes freely.

- Note in the picture below: Sperm head and the acrosome (coat on the outside), Midpiece containing mitochondria for providing energy. Protein receptors on the zona pellucida and cortical granules inside the zona pellucida



Phase 2: penetration of zona pellucida:

After contact with the zona pellucida, the acrosomal reaction is generated.

The acrosome of the sperm starts: Dissolving (disappears), and secreting lytic enzymes (hydrolytic enzymes) which dissolve a layer of the zona pellucida.

Then penetration is done.

Zonal reaction: when the head of the sperm comes in contact with the oocyte surface, the permeability and characteristics of zona pellucida are altered as mentioned before by cortical granules to prevent sperm penetration and inactivate species-specific receptor sites for spermatozoa on the zona surface.

(We can find other sperms surrounding the ovum and probably embedded in the zona pellucida but never penetrate the oocyte, only one sperm is allowed to do so.)

This means that capacitation occurs frequently while penetration only takes place with one sperm.

Phase 3: Fusion of Oocyte and sperm cell membrane:

Both head and tail of the sperm make their way through, the tail faces disintegration and degeneration, and remains the head of the sperm which has the nucleus [Most important part]



Also, we have to know that this is a secondary oocyte in second meiotic division, once penetration, fusion and fertilization have taken place the cell has to go through meiosis II.

In Detail:

After adhesion, the plasma membranes of the sperm and egg fuse.

Because the plasma membrane covering the acrosomal head cap disappears during the acrosome reaction, actual fusion is accomplished between the oocyte membrane and the membrane that covers the posterior region of the sperm head.

In the human, both the head and tail of the spermatozoon enter the cytoplasm of the oocyte, but the plasma membrane is left behind on the oocyte surface.

After swelling and adhesion the nuclei come to division (D), a zygote performing mitotic division giving a two-cell stage. (Zero Time)

If we take a close look we have a second stage division where these 2 cells undergo swelling and adhesion then continue the division resulting in a zygote which takes place in a mitotic division going through 2 cells stage, shape (F) in the picture, forming Identical twins.

But if the cell carries out normally where the zygote gives 2 cells, the 2 cells divide giving me 4 cells and divide again giving 16 cells (cleavage).

If the cell didn't go through the cleavage phase and each cluster was implanted on the uterine cavity wall we will have Identical twins.

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As soon as the spermatozoon has entered the oocyte, the egg responds in three ways:

1- Cortical and zona reactions:

Read slide number 9, please

2- Resumption of the second meiotic division:

The oocyte finishes its second meiotic division immediately after entering of the spermatozoon the cytoplasm of the oocyte

One of the daughter cells gives off the polar body, the other daughter Cell gives off the secondary oocyte [Mature Secondary] made up of 22 chromosomes + X (female).

In the male pronuclei, however, will be made up of 22 chromosomes + X, which results in a female zygote, or 22 + Y, which results in a male zygote.

3- Metabolic activation of the egg:

Protein and glycogen increase in the cytoplasm of the egg.

Read slide number 11, please

Cells become indistinguishable (become very closely related in characters).

Both cells (Female & Male) lose their nuclear envelope and enter Mitotic division.

Tip: Before mitosis takes place the cell has to go through the duplication of nuclei [DNA];

Since one cell will give out two cells and so on, we have to have 46 chromosomes in each cell where we have 23 of these chromosomes Maternal and another 23 chromosomes Paternal;

Maternal: from Mama [Mother] Paternal: from Papa [Father]

These chromosomes come into longitudinal arrangement connected by a centromere, where every chromosome is made up of sister chromatids, at final stages the sister chromatids are separated each goes to and opposite pole and a division of 2 cells will be formed off mitosis.

Result of fertilization:

Read slide number 13, please

- Restoration of the diploid number of chromosomes. Hence, the zygote is a new creation and a new combination since its genes are an even combination of Maternal and Paternal characteristics, as well as the new characteristics gained by the cross over

- Determination of the sex of the new individual.

- Initiation of cleavage.

Cleavage: A series of mitotic divisions and increasing the number of cells that take place once the zygote reaches the two cell stage immediately after fertilization, we get an action of mitosis and repetition of mitosis.

Where 2 Cell stage results which will be followed by 4 cell stage then 8 then 16.

And the 16-cell stage is named a morula, the morula sticks with its initial size but the smaller portion of it is called a blastomere which is a part of the morula.

The morula isn't only a 16 cell structure, 32 cells are called a morula, 64 cells are considered a morula, the only difference between one morula and another is the size of the blastomere evolved where each division increases the number of morula cells but decreases the size of the blastomere.

The 2nd cell stage is evolved a few hours after fertilization and zygote formation.

4th cell stage is said to be 30 to 40 hour after zygote formation.

Until 8th cell stage this cell accumulation is named a clump.

The morula requires from 3 to about 4 days after fertilization to evolve and 5 days until implantation takes place. And at the 5^{th} day it is free in the uterine cavity and it is directed to it by cilia of the uterine tube. This cilia moves in one direction towards the cavity of the uterus, so this movement is considered a helping factor to push the zygote to the uterine cavity.

All these are compared to the Zero time [Time of fertilization].

- If Fertilization doesn't take place, degeneration of the egg will take place approximately 24 hours after Ovulation. [It takes 48 hours for a mature ovum to degenerate]

After the morula grows and multiply (divides) we will get a blastocyst; a cavity inside or between the blastomere of the morula, containing a fluid, and most of the cells migrate to one pole which we'll name (inner cell mass or Embryonic pole) mainly made up of blastomere cells. This accumulation of the blastomere cells as a heavy mass indicates that the endometrium is the site of implantation and causes contact with the endometrium while other cells are arranged to the outside (Trophoblast cells) at the edge of the blastocyst.

Trophoblast is known for:

. In the future stages it will turn into a chorion which is an early stage placenta.

. The trophoblast on the side of the inner cell mass will turn out into a senseteo trophoblast which will release Human chorionic gonadotrophic HCG hormone which is the first hormone indicating pregnancy.

Start of implantation takes place on day 7 after fertilization.

While complete implantation at the end of day 9 or beginning of day 10.

Be careful! these scientific experiments are done on both humans and animals.

Did you realize that at the beginning the Dr. used to say zona pellucida remains around the morula and disintegrates before implantation now he says [On the fifth day where the zygote reaches the cavity of the uterus] once zona pellucida disappears the endometrium is penetrated and implantation occurs.

(Can either say end of fifth day or sixth day, both indicate same thing.)



Trophoblast turns into invagination creating cynsetio trophoblast while the trophoblast will remain on the outer cell mass.

The cynsetioblast is the structure which secretes HCG hormone (Human chorionic gonadotrophic hormone).

Inner cell mass is called "embryoblast" which is on one fold, while the outer cell mass is called a trophoblast it is flattened epithelial cells.

The disappearance of zona pellucida, allows implantation to begin.

Implantation starts at day 7 (Superficial implantation) and is completed at the end of day 9 or at Day 10 (complete implantation).

The normal site of implantation is on the posterior wall of the body of the uterus or sometimes anterior.

Case study: Cervical embryo implantation:

After the zygote is implanted on the cervix of the uterine body the placenta will form but in this case the placenta will be called (Placenta previa), so when the baby grows the pathway is blocked, so when the doctor checks this case out, the patient will require special treatment.

She has to give birth before her due date.

She has to give birth caesarean operation.

Visit the doctor very often all through the pregnancy because she's endanger of excessive bleeding from cervical collapsing.

The doctor continues to read the last slide

Changes in trophoblast doesn't take place spontaneously it's regulated by a specific type of protein secretions controlling changes of blastocyst and arrangements.

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