Human Physiology
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Week - 10
Lecture – 01

Hello everyone, welcome to another new class on human physiology. In this class, we will discuss the menstruation cycle and the hormonal regulation. So, in the last few classes, remember we discussed female reproductive organs; we will also discuss the ovarian cycle. So, in this class, we will again cover the ovarian cycle and uterine cycles; along with that, we will discuss how different types of hormones have a very crucial role to play. So, let us stick with it. So, what different content will be covered for this class? We will discuss the main events of the menstruation cycle.

We will discuss different hormones that are involved in the menstruation cycle. We will discuss the hormone initiations of the cycle and hormonal interactions in the ovary. Then we will see the role of estradiol and the role of progesterone. We will also discuss the role of inhibin and the role of other hormones like FSH and LH.

So, what are the main events of the menstrual cycle? First, we have to remember that the menstruation cycle is categorized into two components, right? So, the first one is the ovarian cycle, and then the second one is the uterine cycle, right? So, basically, the total cycle stays at about 21 days. And in cases of the ovarian cycle, there are certain components that you already remember we discussed in our last class. So, for example, first what happens is that the egg starts to mature, where follicular maturation occurs, which is basically the development of the follicles in the ovary. Then, after the follicular maturation happens, the egg progresses from meiosis I to meiosis II and is arrested in meiosis II. You remember the next stage at day 18; the ovulation of the oocyte, or the ovulation of the egg, happens at day 14.

And finally, after ovulation, what happens is that the remaining granulosa cells, or follicular cells, convert into a component called the corpus luteum. This structure is basically formed after ovulation, and as we discussed, the corpus luteum has a very crucial role to play, and we will see how the corpus luteum is so important. So, this is all about the different kinds of stages of the ovarian cycle, where initially follicle maturation happens, followed by ovulation and the formation of the corpus luteum. In cases of the uterine cycle, what mostly happens is a growth of the uterus. So, initially after the initial periods, which happen like 1 to 7 days, slowly and in the presence of different hormones, the uterine gates develop.

So, uterine growth happens, and endometrium growth happens; basically, the uterus and endometrium prepare themselves for possible embryonic implantation. So, one more time, it is mostly in cases of the menstruation cycle; it has basically two phases. One is the phase called the follicular phase, and the second is called the luteal phase. So, in cases of the follicular phase, as you know, the maturation of the egg mostly happens, where the egg starts to grow, the follicle starts to develop, and in cases of the luteal phase, the corpus luteum develops, and eventually, the total cycle is about 0 to 28 days; the whole cycle is about 28 days. One thing you have to remember is that this luteal phase, specifically, occurs mostly after day 14 and lasts until about day 28.

So, this gap of 14 days needs to be there, and it is always there in cases of a female body; however, in cases of longer and shorter menstruation cycles, the follicular phase can vary. You remember that in the last class we also discussed that in cases of a regular 28-day cycle, we see ovulation on day 14, right? But if the cycle is short. So, for example, if the cycle is short, you still have to remember that the luteal phase still needs 14 days, right? So, this initial follicular phase will only be for 7 days, and in cases of a longer period of time, for example, if it is 35 days, right? So, basically, there would still be the 14 days of the luteal phase, which means there would be about 21 days of the follicular phase. So, there would be about 21 days of the follicular phase with only 14 days of the luteal phase. So, basically, the important part here is that the luteal phase needs to be maintained for at least 14 days, but the follicular phase can vary based on a shorter or longer time period.

So, let us see that the primary reason for today's lecture is to discuss the different hormones that play a crucial role in the ovarian and uterine cycles, right? So, there are mostly five different hormones that are involved. So, we will see exactly what their roles are and from where they are secret, okay? So, basically, the first hormone we will discuss is FSH, or follicle-stimulating hormone; this is secreted from the pituitary, mostly from the anterior part of the pituitary, and it plays a role in follicular maturation. Then the second important hormone that is also secreted from the anterior pituitary, which is called the luteinizing hormone or LH. LH has a different role; LH is highly important for ovulation, and along with that, LH has a crucial role in corpus luteum formation. Then, in terms of the uterine cycle, the role of the uterine cycle is mostly to develop the uterus and grow the endometrium.

In these cases, two important hormones have a very crucial role; one is estradiol, and the second is progesterone. So, what are the five hormones we discussed? Lastly, there is another important hormone we should discuss, which is the gonadotropic releasing hormone. This basically gets secrets from the hypothalamus. So, basically it gets secreted from the hypothalamus, and these are like the precursor hormones that stimulate the anterior pituitary to secrete FSH and LH. So, we will see again how this kind of hormonal signaling happens, but in short, there are 5 different important hormones.

The first one is the follicle-stimulating hormone; this stimulates the maturation of the ovarian follicles. Then there is this luteinizing hormone which has a very crucial role in terms of oocyte ovulation. It is also very important in terms of estradiol synthesis or estrogen synthesis. LH also has a crucial role in corpus luteum formation. Then estradiol, which is a form of estrogen, helps to prepare the uterus for possible embryo implantation.

It is also very important; then progesterone, which is highly important, works simultaneously with estrogen to basically form and develop the uterus and endometrium. And lastly, we said that GnRH, or gonadotropic releasing hormone, is a precursor hormone or stimulating hormone that gets secreted from the hypothalamus, and it basically stimulates and triggers the anterior side of the pituitary to secrete FSH and LH. So, an important thing is that you also have to remember the locations. So, basically, FSH is secreted from the anterior pituitary, and LH is also secreted from the anterior pituitary, right? Then gonadotropic-releasing hormone is secreted from the hypothalamus, followed by estradiol, which is initially produced in the granulosa cells, and then progesterone, which is primarily secreted from the corpus luteum. So, these are the areas from where these hormones are secreted.

Let us see how the hormonal initiation of this cycle occurs. So, as we said, the first thing that happens after puberty, just before each cycle, is that the hypothalamus secretes gonadotropic

releasing hormone, and you know, the hypothalamus is located in our brain. And once this gonadotropic-releasing hormone is secreted from the hypothalamus via the hypophyseal portal system, it comes to the anterior side of the pituitary. So, on the frontal or anterior side of the pituitary, this gonadotropin-releasing hormone is produced. Right, and once it comes to the anterior side of the pituitary, it stimulates the gonadotrope cells that are present in the anterior pituitary, and by stimulating these gonadotrope cells in the anterior pituitary, it kind of stimulates the secretion of two hormones; one is the luteinizing hormone.

The right one is the luteinizing hormone, luteinizing hormone, or LH, and the second is the follicle-stimulating hormone, or FSH. So, follicle-stimulating hormone, or FSH, and then another is luteinizing hormone, or LH. Then, once LH and FSH, which are secreted from the anterior side of the pituitary, travel via the bloodstream to the ovary, what basically happens is that they. So, basically, these two hormones, LH and FSH, come to the ovary, and there the ovarian cycle basically starts. So, let us see how it starts and what the different roles of this hormone are.

So, FSH, which you can see by the name is called follicle-stimulating hormone, stimulates egg maturation and follicle formation. So, you can see that initially there were thin layers of follicle cells, and slowly from the initial stromal cells, it became cuboidal cells, and after that it started to develop into granulosa cells. But the main thing is that these follicular cells or follicles eventually mature and develop, and FSH plays a crucial role in their development and maturation. And then next is the LH, or the luteinizing hormone. LH basically acts on the theca layer, right? So, this is basically the theca layer, this red layer you remember we discussed in our last class as well.

So, it acts on the theca interna cells in the follicle. By stimulating the theca interna cells, it basically secretes a molecule called androstenedione. So, what LH does is basically act on the theca interna cells, and after the theca interna cells are stimulated by LH, they secrete a precursor molecule of estrogen called androstenedione. And now this androstenedione, what it does is it basically affects the granulosa cells, and once it diffuses inside the granulosa cells, it converts to a molecule which is called estrogen or estradiol. So, what we just said initially is that the hypothalamus secretes the gonadotropic releasing hormone, and once the gonadotropic releasing hormone is secreted, this hormone basically stimulates the anterior pituitary.

So, it stimulates the anterior side of the pituitary, and by stimulating the anterior side of the pituitary, it secretes two different hormones: one is the luteinizing hormone, and the second is the follicle-stimulating hormone. This follicle-stimulating hormone basically stimulates follicle formation, maturation of the follicles, and eventually stimulates the formation of granulosa cells. Whereas, on the other side, the luteinizing hormone basically acts on the theca interna to secrete a precursor molecule called androstenedione. And androstenedione can actually diffuse into the granulosa cell to produce the hormone called estrogen or estradiol, and this estradiol plays an important role in uterine growth. So, you see in this chart, what we discussed is that initially, for example, this FSH is slowly increasing; it is almost as if it starts when the GnRH stimulates the anterior pituitary.

The FSH level goes up a little bit in the body and then basically it maintains until about day 9 to day 10, which contributes to follicle maturation and follicle development. And when there is a lot of this granulosa cell formation, what LH does is basically stimulate the theca interna cells, and by stimulating the theca interna cells, it forms androstenedione. Androstenedione is a molecule that diffuses inside the granulosa cells and starts to secrete estradiol or estrogen.

So, basically, this is the estrogen. You can see that slowly, with time, once the granulosa cells are getting thicker and more numerous, the estrogen level is also rising, and what this estrogen or estradiol does is that it basically starts to proliferate, proliferate, and grow, proliferate, and grow the endometrial lining inside the uterus.

So, basically, with the estrogen, it is maintaining the endometrium, growing the endometrium, and preparing the uterus for possible embryonic implantation. So, in the next stage, as you can see, the very interesting thing is that estradiol has a negative feedback effect on both the hypothalamus and the anterior pituitary. So, directly or indirectly, this estrogen, when it is formed, basically has an inhibitory effect. So, up to a certain time, the FSH and LH levels. So, basically, this is the FSH, and the yellow line is the LH.

So, initially they were maintaining a stable level, but once the estrogen starts to form, they have an inhibitory effect because they directly inhibit both the hypothalamus and the anterior pituitary. So, not more than LH and FSH are being secreted, and when it inhibits, you see the LH and FSH levels drop. So, basically, after maybe day 8 or day 9, the LH and FSH levels drop around day 11 to 12. So, you can see that the LHH level is high and the FSH level drops a little bit. Now, what happens is that there is saturation or a threshold level you can see.

By continuously proliferating, the granulosa cells are causing the maturation of the egg, and when there is almost a formation of this graphene follicle or the dominant follicle, there is a continuous increase in the estradiol level. So, at a certain threshold level, this previous negative feedback loop, which was initially established maybe at this range, basically goes away and switches to a positive feedback loop. I know this can be a little complicated, but we will quickly rehearse one more time. Initially, when LH and FSH form, FSH starts to produce the granulosa cells, and LH basically forms androstenedione. Androstenedione basically diffuses inside the granulosa cells to form estrogen or estradiol.

Estradiol has a negative feedback loop effect that basically inhibits both the hypothalamus and anterior pituitary from secreting more and more LH and FSH. So, it prevents the secretion of further LH and FSH. And that is why you can see that from this 8 to 9 days to about 11 to 12 days, there is a decrease in the level of both FSH and LH. But after that day, granulosa cells continuously proliferate, which also causes continuous production of estradiol. So, at a after a certain threshold that negative feedback switch that kind of gets switched off.

So, initially, the negative feedback loop was there; basically, this negative feedback loop gets terminated and it kind of switches over to a positive feedback loop, and whenever there is this positive feedback loop, what happens is that both FSH and LH immediately see a surge in production. So, you can see that FSH, this green line, has also surged, right? And then, in cases of LH, the surge is also much more prominent, which is also called LH. So, in this case, both the surge of LH and FSH together, especially the LH surge, have a significant role because the LH surge is important just 36 hours before ovulation; it basically helps in completing meiosis I and also matures the oocyte to form a secondary oocyte. It also contributes to ovulation, which is the release of the oocyte. Finally, LH or LSH search is also important for forming the corpus luteum.

So, we will discuss the corpus luteum in the next slide, but before that, there is one more important point to consider, which is the FSH search. So, basically, this is the LH, right, and this is the FSH. So, you see that the FSH surge is not bigger than the LH surge. So, the LH

surge is much larger than the FSH surge. And why is this so? Because from these granulosa cells, there is another hormone or molecule called inevin.

So, basically, these inhibin molecules are secreted from the granulosa cells, and this inhibin kind of negatively reduces or hampers too much of the FSH surge. So, what this inhibin molecule does is basically secreted from the granulosa cells, and it suppresses FSH secretion, which explains why FSH is not as high; the surge of FSH is not as high as the surge of LH. So, we already discussed the role of the LH surge, right? What we said is that the LH surge is highly important because it allows the completion of meiosis one step, it allows for the formation of the secondary oocyte, it enables the female body to complete ovulation on day 14, and eventually, it helps to form the corpus luteum. Now, when the corpus luteum forms, basically what happens at this stage is after day 14. You can see that there is a sharp decrease in estradiol because the initial egg and the initial granulosa cells are now converted into the corpus luteum with the help of the LH surge, and this forms a yellow body.

And now there is no presence of any more granulosa cells, and that is why you can see there is a sharp drop in basically this estradiol level, right? So, you can see there is a sharp drop in estrogen levels whenever this granulosa cell is converted to the corpus luteum. Now, what is the basic role of the corpus luteum? The corpus luteum primarily produces progesterone in the early stage, and progesterone is important because, during the early stages, estradiol, which is a form of estrogen, was mostly responsible for uterine growth, but after day 14. So, after day 14, once the corpus luteum forms, it basically secretes progesterone, and now this progesterone molecule helps in terms of further growth of the endometrium, and it also makes the endometrium vascularized. So, there are a lot of blood vessel formations, a lot of capillary formations. So, basically, the body is preparing the uterus with a stable and vascularized endometrium for possible embryonic implantation.

Because if the embryo is implanted, then it needs a lot of nutrients and a lot of oxygen, and the blood capillaries or the blood vessels of the endoneurium facilitate the supply of oxygen and nutrients to the newly formed embryo. So, you can see who basically secretes the progesterone: this corpus luteum. So, you can see that the initial progesterone level. So, this blue line represents the progesterone level for the first 14 days; the progesterone level is too low, with almost negligible amounts of progesterone or almost no presence of progesterone. And now you can see that after day 14, the progesterone level sharply increases.

So, the progesterone level sharply increases because the corpus luteum is forming progesterone. And after a certain time, two things can happen. So, at this point, either fertilization can happen. So, basically, let us consider two conditions if fertilization happens right. So, if fertilization happens, then what will happen? If fertilization happens, then basically the progesterone level will be maintained and we will see why it will be melted, but let us consider if there is no fertilization.

So, let us consider if there is no fertilization; then basically, the progesterone level will drop, right? So, if there is no fertilization, then there is no need for the body to maintain this corpus luteum, and you remember in the last class we discussed that the corpus luteum eventually becomes a white body. So, initially, it was the yellow body that was called corpus luteum. If there is no fertilization, it forms the corpus albicans, or white body. Eventually, there is no longer a role like progesterone formation, and as the progesterone formation has stopped, you can see this sky blue line; the progesterone level also immediately and sharply decreased until day 28. So, we just discussed two conditions, right? If fertilization occurs, then the embryo that

develops or forms after fertilization will secrete a hormone called HCG or human chorionic gonadotropic hormone.

And this HCG hormone will basically help the corpus luteum to maintain itself. So, if fertilization occurs, the embryo will secrete HCG, and this hormone will help the corpus luteum to maintain. So, it will support the endometrium to maintain, and it will support the vascularization and proliferation of the thick endometrial layer to ensure proper embryonic implantation and overall embryonic health and growth. But if fertilization does not occur, as we said, the corpus luteum will become an inactive white body; it will become an inactive white body, which is also called corpus albicans. And once it forms like an inactive form of corpus albicans, it will not be able to secrete any further progesterone hormone.

So, eventually, progesterone levels will drop. One last thing to remember is that for this estradiol or for this estrogen hormone, there is a dark blue line. So, initially there was a dip just because granulosa cells were converted to corpus luteum cells. But you can see in the mid phase of the luteal phase, almost around day 20 to day 22, there is again a second level of increase of this hormone. You can see that initially there was a fast decrease, and we know why: because the granulosa cells are proliferating. After the granulosa cells convert to the corpus luteum or yellow body, there is a decrease, but there is again another round of increase in cases of this mid-luteal phase.

And you know why it happens: because the corpus luteum, around day 20 to 22, does not only secrete progesterone; it also starts to secrete some amount of estrogen. So, at this point, you can see that there is another rise or surge in estrogen levels because the corpus luteum secretes both progesterone and estrogen from around day 20 to day 24. So, what is basically happening is that we have almost completed both the ovarian cycle and the menstruation cycle by day 28, but let us see what menstruation is. So, when there is no fertilization, what happens is that, as you remember from the last slide, we discussed that both the progesterone level and the estrogen level completely went down. And if there are no progesterone and estrogen levels in the blood or in the body, what will happen is that the endometrium of the uterus will eventually start to degrade.

It will basically be all those thick endometrial layers; you can see those initial formations of the endometrial layer. These layers will kind of come off, and eventually, they will start to degrade and degenerate, which will also cause a lot of surrounding tissue layers to come out, leading to a lot of blood loss. Eventually, the blood and the tissue will come out in the form of periods. So, this is basically called menstruation in cases where fertilization does not occur, and the female will experience about the first 1 to 2 to 7 days of menstruation or heavy bleeding, followed by the next phases of the menstrual cycle. So, let us think about how long the menstruation cycle typically lasts, what the role of the corpus luteum is, and why the menstruation cycle is important.

So, can you think about and answer this question? You can also refer to this textbook. If you have further questions, please discuss them with us during the live sessions; you can also drop your questions by email. So, thank you again. Hopefully, you are enjoying the human physiology class. We will meet with you very soon for another new class of human physiology. Thank you.