Human Physiology
Dr. Sudip Mukherjee
School of Biomedical Engineering
IIT(BHU), Varanasi
Week - 09
Lecture - 04

Hello, welcome to another new class on human physiology. In this class, we will start with the ovarian cycle, mainly discussing the female menstrual cycle, and as you know, in the female menstrual cycle, we have two different cycles: one is the ovarian cycle and the second is the uterine cycle. So, in the next few classes, including today's class, we will discuss the ovarian cycle. So, let us stay with it. So, what different content will be covered for this class? So, we will cover the concept of oogenesis. We will then discuss embryonic developments and germ cells.

We will see how the cells differentiate into oogonia. We will discuss the proliferation stages by mitosis, then we will discuss follicular cells and germ cell clusters. We will discuss meiosis, the formation of primordial follicles, and provide a brief overview of ovarian maturation steps in the ovarian cycle. So, let us discuss them one by one.

So, what is basically oogenesis, as we know "oo" means basically egg, right? So, "oo" means basically egg, and "genesis" is basically like formation, right? So, genesis basically means formation. So, this is basically like egg formation. So, in the female body, after a certain time, basically when the female body attains puberty, we have a particular cycle that happens every month. and where the immature egg eventually converts to a matured egg, and after ovulation, the egg awaits the sperm to enter in case fertilization happens. So, this whole step from starting with egg development to egg maturation is kind of called oogenesis along with the ovarian cycle.

So, basically, the process by which female gametes are formed can be called oogenesis, and one thing to remember is that it does not start at puberty. It starts with the fetal development of the baby girl, and we will see how it happens, but you have to remember that it starts long before, whenever there is embryonic development or fetal development, as the female baby oocytes start developing very early, well before the girl is born. So, this is very crucial to remember, and as you recall, we discussed during the female reproductive class that what we have is, like, in females, we have two ovaries, right? So, in females, we have two ovaries, and each ovary has a certain number of eggs. We will discuss how many eggs there are. But each cycle, each of the ovarian cycles, a certain egg will eventually start the ovarian cycle state.

And the process of maturation will happen, and via ovulation, the matured egg will be released into the fallopian tube area. So, let us see how embryonic development and germ cells occur. So, what we just said is that this process starts long before puberty. So, in the case of a female body, it starts during fetal development around 3 to 4 weeks after the formation of the female embryo. At that time in the female body, let us consider that there are a lot of germ cells present in the female fetus, and exactly around 12 to 14 million germ cells are present.

These are basically like stem cells. So, these are basically like different types of stem cells that are present in the female embryo, and what happens is that these primordial germ cells eventually slowly migrate to the ovary of the female. So, what I just said is that about 12 to 14

million initial primordial germ cells, right? They are initially kind of a stem cell type; they get differentiated, and initially those germ cells move towards the female ovary, where the initial step of differentiation happens. So, from the initial stem cells or the primordial germ cells, the cells get differentiated into a cell called oogonia. So, what happens to the primordial germ cells when these cells move to the female ovary during the first 4 to 5 weeks of embryonic formation? They are in the ovary, and the first stages of differentiation initiate, forming the oogonia, which are basically the precursors of the oocytes.

Let us see, once this Ogonia formation happens, you will see a lot of Ogonia clusters, and as we said, initially the primordial germ cells were there; they migrated to the female ovary, and the process of differentiation basically caused the formation of the Ogonia. And this Ogonia starts to rapidly generate and divide by the process of mitosis. So, the rapid proliferation of this Ogonia occurs, and eventually, a lot of clusters of Ogonia cells can be seen forming inside the ovary, right? This happens very rapidly and exponentially. And after some time, you can see this Ogonia. So, on top of the Ogonia, there is another layer of this green cell, which is also called follicular cells.

So, this formation of the follicular cells initiates. So, after the initial germ cell cluster or the agonial cell cluster, each agonal cluster eventually gets surrounded by a new cell layer called follicular cells, which are basically somatic cells of ovarian origin. They have a highly loaded variety of important functions; basically, they support and interact with Ogonia and later oocytes. Along with that, they secrete a factor called the OMI, or oocyte maturation inhibitor. So, basically after mitosis, these follicular cells, like oogonia cells, enter an arrest phase.

We will discuss how they get into the arrest phase, but these follicular cells eventually secrete a factor called OMI, or oocyte maturation inhibitor, which basically stops the meiosis state and puts these cells into an arrested condition. So, we will see how it goes. So, as we said, whenever the initial mitosis happens and a lot of agonium clusters form, slowly the agonium clusters will get covered by the follicular cells, and what happens is that some of these follicular cells start to enter the arrest phase. So, some of these follicular cells start to become arrested, after the mitosis where they form the ogonium cluster, and eventually when this primary oocyte forms after the follicular cells wrap around it. So, basically, initially it was the ogonium, and from the ogonium, the primary oocyte forms.

In the primary oocyte form, many of these old agoniums start to degenerate, and some of the agoniums eventually complete mitosis and enter meiosis one step. But because these FSA follicular stimulating cells or these follicular cells secrete a factor which is OMI or the oocyte maturation inhibitor. What this oocyte maturation inhibitor does is basically erase this primary oocyte in this meiosis one step. So, they are unable to complete meiosis one step, and then they get arrested here. So, to recapitulate what we just said: some of the oocytes start to degenerate, but those few oocytes from the primary oocyte complete their mitosis, enter the meiosis one step, and due to the presence of the OMI, maturation inhibitor factor, which is secreted by the follicular cells.

These are the follicular cells that are secreting the OMI, or the oocyte maturation inhibitor. As a result, the majority of these, like the primary follicular cells, get arrested; they get arrested in the meiosis I phase. If you want to know exactly which phase of meiosis I, it is the prophase I phase of meiosis I. So, basically, in prophase 1 of meiosis 1, they get arrested. And eventually, what we are left with is that some of the agonia got into the arrested phase.

We are still left with a lot of primary kinds of agonium, right? We are still left with a lot of primary agonium, but we said that a lot of this initial agonium starts to degenerate via the process of apoptosis, which is programmed cell death. So, basically, a lot of agonium now starts to die and degenerate. So, once they start to die and degenerate, what we will leave with, we will basically leave with some of the primordial follicle. So, primordial follicles were initially those arrested oocytes, which had a wrapping; these were primary oocytes that were in the arrested condition and had wrapped follicular cells. So, these are basically represented here; if we zoom in on one of these cells, you can see this forms the primordial follicle cell.

So, basically, it goes into the arrested phase; right, basically, it goes to the arrested phase, but the cells are nicely covered with these follicular cells. This is called a primary oocyte. This is called a primary oocyte, and together with follicular cells, they form a primordial follicle. So this is called primordial follicle cells. So, what we initially had was this arrested primary oocyte, and then that got wrapped up in the nice green-colored follicular cells.

Whenever these nice follicular cells cover the primary oocyte, they form the primordial follicle, which basically stays in the arrested phase. This primordial follicle is generally in the arrested phase until the female body reaches puberty. So, basically, this is very important; we have to remember that the primordial follicles are in the arrest stage of meiosis 1, specifically in prophase 1, and those cells eventually remain intact until puberty. But in between, there are a lot of cell reductions in the number that happen, and we will see in the next slide, and the slide after that, how these numbers change from initial primordial germ cells to primordial follicle cells. But when the female body reaches puberty, what we just said is that some of these arrested primordial follicles initiate into the ovarian cycle, where the maturation stage starts.

Now, let us see how the germ cell number eventually changes. So, what we said initially is that we have a lot of these primordial germ cells, or like stem cells, and that a female has 2 ovaries if you consider a female as having 2 ovaries. So, each of these ovaries basically has about 7 million primordial germ cells. Total how many primordial germ cells they have during this embryonic development is almost 14 million primordial germ cells the female body has. But after that, as we said, when it forms like this primary agonium or like the matured agonium by the process of mitosis, a lot of this, like this, the differentiated agonium starts to degenerate.

So, from 14 million, the number eventually drops to about 4 million when this primary oocyte forms. So, when the primary oocyte forms and they are basically arrested, the number goes down from 14 million to about 4 million, and in this process, you remember that apoptosis happens. So, basically, a newborn baby girl has about 4 million primordial follicles; this is highly important to remember. A newborn baby girl has about 4 million total primordial follicles, which can also be called oocytes or primary oocytes. So, basically, these 4 million oocytes eventually remain until puberty, right, and they are arrested in the prophase 1 stage.

So, basically, whenever the body reaches puberty, a few cells eventually initiate the ovarian cycle, but one thing to remember from the birth of this baby girl is that we have 4 million oocytes or primordial follicular cells, and during puberty, a lot more reduction of the cells happens. So, eventually the 4 million cells do not stay; it becomes about 500k cells, with further and further degeneration happening. So, one crucial thing you have to remember is that each baby is born with a finite number of primordial follicle cells, which is 4 million primordial follicle cells. But it is highly important to know that in the case of males, there are no limitations on how many sperm cells are produced, right? Because males can produce sperm cells until a

very late age in their life. So, unless there is any hormonal deficiency, we discussed in some classes what the disease conditions can be.

So, unless there is an infertility condition in males, generally males can still produce sperm cells. But in the case of females, it is very tricky because each female is born with only 4 million primordial germ cells or primordial follicular cells, and from these, only 500,000 of the oocytes survive, resulting in a finite pool of about 500,000 oocytes that survive. So, a female has a highly limited number of cells—only 500k—and that's why a female needs to take care of her body in a way that prevents her egg cells from degenerating faster, because only a few of the oocytes can participate in the potential chances of fertilization whenever a sperm cell enters during intercourse. So, it is very tricky. So lastly, at the fifth month of fetal life, initially, 14 million germ cells, the primordial germ cells, are present, and then through apoptosis, a lot of these cells die; even in the newborn baby, 2 million primordial follicles are present per ovary, with each ovary having about 2 million primordial follicle cells.

So, together it becomes about 4 million primordial follicle cells, and they are arrested, you remember they are arrested in the meiosis one phase, right? And then what happens to each eventually until puberty? So, when the female reaches puberty, eventually some more degeneration happens. So, from 4 million initial primordial follicles, they are left with only 500k oocytes. So, from the 500k oocytes in each menstrual cycle. So, each menstrual cycle only 15 to 20 of these oocytes actually participate per ovary in the ovarian cycle. So, you have to remember that the female has only a limited number of 500k oocyte cells, and from there, per ovarian cycle, only 15 to 20 oocytes per ovary undergo the process of maturation.

Followed by when ovulation happens, the matured egg, only one matured egg, comes out from the ovary to the fallopian tube. And in the fallopian tube, they wait for potential chances of fertilization whenever sperm enters. So, eventually, the ovarian cycle is a series of changes that occur in a body that lasts about 28 days. And during these changes, what happens is that the immature oocytes, which were initially in the arrest phase of meiosis 1, complete their meiosis 1 stage, then they go to the meiosis 2 phase where they again get arrested. And eventually, on day 14, ovulation happens, and the mature egg eventually comes out in the fallopian tube.

There they wait for another 14 days for a potential sperm infusion, and if that fertilization happens, the final meiosis II step occurs, causing embryonic formation or development. And in the next class, we will thoroughly discuss the ovarian cycle. So, basically, we will see how all this maturation happens step by step, from initially these primordial follicle cells or oocytes. We will see how the stages of maturation happen, and at day 14, when ovulation occurs, eventually this matured egg comes out. So, in the next class, we will thoroughly discuss this: think about what the three phases of the ovarian cycle are, when ovulation occurs, and what primordial follicles are.

You can refer to different books, including Guyton's medical book and Tortora's textbook. Thank you again for attending today's class. If you have further questions, please drop your question by email or you can also discuss it during the live sessions. Thank you again for attending the Human Physiology class. So, we will meet very soon with another class. Thank you.