Let’s talk about sex - females
Ep 3

I like the way you work it…. No diggity, got to bag it up.

Okay, hold up - I know the perfect song for this episode.

akwafina’s “My Vag” “my vag like an operatic ballad, your vag like grandpas cabbage.”

Let’s be perfectly honest about a few things 1- I can't sing, 2- there is no way I could do this song justice, so do me a favor. Pause this podcast, go and listen to akwafina’s song “my vag” then hit play on this podcast. And if that song doesn’t get you seriously excited to learn about the female reproductive system, then listen to it again. And don’t @ me about a vag song because there are so many songs about pensis.

https://www.youtube.com/watch?v=z726OPwCnjE

Maybe I should mention that this episode does have sexual health material - so this is your warning. We’re gonna be talking about vagina’s and periods and all of those hormones that make it all happen.

Welcome to the Cell-fie Life. This is nikaela and i wanted to Thank you, so much for listening. If you have questions or comments, or corrections. Please let me know- the best way to reach me is either the website: CellfieLife.com or on insta: @thiscellfielife.

You guys, subscribe to this podcast, just hit that little button and then you will get the latest episode automatically. There really is no downside to subscribing. Seriously.

Are you guys ready for this? You all know that females have a complicated reproductive system and its cause we can grow new humans. NEw humans. That is just crazy to me. So take a deep breath and dive in.

Last note before we begin in earnest. This episode is about biological sex and not gender expression.

Okay now, let's talk about the ladies - which are hella complicated but we can get this all sorted.

The major reproductive organs for females include: the ovaries (which are homologous to the testes - meaning they came from the same precursor during development)
The ovaries are where the ova, aka the gametes, are produced.

The uterus,or as i like to call it sometimes, the baby box, but we're being sciency here so its the uterus, the uterus is where a viable progeny develops. I say viable because ectopic pregnancies are pregnancies where implantation happens other that the uterus and this is super dangerous for mothers if not caught in time. And breasts are also included in reproductive organs; breasts because of lactation. So these are all included in the reproductive system, as well as the brain. Because as we learned from the last episdoe, sex starts in the brain.

Q do you remember what part of the brain releases gonadotropin releasing hormone?
A: the hypothalamus? Do you remember where the GnRH travels to and acts upon?
A: the anterior pituitary.

Nice job, you guys are so smart, you should all be doctors.

If you missed those questions, no worries. We will review them in like 30 seconds; you could also review the last episode which goes over the male reproductive system.

The ovaries produce some major female hormones - like estrogen and progesterone. Estrogen is also responsible for the sexondary sex characteristics, such as breast development, and the widening of the hips.

But just as in males, it all starts in the brain. The hypothalamus regulates the hormones released by the anterior pituitary through the portal blood that travels from the hypothalamus to the anterior pituitary.
In males, the hormone released from the hypothalamus is Gonadotropin-releasing hormone, GnRH. GnRH runs up to the anterior pituitary and tells it to release the luteinizing hormones LH and follicle-stimulating hormone FSH.

Hell yes. Those are the exact same hormones that are released in male brains. I love when I go to learn something and i'm like wait a second. I already know and understand that because I learned all about it, over there(over there being the podcast that talked about the male reproductive system).

The hormones FSH and LH travel through the blood to the ovaries. We are going to pause there for a minute with the hormones and we are going to do a broad overview of meiosis in females. And really get a general idea about the different aspects of meiosis, aka ova development and the ovarian cycle.
Let's start with the specifics of female meiosis.

There are some very big differences between males and females. I can hear all of you that just said, duh. First females do not have the same unending supply of stem cells, as men do in spermatogonia.

Females have ALL their eggs, at birth.

The ovaries created the eggs during baby girl's gestation and the eggs just remain in an inactive state until puberty.

The production of female gametes, eggs, is called oogenesis.

Q: Do you remember what the production of males gametes was called?
A: spermatogenesis

The double OO thing you will see is because OO - i don't know how to pronounce it, but the oo means egg in Greek. So the word oogenesis - literally means egg - birth.

Early in uteral development the precursor germ cell is called an **oogonia (** sound familiar the male germ cell is spermatogonia) anyway. The oogonia undergoes a ton of mitotic division to make loads of themselves, at around 7 months the division stops. and this is the egg supply that the baby girl will have for the rest of her life, but there are actually a ton of them, anywhere from 2- 4 million.

Which would be a ton of babies.

So females have all their eggs at birth and all the eggs have already gone through interphase and replicated their DNA and entered Meiosis 1. So the eggs are really just hanging out as **primary oocytes**. They have started meiosis but have stopped immediately in the first stage of meiosis 1.

Q: what is the first stage of meiosis 1? A: prophase 1 - so these cells are in meiotic arrest. Meiosis has been stopped, arrested. So when a baby girl is born, her eggs will be in meiotic arrest in prophase 1 until she enters puberty and has her first period, which is called menarche. (men-arch-EI actually didn't know that was the name of your first period until I started fact checking this episode.

I didn't mention this in the last episode but biological sex is determined by the 23rd pair of chromosomes. Males have XY chromosomes, and females have the XX chromosomes. So ova only carry the X chromosome and sperm can carry the x or y. Which I find slightly vindictive because back in the day women were blamed for having girls and then BAM science is like, yah no that's on you sperm donors and i'm pretty sure all the ladies that were ever harassed for having daughters just felt so vindicated when they got to heaven and were like ya, no dudes, that's on you.

So every month, 1 primary oocyte will complete **Meiosis I** and become a **Secondary oocyte** this is what gets ovulated. (This is a side note that I googled to learn. Meiosis 1 isnt completed until the day before ovulation.) Now you have listened to episode 1 and have meiosis down

and you are like, hold up. 1 - 2n cell splits into 2 n cells with meiosis 1. Which is true. But in females, one of the cells gets all the cytoplasm and the other is called a polar body. The polar bodies just wither up and die because they didn't get any of that cytoplasm. We are basically putting all of our eggs in one basket, or all of our cytoplasm in one ova.

So every month. 1 primary oocyte will complete **Meiosis I** and become a **Secondary oocyte** this is what gets ovulated. Along with the secondary oocyte, a polar body is produced. So with each round of meiosis, 1 polar body is produced. Which leaves our end count at 1 ova and 2 polar bodies discarded.

Q: were you paying attention: what stage is the egg in when it gets ovulated?
A: a secondary oocyte is ovulated.

The secondary oocyte then pauses in **Metaphase II** and will not complete Meiosis II unless fertilized.

So, the egg is just hanging out, in the fallopian tubes and for kicks and giggles. let's say that the egg is fertilized. Sperm has managed to penetrate the zona pellucida and corona radiata - which are layers that surround the egg. This triggers Meiosis II to proceed forward to an ovum and a polar body, the ovum is successfully fertilized and is now a zygote.

I know that was kinda thick so lets do a review/ questions.

What phase is are all oocytes arrested in until they are chosen to mature during an ovarian cycle?

Prophase I

What specific phase is an ovulated egg arrested in?

Metaphase II

When will an oocyte undergo Meiosis II?

Not until a sperm cell penetrates the zone pellucida and Corona radiata.

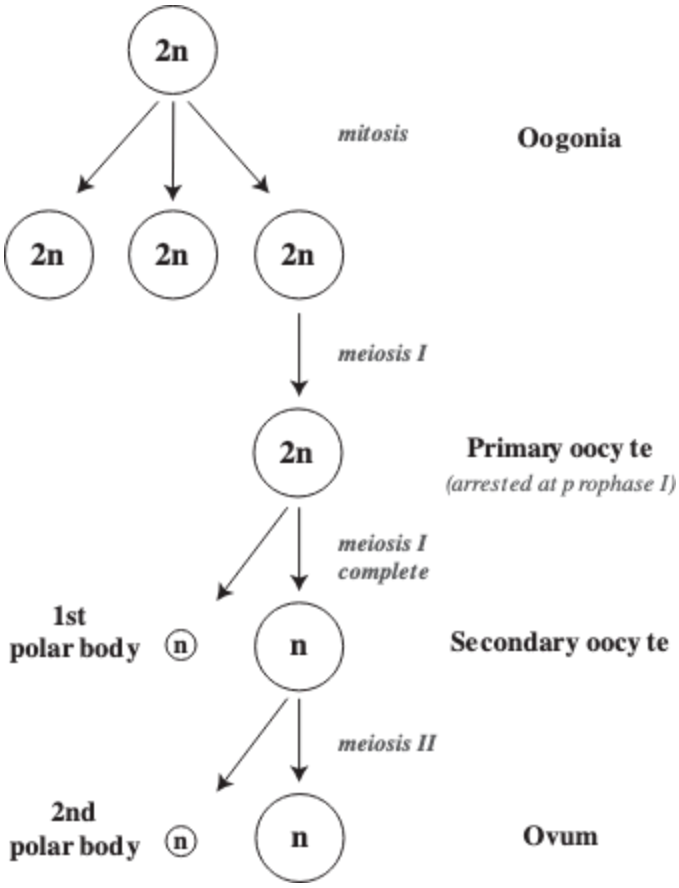
You guys might be thiniking the zona whats'a and a beer?

So the corona radiata and zona pellucida are just layers that surround the egg, and the acrosome fusing sets off enzymatic reactions that help the nucleus of the sperm get through the layers to the nucleus of the cell. This reaction is what singnals meiosis 2 to finsih

How are we gonna remember what phase the ova get arrested in?
okay. arrested in Meiosis I in prophase I,

arrested in Meiosis II in metaphase II.

I Remember this because prophase is the FIRST phase so meiosis I - so the primary oocyte is arrested in the primary phase of meiosis.
And meiosis II it is hanging out in Metaphase II which is the secondary phase of meiosis. If you don't remember this, give episode 1 another listen.



https://www.khanacademy.org/science/how-does-the-human-body-work-class-12/x7babbc170453fdb8:human-reproduction/x7babbc170453fdb8:gametogenesis/a/oogenesis-and-follicular-development-review

Now let's talk about the path the egg takes from the ovary to the uterus

It is, in my opinion the egg's path is a simpler path than the sperm takes in males. So we don't really need a terribly awesome roller coaster analogy to remember this pathway. The ovary actually release the egg into the abdominal cavity and the oocyte will get pulled in by the fimbriae, which are just beating cilia, and travel through the fallopian tube. The fallopian tubes are where eggs often get fertilized, then the egg continues to the uterus. This is where the fertilized egg should implant. From the uterus there is the cervix, that separates the uterus from the vagina. Then the vagina which is where the sperm are often deposited.

Phew, you guys got that!? You're doing great.

Now let's take a look inside the ovary - remember the oocytes are hanging out as primary oocytes arrested in Prophase I of Meiosis. Actually Before we start that lets do a broad overview of an ovarian cycle.

Each month an egg goes through a maturation process. This cycle creates the secondary oocyte that can then be fertilized by a sperm and if all of these exact processes happen, ta da, BABY this ovarian cycle is responsible for the menstrual cycle. So we will look at them in tandem. It is also imprtant to remember that fluctuations in female sex hormones, released from the ovaries, control the development of the egg and the menstral cycle.

The main sex hormones released from the ovaries are: Estrogen, Progesterone and Inhibin.

Do you remember what major sex hormone the testes make?
A: testosterone.
Do you remember what cells make testosterone?
A: interstitial cells of Leydig, which creates secondary sex characteristics - like bigger muscles, which is why they are so good at digging holes. ;)

Okay - let's start with a broad overview of the ovarian cycle.

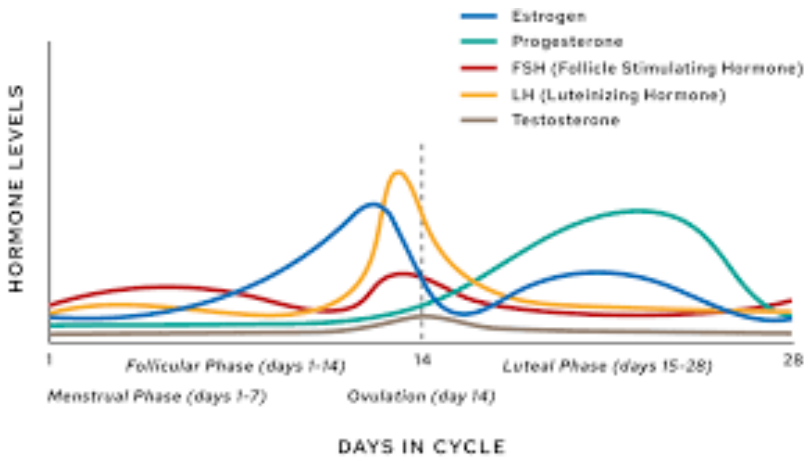
Cycles are approximately 28 days long, and day 1 is the first day of menstruation.

Day 1 through day 14 is called the follicular phase

Ovulation happens on day 14 - so halfway through the cycle - ovulation occurs.

Day 15 through 28 is the luteal phase. We will be going into more detail but I think that having a broad picture going in helps.

It's a basic bell curve - going up its the follicular phase. At the top in the middle is day 14, ovulation, and going down the other side of the curve is the luteal phase.



https://www.palmhealth.com/sync-your-cycle-and-exercise/

So first I need you to picture an american football, or rugby ball, they are round but has those pointy-ish ends. YOu are holding this ball out in front of you with the pointy ends out horizontally so they are lining up with the earth. The pointy ends run left to right in front of your face. Or a lemon --- you know-- for those of you that are totally like, that's the sport that has a ball, right.

Now this is the shape of an ovary (roughly) Starting at the point on the right, as day 1 and tracing the outside of the ball, going counterclockwise, over the top to the other point. This other point is day 14. Now continue around the ball going counterclockwise, along the bottom, back to the point on the right. Back to day 1. In a full circle. Or you know, a cycle….

Having this imagery really helps me in understanding where we are at in the ovary, on the day, which translates to having an understanding of what hormones are increasing, decreasing, spiking, etc.…

*inset pic of football/lemon cycle

Now let's follow one of these eggs through to ovulation and see what happens.

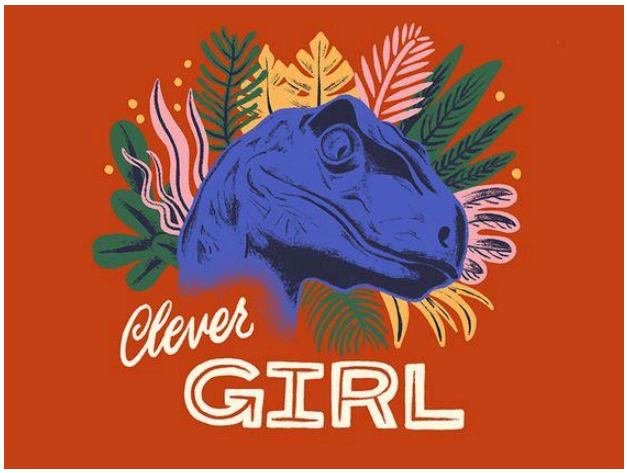
Now in the ovaries females have a ton of these primordial follicles and primordial follicles are the most immature stage of an ovarian follicle's development. It's the oocyte that is surrounded by a single layer of cells. And for me, when I hear primordial follicle, I'm thinking of old-school Jurassic park. Like the first Jurassic Park, with Jeff Goldbloom. Where they watch the egg hatch at the beginning.

"Life, ahh, find a way"

All of this imagery really helps me remember that the most basic stage of egg development is called a primordial follicle. Come on, they named it primordial, which, yes makes sense since it means giving origin to something. But all I can think is Dino's

"Cleaver girl" okay. I'll stop but Im gonna watch that movie tonight and i'm gonna link the egg hatching scene in the script notes. You're welcome.

https://www.youtube.com/watch?v=zP2m95JAD4g



Inside the ovary, eggs develop in follicles. (The follicular phase is starting to make sense, huh?)

So day 1 we are looking at the ball in front of us, we are focusing on the pointy end on our right. We are calling this Day 1.

So Day 1 a follicle is one egg surrounded by a layer of granulosa cells. Remember granulosa cells they are very important and we will talk about them more but the granulosa cells become more and more numerous as the follicle matures. I like to think of this follicle starting out on the right side and moving slowly counterclockwise to the other point. During this time the granulosa cells increase and get larger.

The granulosa cells are responsible for some of the sex hormones, specifically estrogen(which we will go into the detail of). So thinking of the number of cells increasing over the next 13 days, what would you expect to happen?

You would expect the hormones that the granulosa cells make to increase, more cells = more hormones.

So while the oocyte is progressing towards day 14 and getting more granulosa cells and growing in size its making more and more estrogen. During this progression of the follicular phase there is a layer that develops between the granulosa cells and the the oocyte. This layer is the zona pellucida (wait a second, that sounds familiar!? Remember the zona pellucida is one of the layers that surrounds the cell that the sperm has to penetrate)

I say that and then i hear fat amy say, “not a good enough reason to use the word penetrate)

So even though there is now this wall, the zona pellucida, that separates the egg from the granulosa cells the granulosa cells can still nourish the egg through gap junctions. So it's a wall that has all these gateways that are open.

The egg at this point is still stuck in meiotic arrest - it hasn't completed meiosis 1 yet.

Do you remember what phase of meiosis the egg is stuck in right now?

A: prophase 1! You all got that right, didn't you!! If not don't worry about it. You will pick that detail up on your next listen of this episode.

For those of you that have already listened to episode 1 - Meiosis - how many chromosomes does the egg have at this phase? So the egg is in meiotic arrest (kinda like house arrest) in prophase 1 - has how many chromosomes?

A: 46 Chromosomes.

How many sister chromatids?

A: 92!!!

If you just got that without even stressing a hair, I am legit proud of you - and you should probably buy yourself a cookie. If you didn't get it or if it took you a little longer than it should. Don't sweat it. Buy yourself a cookie and listen to episode 1 to freshen up on the details of Meiosis.

If you guys haven't noticed by now I am really going to try and build and pull information from previous episodes into the new episodes. So that we are repeating everything and really building those connections.

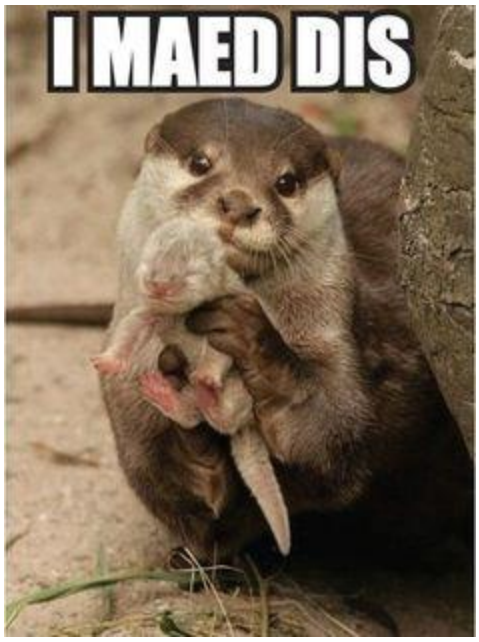
Okay - back to the ovary - so we are in the follicle and we have granulosa cells that all around and increasing in number. We also have a layer separating the granulosa cells from the egg but it has gap junctions so that the egg and the granulosa cells can still chat through hormones and the egg is still stuck it prophase 1 of meiosis 1.

Now another layer starts to form around the outside of the granulosa cells. These cells are called Theca cells. Theca cells are important because they have receptors for luteinizing hormone which is the hormone that is released from the anterior pituitary.

Starting from the outside of this follicle working our way in, lets go over the layers, as of right now. So the outermost layer is the theca cells, then the granulosa cells then the zona pellucida, then the egg.

So once the Luteinizing hormone from the anterior pituitary binds the theca cells the theca cells produce a hormone called(andro - sten - dione) androstenedione. Once the theca cells make the androstenedione they hand it to the granulosa cells who convert the androstenedione into estrogen.

Legit what came to my mind when i was researching this. Have you seen that otter meme? It's super old. But its an otter holding up a baby otter and there are the words " I MADE DIS" this is how I ace'd my classes, converting complex science principles to memes and gifs. And i kinda picture the the theca cells holding out the aderiostonedione to the granulosa cells being like " I made Dis"



And obviously, in my mind, the granulosa cells reply, and they pat the little otter on the head, like you would a child, and they say, o that's so nice, I love it. Then, they take the aderestonedione and make it into something usable. Estrogen and then release the estrogen levels into the blood. So the blood estrogen levels start to go up-

Estrogen will increase until ovulation and then drop slightly.

Eventually, at around day 14 the follicle is so large that it presses up against the edge of the ovary and the egg ruptures out with the help of some enzymes. Leaving behind it's house of granulosa cells.

Now normally only 1 egg develops to the point of rupturing out of the ovary, even though several start along the path. The one that makes it and is ovulated is called the dominant follicle, now if you have a few eggs that all make it and are ovulated this is 1 way of how to get twins, or multiple births.

So the egg has left the follicle and ovary behind and getting swept up by the the fibrae and taking its own journey. But what happens to the house that was left behind? All those granulosa cells?

Just really quick, for reference, we just passed day 14 so if we are looking at that football or lemon, we went from the point on the right, counterclockwise to the point on the left day 14 and the egg was expelled from the ovary. Now we are continuing our cycle, counterclockwise, back to day 0/1.

The follicle that expelled the egg now transforms itself into a structure called the corpus luteum. Which is basically a dead follicle. I mean it's called a corpus. The corpus luteum secretes 3 hormones: estrogen, inhibin, and progesterone- let's delve in.

The corpus leuteum is like when you move out of your parents house and your entire life they went to bed at 10. and you go home for a surprise visit and arrive at 11 thinking they are going to be alseep, but instead they are having a pool party with all the neighbors and your house is really just not the same. This is basically what happens. the egg is out and the follicle becomes the corpus leteum. (leteum, as in leutal phase - sound familiar?

In this new house the granulosa cells actually get a lot bigger and continue producing estrogen but the corpus leuteum really starts pumping out progesterone and some inhibin. Some progesterone and inhibin is produced during the follicular phase, but a lot is produced in the luteal.

-Estrogen will increase until ovulation and then drop slightly. inhibin is present after ovulation and will increase after ovulation, because of the corpus leuteum.

-Progesterone levels were low until after the ovulation and will continue to increase after ovulation during the luteal phase.

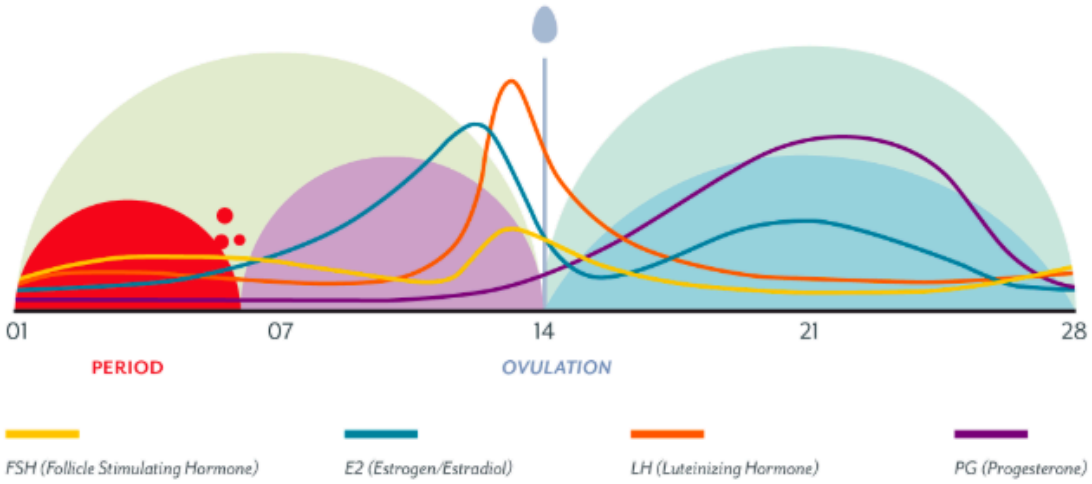
So at day 21 of the female reproductive cycle, progesterone is increasing, and inhibin is increasing.

Inhibin, inhibits so it will inhibit the secretion of FSH. we are in the leuteal phase; we don't need any more follicles stimulated. We don't need any more eggs to mature just yet

Inhibin lowers the amount of FSH - follicle stimulating hormone that is released from the anterior pituitary. Which think about the words and it literal is telling you what it does and makes sense. So follicle simulating hormone, stimulates the follicles to develop and mature. But when we are the second phase of the cycle, the luteal phase we don't want follicles stimulated. We don't want eggs to keep developing. So when the follicle becomes the corpus luteum and starts producing inhibin to inhibit the FSH so that follicle growth isn't stimulated….

Nifty little system right.

Women's hormones and cycles can look like a lot at first glance, but i have found if i really understand what is at play they aren't as terrible as that graph you are shown in physiology. Where you are like, holy shit. Women are so freakin complicated. And not to say that we aren't complicated. But if you break down the cycles and hormones, it's not so bad.



Taken from clue - the app that helps you track your cycle. Find the article here https://helloclue.com/articles/cycle-a-z/the-menstrual-cycle-more-than-just-the-period

Progesterone is the most important hormone in the luteal phase

Progesterone stimulates endometrial growth. Which is great, because the name, progesterone is telling you what it does. Pro - as in favor of, gest - as in gestation Actually gest is latin for carried (as in carrying a baby) progesterone the word basically means in favor of carrying a child. So it make sense that your endometrial lining will grow to get ready for implantation to occur. And the lining would need to be ready for this implantation after ovulation. So progesterone levels go up drastically after ovulation.

If you ever get stuck on a hormone question go back, in your brain, to the thing that you absolutely know. And now you know that progesterone is pro baby. To get ready for baby the uterus walls need to be ready. When do the uterus walls need to be ready? They need to be ready after ovulation when there is a chance for pregnancy.

And you won't ever forget that is what progesterone does because the word tells you what it does.

Progesterone also has a negative feedback loop with they hypothalamus and inhibits GnRH.

At the end of the cycle the corpus letuam is going to degenerate, so all those hormones will decrease. So the progesterone and the estrogen and inhibin will stat to decrease because the corpus leutum is degrading so it can't produce those hormones at the same level, makes sense

huh. The decrease in progesterone means that progesterone is no longer at a high enough level to inhibit the GnRH. and inhibin isnt inhibiting, so a new cycle will be able to start. It also means that these hormones cannot maintain the endometrial lining of the uterus so it will shed. Aka the period.

***feedback loop pic

So if the egg doesn't get fertilized the corpus letuem reaches its max size the corpus leteum undergoes apoptosis. SO this is around day 25 in the 28 day cycle.

But if the egg does get fertilized the corpus letuem hangs out, and by hangs out, I mean it keeps living and producing estrogen and progesterone. THis is really important because it is this estrogen and progesterone that takes care of the endometrium where the egg will be implanted.

Wow, that was a lot. To reward you I will ask you a question.

Q: what the two phases of the ovarian cycle are called?
A: 1-14 is the follicular phase and 15-28 is the luteal phase.

Boom, aced it.

There are some really great graphs that give good visuals of the hormones, if you have a second google that. But we are still going to create a really good understanding so that you can picture this in your head so that when it pops up on the mcat you will be like, o ya, i have that filed right here in my mind palace.

Now, let's talk about the uterus and do a little review.

Did you guys ever see the movie with Ashton Kutcher and Natalie Portman- I can't think of what it's called.. No

I googled it - it's "no strings attached" i still get a kick when Ashton brings cupcakes to the apartment full of doctors all on their period and recites what is happening to their bodies from an excerpt he found on google.

https://www.youtube.com/watch?v=pJFZLCoqB9w

Anyway- the uterus is that organ that is kinda a pain in the ass, as it causes periods. I mentioned earlier that day 1 is the first day of the period, medically called menses. This is when the uterine lining sloughs off. Meses is considered to be day 1-7 but they usually don't last a full 7 days. Then after the endometrial lining is gone there is what is called the proliferative phase where the lining starts to build back up in hopes that an embryo will be implanted. After day 14 is what is called the secretory phase.

So the endometrium has 3 phases: 1- menses day 1-7. 2-proliferative day 8-14. 3- secretory day 15-28.

After the end of menses, roughly day 5-7 the endometrium will grow increasingly thick in preparation for the implantation of a zygote. If implantation does not occur the uterine lining will slough off and start over.

point of clarification, you will hear/see day 0 sometimes. Day 0 is Day 28 of the previous cycle so there isn't ever a space it doesn't go day 28, 0,1 its 28/0 then 1

So from the anterior pituitary we have FSH and LH being released. The FSH is stimulating the growth of the follicle. I mean come on. It's called follicle stimulating hormones. So down in the ovary the follicle will start to develop and get surrounded by those granulosa cells. As it gets bigger the number of granulosa cells are increasing.

The more granulosa cells there are the more estrogen they will secrete so the estrogen levels start to go up in the blood.

Remember the LH cells causes the Theca cells to make androstenedione, which it hands over to the granulosa cells which convert them into estrogen.

So, as the follicles grow, the estrogen really starts to rise. These estrogen levels really start to rise around day 7-9, which mean that the uterus is in the proliferative phase. The uterus is proliferating because the estrogen levels tell the endometrium, "Hey it's that time again. Let's start building up in hopes of a baby.

Let's check back in with the brain. The hypothalamus in the brain is really responsible for homeostasis, which means it is always keeping track of what's going on in the body, what's going on in the blood. So the brain senses that the estrogen levels are getting high so the levels of FSH and LH decrease slightly.

The granulosa cells are still producing estrogen but they also start so produce more inhibin and progesterone.

Q: do you remember what inhibin does?
A: inhibin inhibts FSH release.

Q: where is FSH released from?
A: the anterior pituitary

This inhibin causes a drop in the FSH.

So at this point, you can see that there is a type of negative feedback loop where the estrogen levels signal the brain to decrease FSH and LH.

***hormone loop

But at this point the granulosa cells are like no, we got this. They are a runaway train. So what happens is that the level of estrogen gets so high that it actually triggers a spike in the FSH and LH.

But remember the granulosa cells have also been spitting out inhibin so the spike in FSH is not as high as the spike in LH.

This huge rush of LH from the anterior pituitary is called a Luteal Surge. In my head, I think of it as a hallway that is getting flooded violently—a surge coming at you. This LH surge is what pushed the follicle to ovulation. After this spike, the FSH and LH slowly decline due to all of the progesteone and inhibin being pumped out by the corpus luteum.

https://makeagif.com/gif/titanic-hallway-flood-CnW6db

So let's think. On day 14, we are at the left point of the lemon/football. So we are at ovulation, and the follicle is about to turn that corner and become a luteal body. In the uterus, we are on the last day of the proliferative stage and moving into the secretory phase.

Yes, we are champions.

I know we just covered a lot in this episode. It was a lot. I really hope that this podcast helped you get a solid review in while driving or working, or hitting the gym, or wherever. If you are listening I tremendously appreciate it.

Study hard, friends - and do me a favor and compliment a stranger today.

PS. I am a fan of the podcast Ologies, and today I actually listened to the episode on gynecology I found it so serendipitous that I listened to that episode at work earlier today and now I'm recording this episode, so if you want to listen to a really great interview with a

gynecologist check out the gynecology episode on “ologies” I will also put a link in the script notes on the website. Cellfielife.com

https://www.alieward.com/ologies/gynecology?rq=gyno

Study hard, friends.