

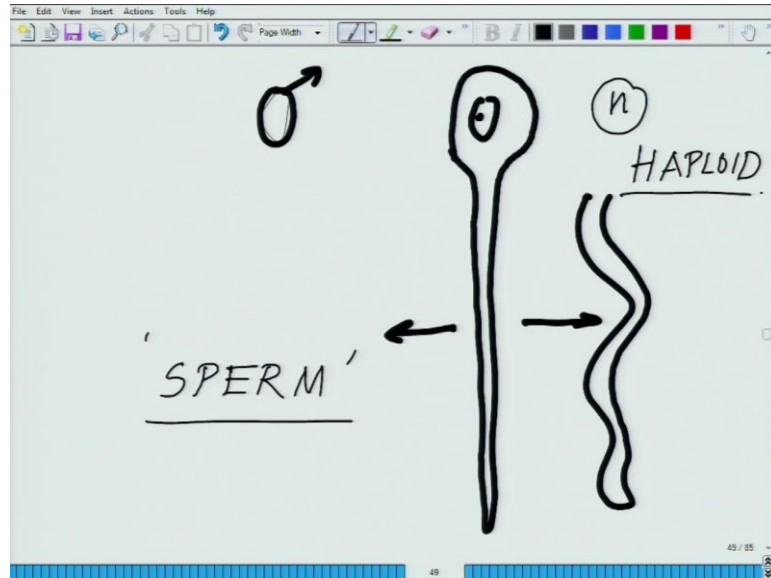
Animal Physiology
Prof. Mainak Das
Department of Biological Sciences and Bioengineering
Indian Institute of Technology Kanpur

Lecture – 26

Welcome back to the lecture series in animal physiology. We are in the endocrine and reproduction section. We have pretty much covered all the different hormones, except the digestive hormones from the pancreases, which we will be coming back just after this, when we will be starting the digestive system. So, the TLPs which is left is one of the most important piece; the reproduction. What really governs reproduction? Before I get into the notes and how that works, I have already explained you, what is a diploid cell and what is a haploid cell.

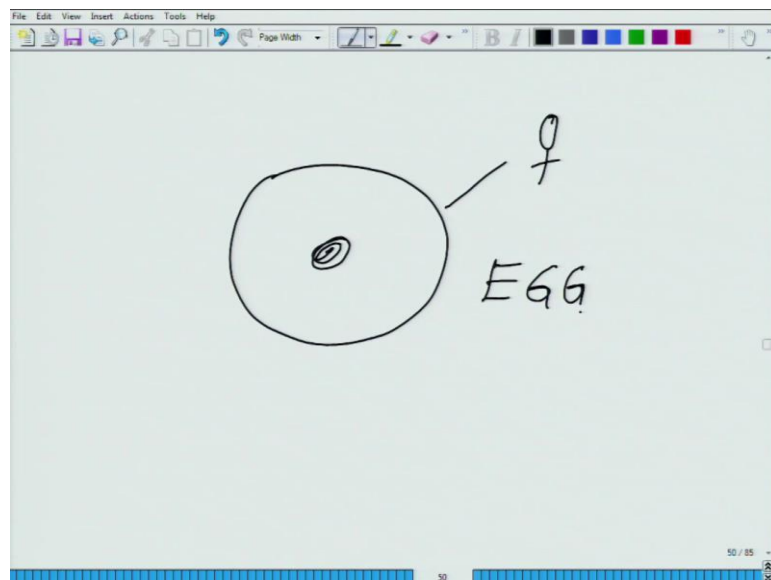
We have already went through the circuit, that it is a hypothalamus which is governed by higher centers of the brain, which release gonadotropin releasing hormone. Then, this gonadotropin releasing hormone comes to the pituitary. Pituitary releases follicle stimulating hormone and luteinizing hormone; FSH and LH. This FSH and LH surge leads to the secretion of the sex hormones by the gonads of our body, and they regulate the sexual behavior as well as, sexual function of the body.

Here, before I get notes, let us get some concepts clear. There are some concepts which have to be cleared here. In the case of males, we all know that the fertilization takes place, when there is sex between a male and a female, and at the level of cells, it is basically, a sperm fertilizing an egg. So, sperms are the male sex gametes, and eggs are the female sex gametes. There are some very star differences between the two, apart from their structural differences. Structurally, if you look at it, the sperm pretty much looks like.(Refer Slide Time: 02:02)



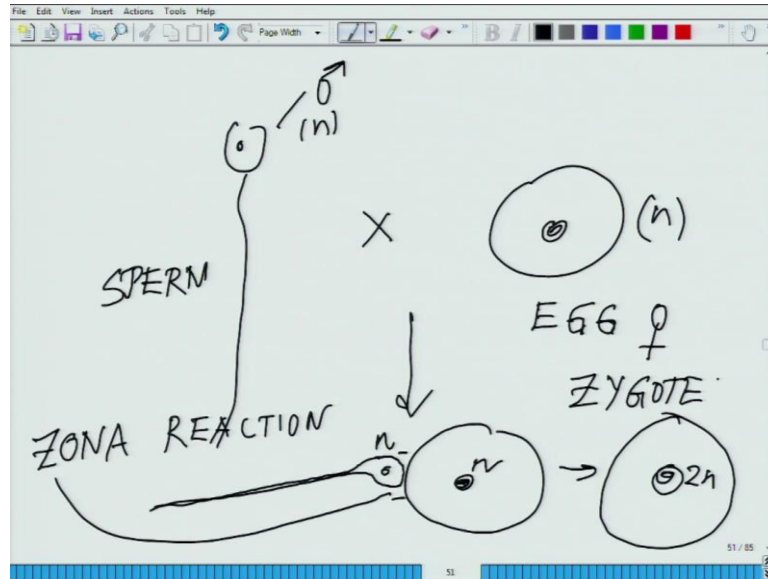
A sperm, this is the male sign of sperm, something looks like this. It has a huge tail and here, you have a nucleus and everything. This tail is basically, what it helps it to mobile; it makes it mobile. This movement is because of this tail. This, we call this, one second, this is the sperm, which is the male sex cell and as I explained you, that these are all haploids.

(Refer Slide Time: 02:42)



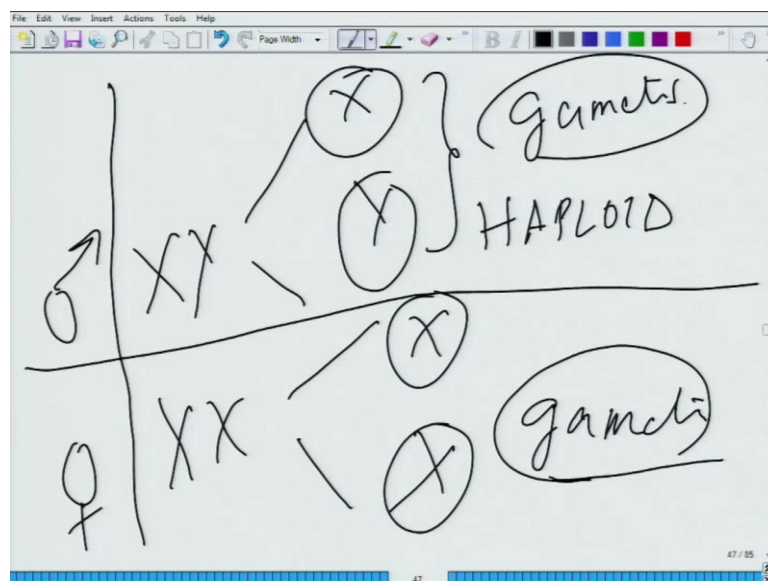
Whereas the female one, looks more like a round structure. It is like, something like an EGG. This is called the female; and this is called an EGG.

(Refer Slide Time: 02:53)



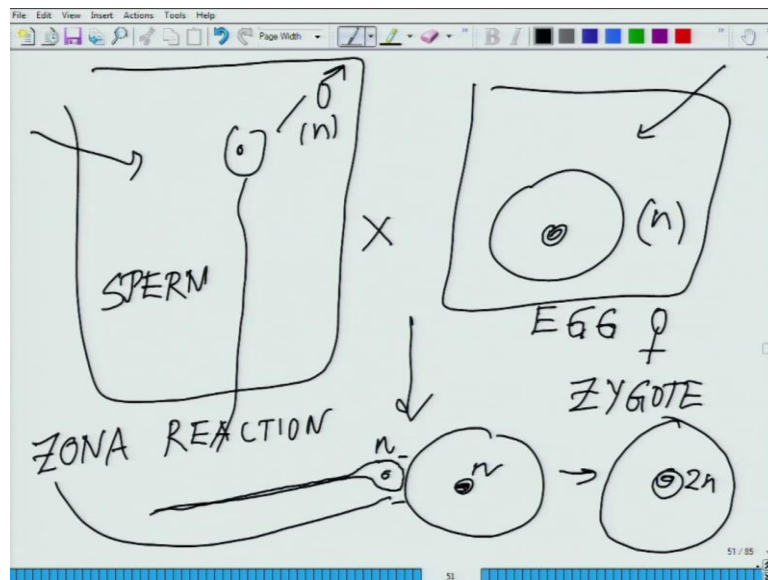
Basically reproduction is all about, when a sperm like this fuses with an egg, which has huge cytoplasm; if you look at the size of the cytoplasm, the cytoplasm of the egg is much larger as compared to. This is n ; female n ; and this is the male n , which is the sperm. When there is a cross between the two, basically that is how it works. Here, is the egg, here the sperm comes. Then there is set of reaction here, called come to that zona reaction. When this n fertilize with this n then, it leads to something called, which has two n , this is called a zygote.

(Refer Slide Time: 03:49)



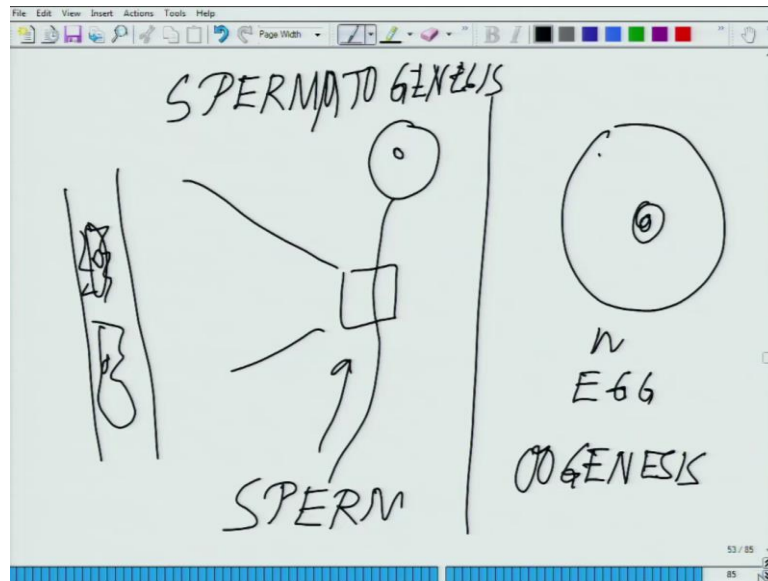
This zygote is the first cell, which is formed in the mother's womb; two n . This is a zygote. A zygote has two possibilities; it could be, say for example, if it is in the case of male, which is basically, a zygote could be, we call it as XX or XY; if it is an XY zygote, then this is male. If it is an XX zygote then it is a female. So, this is the contribution; this is the male. The female contributes two X, whereas the male contributes; either it could contribute an X or a Y. If it contributes a Y, then it leads to a male. If it contributes an XX, then it leads to a female. In other words, whether it is a male or a female is actually, not determined by the woman; it is actually determined by the male. If you look from the chromosome perspective, that is how it looks like. Now, what is so important about this.

(Refer Slide Time: 05:01)



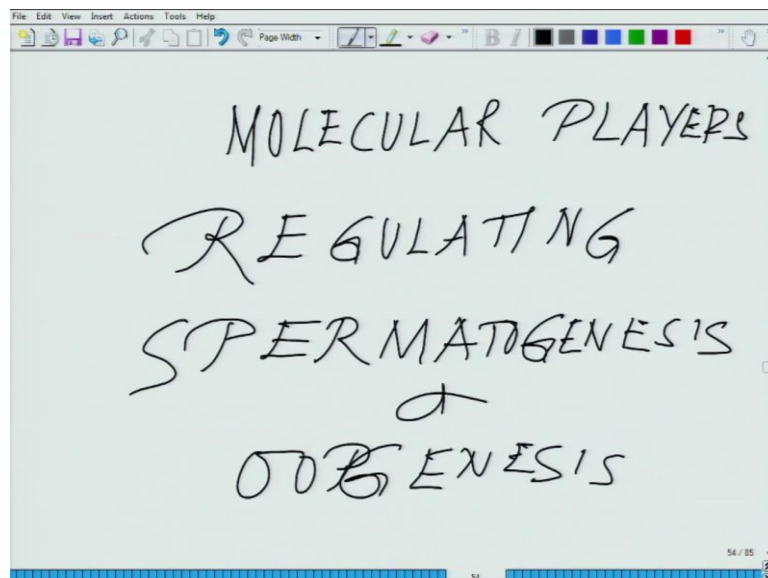
What we will be studying is this part and this part. How these are regulated? What regulates the formation of this and the formation of this in the body?

(Refer Slide Time: 05:14)



The formation of this in the body, as I have already mentioned, the formation of this sperm and the egg; this is the egg and this the sperm, and the sperm tail has a lot of section of this tail. You will see a lot of mitochondrias out there, which generates a lot of energy for its movement, because it has to move a lot. It is very motile structure. This formation of a sperm is called spermatogenesis, whereas, the formation of the egg is called oogenesis.

(Refer Slide Time: 06:00)



What we will be studying essentially is the molecular players regulating spermatogenesis and oogenesis. So, after defining the problem, what we are going to discuss here, I will highlight two specific aspects. One aspect, what I wish to highlight is that, these major molecular players in the game are the hormones, which play a critical role. But, there is a distinct pattern by which it regulates. In the case of males as we hit upon the puberty, at the age of 15 or 16, our reproductive organ or the testis; they have the potential to produce hormones. In other words, those testicular cells which are present in the testis, they are initially also diploid; they are $2n$. But, they have the potential to divide to form n and n . Then, each n forms another two sets of n and n .

So, each sperm cell could produce, sorry, each reproductive cell could produce four different sperms. This sperm production continues in the case of male, for the rest of the life. There is no limit, pretty much, there is no limit. Of course, the quality of the sperm goes down as we hit upon the age of 50s and 60s, the sperm quality goes down. They are much more fragile; their chromosome elaboration and everything. Chromosome elaboration; there are defects in the chromosomes because of the aging process pitches in, whereas, in the case of female the story is slightly different.

Females have a limited reproductive age. At the age of say, 15 or 13 or 14, their reproductive age starts. In other words, what the reproductive age continues up to 45 or 50 or may be, extended up to 50 maximum, most of the time. But there could be some exceptional situation, but those are rare; that does not happen every day. You would not come across individual, who are fairly reproductive at the age of 60. Now, what really does that mean? For the males, I told you, we can produce; a male can produce sperm for all his life.

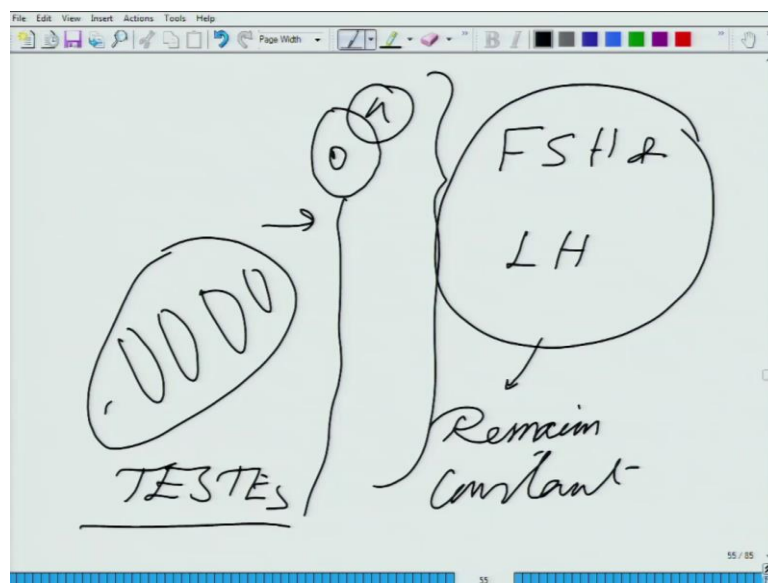
For the female, every month one egg matures and that one egg is capable of fertilizing a sperm, or a sperm is capable of fertilizing that egg. So, every month, that monthly cycle of the maturation of an egg is called menstrual cycle, which a female undergoes from the age of say, 14, 13 or 15, all the way up to 45 or 50. That is the phase, when a female is reproductively active, other than that, after that, it ceases that whole process of menstrual cycle ceases, and they do not produce any fertilized eggs after that.

What is essential here, to highlight is that, it is a very cyclic phenomena. In the case of males, across the month or across the years or across the whole life on, they hit upon

puberty; they can produce sperms. But in the case of females, it is a very cyclic fashion; there is a regulation of say, 21 to 28 days, depending on the female. It could be even up to say, 18 days to 28 days to 31 days, depending on which, I mean; it could be Caucasian female; it could be an Asian female; it could be an African.

Whatever, depending on the individual race or place, from where the female belongs to, their menstrual cycle varies; it could be 18 days to 31 days. During this phase, what will be actually highlighting is that, during this phase there is a cyclic fashion of secretion of those gonadotropin hormones, specially, the FSH, LH; follicle stimulating hormone and luteinizing hormone. That is what regulates the whole cyclic process, and the tail end, we will be talking about, when the egg gets fertilized, when a women is ready to give birth, when the zygote is formed, how this cycle gets stopped, and till the child is not born, that cycle remains stopped, and how that takes place, is what we want to discuss.

(Refer Slide Time: 10:57)



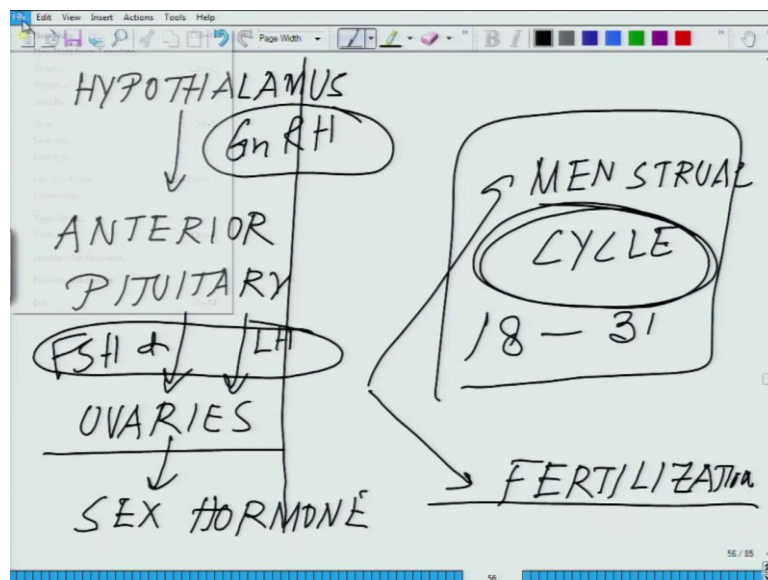
Talking about this, we will be talking very briefly about the male situation; what happens in the male? In the case of the production of the sperm, as I told you, in the males continuously, FSH and LH are being produced. This concentration in FSH and LH remains fairly constant and as I already told you, that there are ledic cells in the testis.

Testis structure is something like that, and this is where, these different cells are being produced. Testis is the one, which is responsible for the producing of the sperms. So,

there are leydig cells, which support in this whole process; FSH and LH helps in the maturity of these sperms and everything. So, this is how the male sex production takes place, where there is not much complexity; it is much simpler, and there is no cyclicality. It is all throughout the reproductive phase, it goes on and it may goes on forever for the whole life.

But, best quality of sperms come in the age like, in 20 to 35 or 40, when the best quality which are healthy sperms, which have the ability to fertilize the female egg, and led to reproduction of a healthy baby, remains in that age. Now, talking about the female which is I told you, that this is a very cyclic phenomena.

(Refer Slide Time: 12:19)

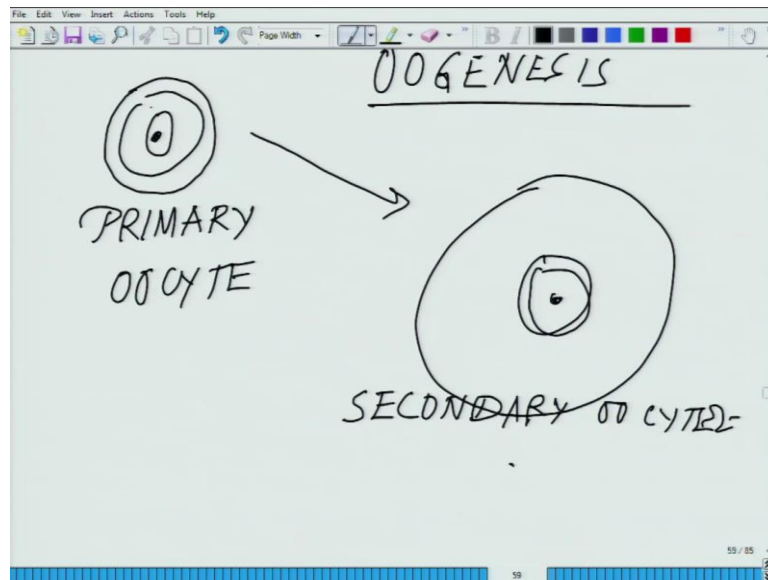


Let us talk about what is happening in the case of females. In the case of females, let us get back to the circuit. So, you have hypothalamus. I am repeatedly drawing this circuit to keep the exact track of how this whole circuit is functioning; anterior pituitary and then, you have the ovaries where, these are acting. These are gonadotropin releasing hormones, and anterior pituitary is releasing FSH and LH. These FSH and LH act on the ovaries and leads to the production of different sex hormones. What we will do now, we will talk about two aspects here. We will talk about menstrual cycle which I have already mentioned; last for some, it is from 18 days to up to 31 days.

What is this cycle? This is an important part of this cyclic fashion, and we will talk about the fertilization; what happens after fertilization? These are the two aspects, what we are

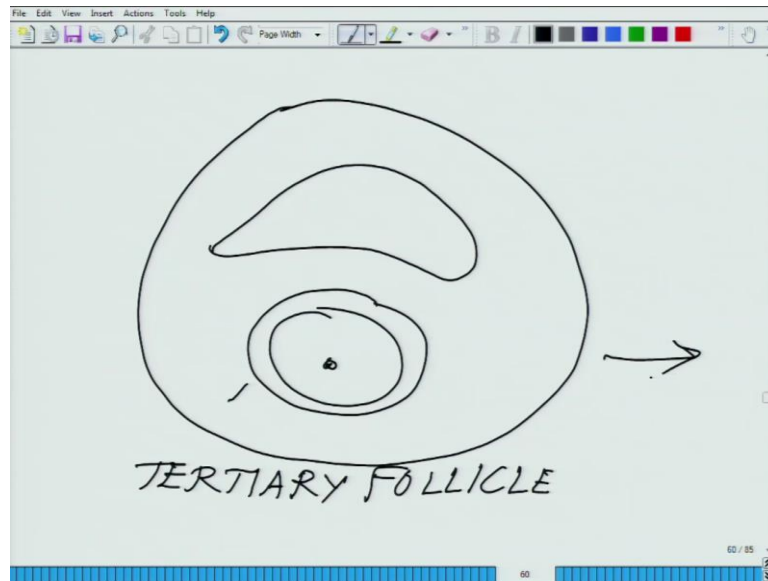
going to deal in the reproduction. So, we have already talked about the production of LH and FSH. Now, let us start with. What I will do, I will talk about four parameters. Assume a cycle is happening in a female. Before I get into this cyclic thing, let me explain something else here. How that maturity is taking place?

(Refer Slide Time: 14:15)



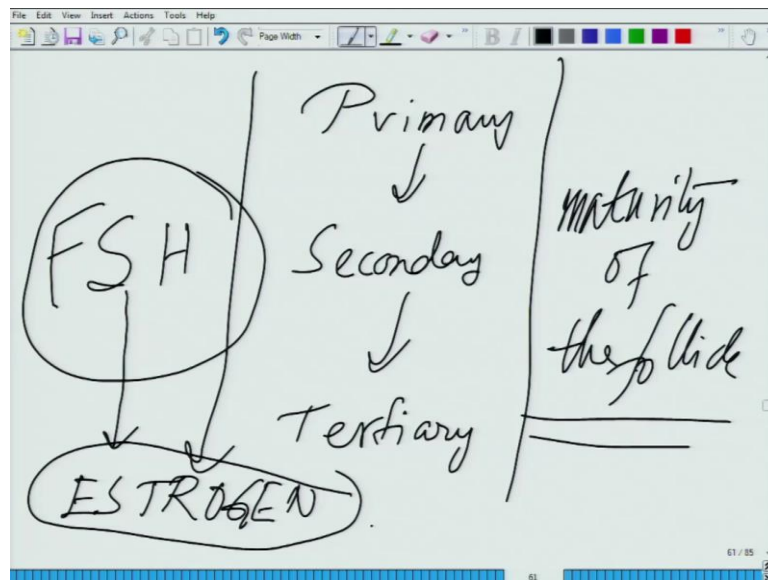
Initially, what happens, you have something called as primary oocyte; it is something like this. This is a primary oocyte. I am in the oogenesis now. This primary oocyte leads to the formation of something, called as secondary oocyte where, the cytoplasm increases in the egg. These are the secondary oocytes.

(Refer Slide Time: 14:55)



Secondary oocytes leads to the formation of something called a tertiary follicle. This is called a tertiary follicle.

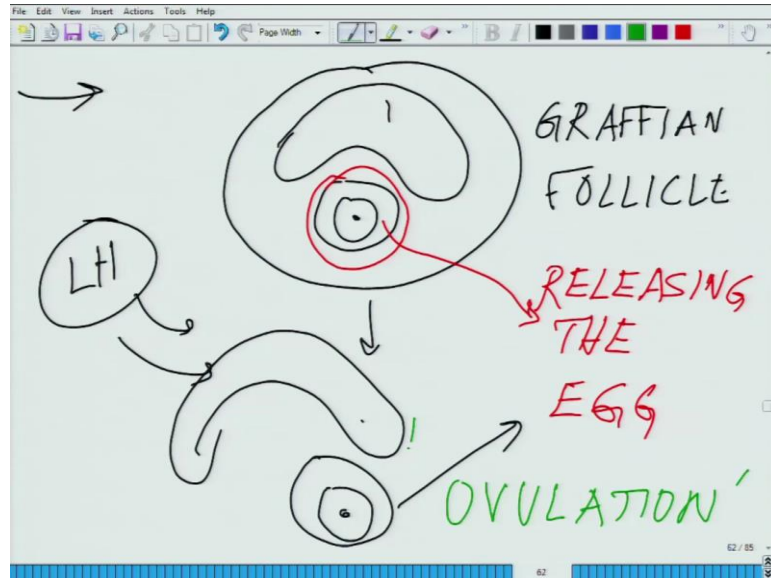
(Refer Slide Time: 15:17)



From the tertiary follicles, this whole process of formation of primary to secondary to tertiary follicle, is governed by; this whole maturity is governed by FSH; follicle stimulating hormones, which is essentially, is responsible for the maturity of the follicle. After this, what happens, and this does so, because FSH leads to the secretion of

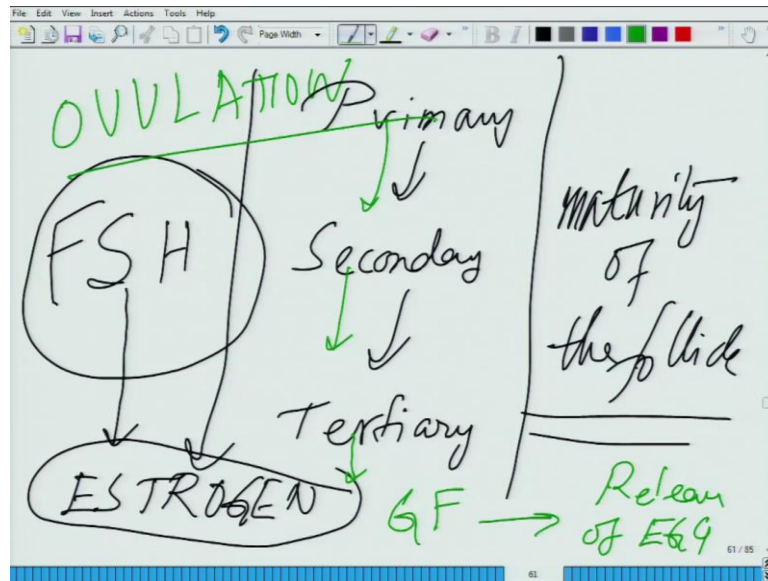
estrogen. It is the estrogen which is secreted by the cells, in the ovary, which leads the maturity of this from primary to secondary to tertiary.

(Refer Slide Time: 16:02)



After the tertiaries are formed, then its leads to another level of maturity, which is basically, called formation of graffian follicle. Continuing from the previous one; from graffian follicle, because of LH surge luteinizing hormone, we have talked about the other hormone; the FSH. The FSH is involved in all the maturity part. Then comes the role of the luteinizing hormone. What luteinizing hormone does is, that it leads to basically, this part is released; this egg is actually releasing the eggs and this releasing phenomena is something like this. You have eggs and here, the egg is getting released and this process is termed as ovulation.

(Refer Slide Time: 17:13)



This whole process by which, from primary to secondary to tertiary to graffian follicle to the release of EGG, falls under something called ovulation. This whole cycle, up to ovulation and after ovulation, falls under something called the menstrual cycle, which we are going to discuss now. What exactly is happening and how this process is taking place? Now, what I will do, I will just, let me check out that. Now, I will draw how the surge of follicle, this whole process, if you look at it, if you just think before I draw all the graphs and really show you.

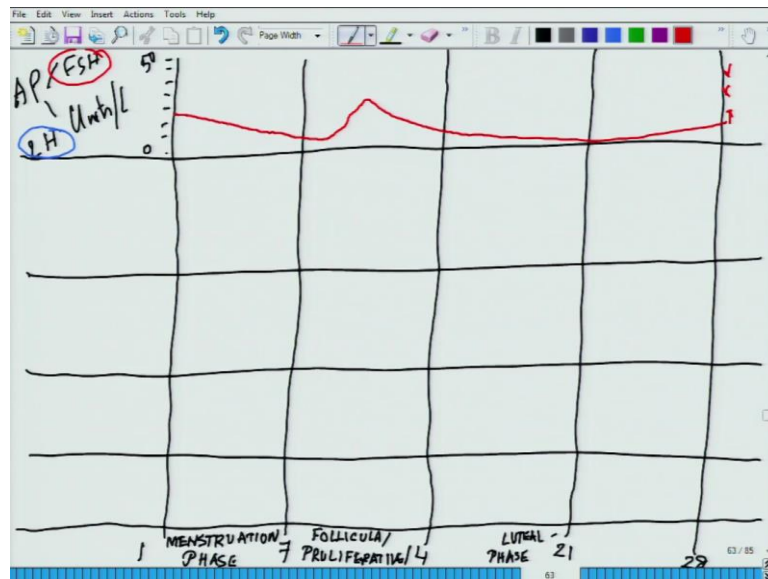
This whole process, if you look at it very carefully is happening. There is a FSH which is coming, which is leading to the maturity of the primary follicle to secondary follicle to tertiary follicle. Then, there is a surge of the next hormone, which is luteinizing hormone. That comes and leads to the egg to be released from the follicle. That process is taken care by the LH. LH does so, by making those cells to secret another hormone which is called progesterone. In other words, we are dealing with four hormones here; FSH, LH; which are secreted by the pituitary; step one.

Step two; of course, let us talk from even top that hypothalamus secreting gonadotropin releasing hormone at pituitary; it is secreting FSH and LH at third level, because of the surge of FSH and LH, there are two more hormones which are secreted, which is estrogen and progesterone. In other words, we are talking, what we will be seeing in the case of female; how the FSH level changes over a period of a cycle; of a menstrual

cycle? How the LH level changes? These two from pituitary and then, at the gonads, we will be talking about the change of the profile of the estrogen and the progesterone.

In other words, there will be a graph which will be showing four different lines of cyclicity, by which it is changing. Top of that, what are the physical changes happening in the body, in terms of the body temperature, basal metabolic rate and behavior. So, we be talking about those. Now, what I will be drawing, I will be drawing four graphs showing the way, the FSH level shifts, the way the LH level shifts, the way that leads to the secretion of progesterone, the way that leads to the secretion of estrogen. Let us draw the graph and that will help you to appreciate the whole process.

(Refer Slide Time: 19:58)



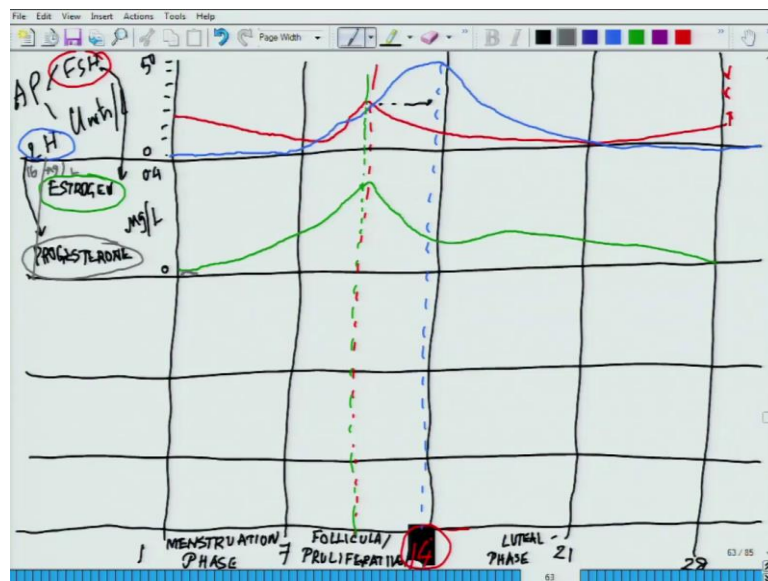
Simultaneously, what I will do, I will draw all the concentration; how that is happening? Let us divide this, say for example, and let us talk about an average cycle of 28 days. Day 1, day 7 and so, underneath, what I am drawing is the day 7, day 14, day 21 and this is day 28. We are taking an average female, who has a cycle of 28 days. This is the cycle, fine. **So, after every.** Basically, what is happening is this.

Let us divide the phases; this is called menstruation phase; then, the next phase is called follicular or proliferative phase; then day 21 is called the luteal phase; luteal secretory luteal or secretory phases. These are the different phases. Now, what I will do, I will divide the graphs into five different parts, which will help you to appreciate it in one go; 1, 2, 3, 4, 5. Now, the first graph will be talking about from the level of pituitary.

Let us get the scale right. At the level of pituitary, we are talking about like, 1, 2, 3, 4, 5. So, the highest limit is 50 and the unit is, here this is 0, 1, 2; just assuming units per liter. So, this is the level of the AP; anterior pituitary; FSH and LH; in the blood. These are all done in the blood. I am marking FSH with red and I will be marking LH with blue. Let us talk about how the FSH is shifting. The FSH shift is something like this. It has the basal level somewhere here, and then the FSH goes down like this.

As we reach somewhere out here, FSH level picks up and then, it slowly goes down and again, starts to the next cycle. So, here begins the next cycle. From here on, the next cycle begins. This is how the FSH is shifting. If you look at it, at sometime out here, in the case of 20 day cycle, one more thing I wish to highlight, I will come back to this graph once again. Depending on your days like; if the cycle is of 18 days; if the cycle is of 28 days or 31 days, the date of ovulation changes. In case of an average 28 days cycle, the ovulation generally takes place at the time of 14th day.

(Refer Slide Time: 23:39)



Now, if you come back to the graph, you will see that the major rise took place around just before day 14 out here. So, if this 7th day, this is day 14. This is, one second, this is day 14. Just before day 14. So, this is ovulation, that is why, I marked it as a red circle. This is the ovulation phase, when it is taking place. Now, let us see how the LH is going. Simultaneously, LH remains fairly low all throughout and then, it starts picking up here, and it reaches somewhere, like this; it reaches the highest peak and then, it starts

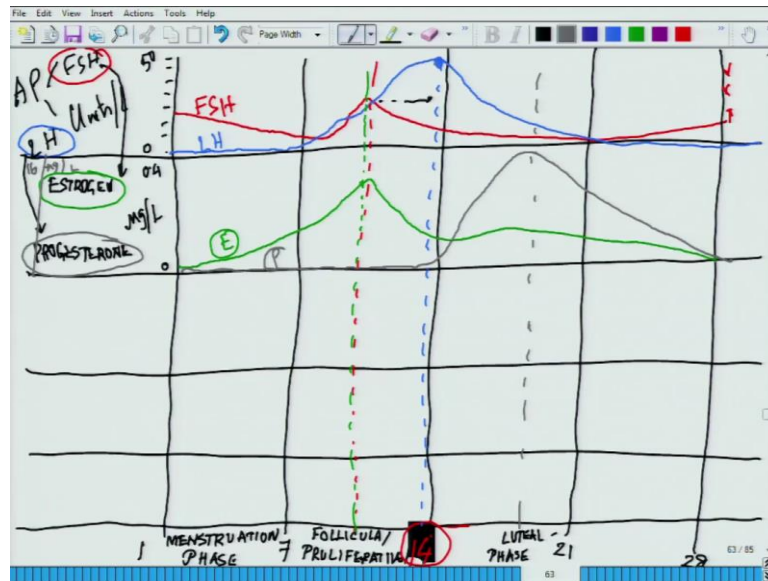
falling down; again, it goes down; stop like this. If you look at it around day 14, which is here; here LH is maximum. As I was telling, there is a cyclic fashion. The FSH, just before day 14, FSH hits the peak and then followed by, with a slight delay out here. Look at here; there is a small delay, then the next peak starts. Now, simultaneously what is happening?

Because, we know FSH leads to the secretion of, now, let me; FSH leading to the secretion of your estrogen or oestradiol, whereas, LH leads to the secretion of progesterone. Now, we will define how these two hormones are changing their profile. Their level is, if in this graph, we again put the amount which is essential. They are far more low; 0.4. This is micro gram per liter of blood. Now, this is the estradiol level, and compared to estradiol, the estrogen level is higher. If I am having a corresponding, let us pick up two colors first. So, I am putting estrogen as in green.

I am using a grey color for progesterone. The progesterone level is higher. Actually, progesterone level, if I have to draw a graph for progesterone, which will be like, the top thing will be 16 micro gram per m m, per liter. Progesterone level, progesterone secretion is much higher, as compared to estrogen level. If you tally this, what happens? Now, let us talk about what is happening to the estrogen? How the estrogen behaves? The estrogen level moves like this, and as you could see, where this one is picking up estrogen level, exactly picks up clearly close to it.

Then, there is a small hump and then it goes down like this. If you tally estrogen level, estrogen is close to the same peak of, as almost, as the same peak as the FSH. Because, FSH stimulates the secretion of estrogen. That is why; you see they are in close sync. FSH leading to the secretion of estradiol or estrogen. What happens next?

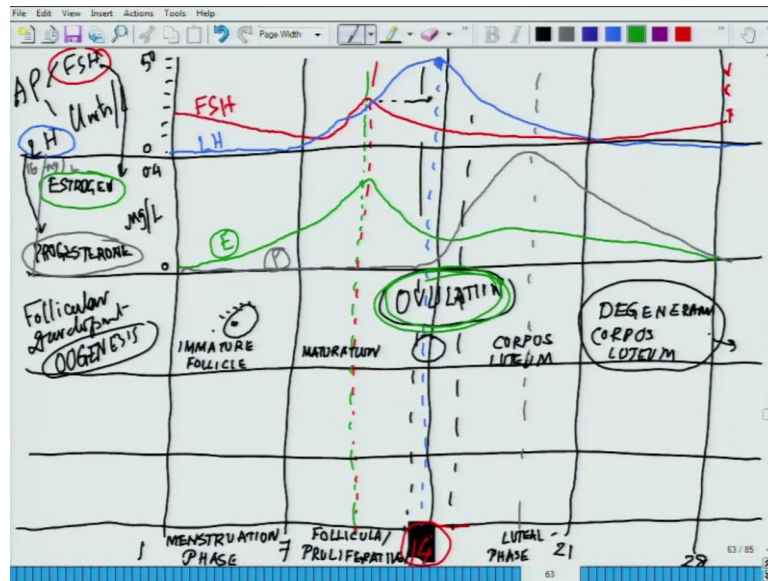
(Refer Slide Time: 27:11)



Now, let us talk about the progesterone level. Now, the progesterone level; this is just like your LH; that means, fairly low out here, and mind you, the progesterone secreted fairly high amount, and as it reaches and it remains like, that almost after day 14. Then, there is a rise in progesterone, big time out here, and that continues and then, it goes down. So, the progesterone level here, you see the peak of the luteinizing hormone and here, you see the peak of the progesterone. If you look at this cyclicality, the FSH out here, here you have the LH, here you have the estrogen and here, you have the progesterone. This cyclic fashion continues month after month during the reproductive phase of women, and this cycle is actually called the menstrual cycle.

But in this process, this is what you are seeing, what is happening inside your body. These molecular players are changing their concentration, but there is something else, which is expressed. Every month there is a blood discharge from the women's body, in the form of menstrual discharge. That menstrual discharge is nothing, but the process by which a female rejects the unfertilized egg from the body. This process, what we are going to deal now, is how I will tell you. I showed you this diagram, just before this. This, how to primary to secondary to tertiary to the whole process is...

(Refer Slide Time: 29:05)

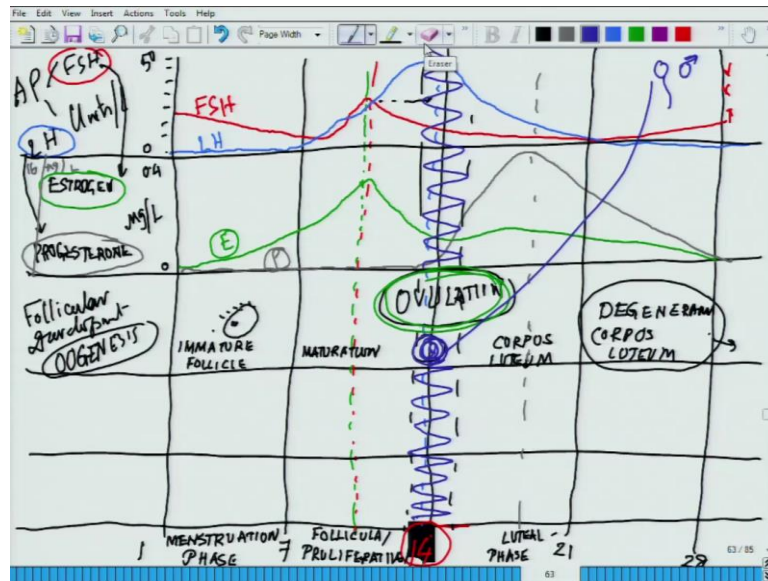


Now, I will explain it in terms of where exactly, this thing is happening. Now, we will talk about the follicular development. Let us come back to the follicular development. With respect to this follicular development, or you can call it; a part of the whole game of called oogenesis process. So, what essentially, is happening at this part of the graph? Basically, you have an immature follicle like this, what I draw is a primary follicle; immature follicle. Then, during the phase two out here, there is a maturation of follicle; maturation phase.

It is at this phase out here, if I have to just put 2 days back and 2 days forward, this is called the ovulation phase. This is very critical phase. Then, comes after the ovulation, if the EGG is not being used for fertilization, then this is lost. It forms something called corpus luteum, and this is degenerating corpus luteum. It is at this phase out here, if you look at it, when a new cycle starts. Basically, this degenerated corpus luteum is being discharged out from the body.

And what really this ovulation phase; this is the most critical phase. This is the phase when a female is reproductively active. This is, in other words, those during in the menstrual cycle, that phase, when a female sexual activity is at its highest. That particular balance of LH, FSH, progesterone and estrogen; is a unique phase of 2 to 4 days, when a female is reproductively active; this is the time.

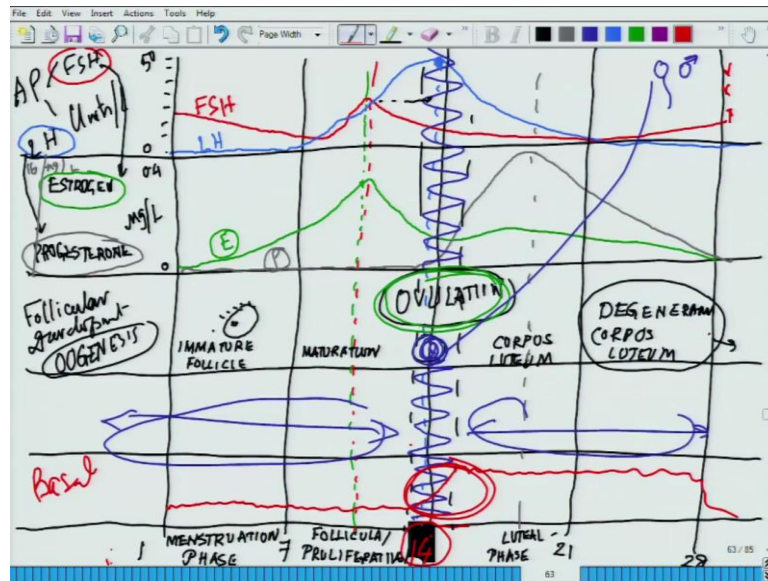
(Refer Slide Time: 31:23)



If this egg which is formed, is fertilized by a sperm at this phase, if a female has a sex with a man and this is the time if it is fertilized, and there is a possibility that this egg will become a zygote after fertilization. This critical window, if I am just shading it, is the most critical window in all the menstrual cycle; in the complete menstrual cycle, in terms of reproduction ability of the women. In other words, you can translate it back in terms of, if you look at the female cycle, every year a female has, if I tell, let us start from the month, every month there is window of 2 to 4 days, when a female is able to fertilize; as the egg has the ability to get fertilized by an sperm.

Every month, technically, there are 4 or 5 days or 3 to 4 days window, when a female has potential to fertilize its egg to produce a zygote and eventually, a baby. In other words, if you look at it, the actual reproductive activity of a female over a period of a year will be around 48 to 60 days. That is it; every month.

(Refer Slide Time: 32:49)



Other than that, at any phase, if a female is having sex at any phase, other than this, if I go back to any of these phases, most unlikelihood that could lead to a formation of a baby. But, this is the phase which is very critical for you to understand. It is a very well cyclic and very well tuned activity. If you look at the way the basal body temperature changes, which I wanted to show here, one second, the basal body temperature remains. Let us talk about an average temperature is moving like this. At this phase, the basal body temperature goes fairly high and then, it falls down. This is the zone when the body temperature of a female goes fairly high, because of the action of these different hormones, which are there and metabolically, it is very active. This whole cyclic process is many a times disrupted.

But, as I told you in one of the previous classes on endocrinology, that please look for the endocrine disruptors, and all those kinds of drugs. Many a times, because of an imbalance of other hormones, the cyclicality of several women; they suffer from lot of gynecological disorder, in terms of because, this whole cycle is being disrupted. They do not get the proper menstrual cycle. They do not get them anything on the right time. It leads to a lot of complications and lot of irritability, lot of behavior traits, which are very asynchronous behavior traits, which happens.

But, if you translate it, without getting emotional, if you translate it in terms of the hormonal, you realize it is a very tightly scheduled molecular event, which is taking

place within the body of a female. Any imbalance or any shift from that kind of tightly regulated chemical phenomenon, could lead to a whole array of behavioral changes, which we really cannot explain straight away; that needs a lots of probing. So, this is very important. I expect you people to appreciate this whole thing, that this is a chemical game of three or four players.