# Implantation and bilaminar germ disc

Summary of previous lecture (about fertilization)

Oocyte is fertilized in the lateral third (or ampulla) of uterine tube.

Zygote undergoes cell division (mitotic divisions) which is the cleavage and then moves towards the uterus by the help of cilia of fallopian tube.

The morula is formed by successive mitoses (cleavage) 3 or 4 days after fertilization, and it stays in the fallopian tube until the 5th day where it moves to the uterus.

The morula is covered by zuna pellucida and it's about the same size as fertilized oocyte. The cells inside are called blastomeres, and since the zygote (morula or fertilized egg) doesn't grow in size, at each division the blastomeres increase in number but they become smaller in size.

At the center of the morula a liquid-filled cavity develops and the blastomeres arrange themselves in a peripheral layer called trophoblast, while a few blastomeres accumulate inside the cavity forming the inner cell mass.

The embryo is called a blastocyst when it arrives to the uterus at the 4<sup>th</sup> or 5<sup>th</sup> day after fertilization (not after ovulation as written in the slide).



The zygote has a nucleus inside that contains the hereditary factors and an alarm that is similar to our alarms, thus everything is programmed in the nucleus with the organization of factors, so just like when your alarm goes on at 3 o'clock for instance and you wake up and start doing the things you planned for, this happens in the zygote for 9 months; each specific time there is a change due to factors, enzymes, proteins or hormones secretion. This way, the inner cell mass, the trophoblast and the blastocyst cavity are formed. In the 5<sup>th</sup> day after fertilization, the morula should arrive the cavity of uterus and the inner cell mass is formed and goes to one pole of the blastocyst because the implantation starts from it.

Keep in mind that all the changes we will talk about are programmed and any change in this programming would cause abnormalities in the fetus. For example if the blastocyst didn't arrive on the 5<sup>th</sup> day, implantation wouldn't happen and that would cause abortion.

From the picture: Fertilization is at day 0 Formation of the morula is at Day 3 to 4 Arriving to the cavity of uterus: at Day 5 Superficial implantation: at Day 7 Complete implantation: at Day 9 or 10



We'll talk about implantation from the  $7^{th}$  day to  $9^{th}$  or  $10^{th}$  day

Changes of the trophoblast occur, to have the ability to penetrate the endometrium for the implantation of the blastocyst. The endometrium is also prepared by the progesterone hormone secretion to be thicker and receive the blastocyst. Those are examples of proteins secreted either from the blastocyst or endometrium:

Integrin receptors for laminin which promotes attachment, while those for fibronectin stimulate migration. These molecules also interact along signal transduction pathways to regulate trophoblast differentiation (it transforms to synsytiotrophoblast and cytotrophoblast due to protein secretion as we'll see later) so that implantation is the result of mutual trophoblastic and endometrial action.

From the picture, we see the epithelial cells of the endometrium and the endometrium glands. There is a decidual reaction which means the endometrium- in the place of implantation- has its glands dilated and filled



with glycogen and protein, and this secretion has fluid for the nourishment of the blastocyst and for the growing of the fetus, that's why it is called edematous endometrium. (Just like how seeds need to be planted in a moisturized wet soil to grow)

Decidua: endometrium which is related to blastocyst only (not all the endometrium, just the sight of implantation)

Before implantation zuna pellucida dissolves and disintegrates, that is in the end of day 5 or at the beginning of the 6<sup>th</sup> day.

The trophoblastic cells invade the endometrium by a process of histolysis (i.e. there is an enzyme that lyses only a small opening which is related to the inner cell mass by which the blastocyst can enter , and after complete implantation it regenerates and the endometrium is closed).

The first part of the implantation is called embryonic pole, and the last part implanted is called abembryonic pole.

**Important:** The difference between synsytiotrophocblast and

cytotrophoblast: is that the cytotrophoblast has distinct boundaries between the cells, and mitotic characters. While the synsytiotrophoblast has no boundaries and no mitotic characters( no division or mitosis), it is formed from the cytotrophoblast; that is the cytotrophoblast gives synsytiotrophoblast in a specific region and it loses its characteristics ( becomes with no boundaries nor mitotic characters).



This is because the function of the synsytiotrophoblast is different which is the invasion of the endometrium to form the placenta in the future, and it secretes the human chorionic gonadotrophin (HCG) (some books say it's secreted by the trophoblast which is correct since the synsytiotrophoblast comes from the trophoblast, but to say synsytiotrophoblast is more precise). This is called superficial implantation ( at the end of the 6<sup>th</sup> day , the beginning of the 7<sup>th</sup> day). Now when we talk about the embryo , we mention two things; the changes of the blastocyst and the changes of the endometrium.

The inner cell mass also differentiates into two layers:

Epiblast: which is primary ectoderm, simple columnar cells.

Below it is the hypoblast which is primary endoderm and its cells are small simple cuboidal. The blastocele is below it, in the future it will give the primary yolk sac.

• When we say primary that means that there is another stage that will give the secondary layers.

The two layers (Epiblast and hypoblast) are called bilaminar germ disc or embryo( this is the beginning of the emryo).

Within the epiblast appears an important cavity <u>called Amniotic</u> <u>cavity</u>, and in the future it will enlarge to surround the whole emryo, it also contains the amniotic fluid that covers the fetus. When the baby is born an amount of fluid is seen, this is the amniotic fluid.

The cells surrounding the amniotic cavity are called amnioblast cells that come from the cytotrophoblast ( the cytotrophoblast surrounds the whole blastocyst from all sides)

A question was asked: the mesoderm is formed later in the 3<sup>rd</sup> week of development between the two layers.

On about the ninth day after fertilization, the embryo is totally submerged in the endometrium, from which it will receive protection and nourishment during pregnancy from endometrium. So on the 9<sup>th</sup> or the 10<sup>th</sup> day the opening is closed by a fibrin clot and the epithelium regenerates.

Finally, the whole embryo is embedded in the endometrium. Eventually, the syncytiotrophoblasts come into contact with maternal blood and form <u>chorionic villi</u>. This is the initiation of forming the placenta, which is formed in the 5<sup>th</sup> month of the embryo's age.

The umbilical vessels are formed in the <u>connecting stalk</u> which provides a connection between the placenta and the embryo.

The endometrium has vascular lacunae (spaces where the blood comes from the mother), the chorionic villi then undergo processing towards these vascular lacunae and form the umbilical vessels to connect between the placenta and the embryo.

The placenta consists of two parts :

a) Chorion: a wall in the blastocyst, the part coming from the emryo.

b) Decidua basalis : in the posterior wall of uterus where implantation happens, the part coming from the endometrium (maternal part of the placenta), thickened, edematous, with glycogen and protein, opposite to it vacuoles and blood vessels they are tortuous and engorged with blood for the formation of placenta.

Decidua capsularis: covering the embryo from the other side (anterior wall) like a capsule.

Decidua marganalis: on the margins

Decidua parietalis: away from the fetus but in the uterus wall.

The placenta is also an endocrine organ, producing hormones such as HCG, a placental prolactin (helps breast formation of milk), estrogens, and <u>progesterone</u>(secreted by corpus luteum of pregnancy but in the 5<sup>th</sup> month the corpus luteum stops secreting the hormone, and it's secreted by the placenta).

Hence, by the end of the first week of development, the human zygote has passed through the morula and blastocyst stages and has begun implantation in the uterine mucosa.

Second week:

<u>At day 8</u>:

In the picture notice the hypoblast , the epiblast, the amniotic cavity above and the cells surrounding it called amnioblasts, Syncytiotrophoblast that invade the endometium and cytotrophoblast.



The hole is still open on day 8 and it's closed on day 10. Some changes are noticed on day 8; the embryoblast differentiation( epiblast and hypoblast), the trophoblast differentiated to two layers (cytotrophoblast and synsytiotrophoblast), the amniotic cavity and amnioblasts( cells adjacent to cytotrophoblast) formation.

The endometrial stroma adjacent to the implantation site is edematous and highly vascular. The large, tortuous glands secrete abundant glycogen and mucus.

### <u>Day 9:</u>

The amniotic cavity enlarges, the hypoblast cells are clear, cytotrophoblast have mitosis and some transform to syncytiotrophoblast. Excess of cells lining the cytotrophoblast forming <u>exocoelomic (Hauser's) membrane</u> : growing (development) from the hypoblast cells lining the cytotrophoblast. Lacunar stage: Synsytiotrophoblast has trophoblastic lacunae (named according to its place since the synsytiotrophoblast is originally from the trophoblast) and near it maternal blood vessels, so the blood can enter the lacunae and supplies the embryo.

#### Day 11 and 12

Epiblast is the primary ectoderm, hypoblast is the primary endoderm, exocoelomic (Hauser's) membrane, cavity called extraembryonic ceolom. Synsytiotrophoblast receives maternal blood called maternal sinusoids "Joyoob Damaweyah" from the mother that filled the trophoblastic lacunae.

Extra embryonic splanchnophleuric mesoderm (inner), extra embryonic somatophleuric layer (outer) and between them is the extra embryonic cavity or chorionic cavity.

## Infertility or sterility

Could be in males or females, but when a married couple come (they are only accepted after at least 2 years of their marriage because she might be pregnant during this period) the male is diagnosed first, he is asked to do semen analysis ( for the fluid of males containing the sperms) the number of sperms is important and it should be more than 20 million (less is considered infertility), and to have a high ability for fertilization the number should be more than 60 million (usually 100 million,200 or 300 million), this is because there is a long journey for the sperm from the ( vagina to cavity of uterus, fallopian tube to ambulla), capacitation for number of sperms( passing through corona radiata) then zunal reaction and acrosomal rection, then penetration of zuna pellucida. Sperms should be motile and viable (some sperms could be dead or have abnormalities like 2 heads or 2 tails). Infertility in females:

No ovulation (it is important in the 14<sup>th</sup> day of menstrual cycle). Closed fallopian tube due to infection in the lower abdomen, the mucosa adheres to each other so the sperm wouldn't be able to enter. If the fallopian tubes were tied there would be no pregnancy at all and it could be reversed surgically.

Note: tiding the fallopian tube of a female would make her infertile and this is what is known as "rabt el-mawseer in Arabic", and tubal ligation in English

A student asked: Why is the number of sperms varies normally?

The answer: many causes; genetic, radiation, some chemical weapons.

Occluding of oviduct (due to inflammation), cervical mucosa (inflammation of cervix) preventing the sperm to pass upwards.

These days a medicine could be taken so that the ovum gives more than one mature ovum.

vasectomy: the vas deferens is tied so that the male becomes infertile. (ligation of vas deferens for males).

In vitro fertilization (IVF): these days there is no need to worry about asospermia (no sperms at all in the fluid) since they take one sperm from the wall of the testis and puts it on a mature ovum, fertilization happens and then they implant it in the uterus, so she becomes pregnant. There is a unit for IVF in the JU hospital <sup>(2)</sup>. The guaranteed stage for the fertilized egg is the 8 cell stage and then it is implanted.

#### The contraceptive methods:

The contraceptive pills for females: a combination of estrogen and the progesterone analogue progestin, which together inhibit ovulation but permit menstruation.

Ectopic pregnancy: Implantation outside the uterus. Either in the fallopian tube, in the ovary (no ovulation and the sperm enters the ovary), or after the fetus formation it drops to the abdominal cavity and adheres to the peritoneum.

<u>Placenta previa:</u> implantation on the cervix (lower part of the body of uterus) block of canal of cervix and the delivery should be a cesarean section.

Good luck

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