Embryogenesis (1)
Episode 4

“Come on baby, Baby baby baby baby baby”

Can anyone name that movie line…? It's Reese Witherspoon in “Walk the Line.” I really love that movie and

https://www.youtube.com/watch?v=6bR-BPDwdXo

I know you’re all surprised I'm not singing at you. I considered doing a rendition of Britney Spear hit me baby one more time.

https://www.youtube.com/watch?v=C-u5WLJ9Yk4

But when I'm animating the word baby in my mind, Reese beats Britney to the punch.

Hello, everyone; welcome to the Cellfie life! Here, we are reviewing topics covered by the MCAT.

My name is Nikaela, and today, I’m going to be reviewing embryogenesis. And I'm not going to lie to you. It is complex. It is probably as complex, if not more so, than the female reproductive system. But I mean, come on, does anyone out there expect growing babies to be easy?? But I am going to do my best to break it down and tie it all together.

Human babies blow my mind. I mean, growing any type of baby is crazy, but human babies are next level. How cells are this smart to pull off this sorcery(like witch fingers and bunny ears) is just another reason that I love science. This really is so cool.

Let’s jump in and start with the basics.

What is embryogenesis!?

Embryogenesis is the formation and development of the embryo in the first eight weeks after fertilization. And it really is kinda a whirlwind of mitotic activity and cell differentiation. This makes sense because you are taking a single-celled organism and turning it into an organism that is developing brains, intestines, limbs, and eyelashes. Okay, let's be honest. At the end of embryogenesis, it's basically a ball of cells with tubes, but they will develop into the guts, brains, limbs, and all that stuff.

So without further ado, let's get into embryogenesis.

Actually, there is some more ado….

This episode may contain some sexual health material

It's really more of a review of embryogenesis, but there might be some flashback material.

Okay, pop quiz time.

You didn't know that you would be starting this episode with a pop quiz, did you!? It's okay, this is one pop quiz you're gonna ace, because im grading and I make the rules.

Question 1:

Q: a spike in what hormones causes ovulation?
A: LH and FSH

Follow up:
Q: which surge point, LH and FSH, was highest and why?
A: the LH surge was greater because the inhibin being produced is already inhibiting FSH.

Okay, so ovulation of a secondary oocyte has occurred. Like just occurred.
Q: and the egg is arrested right now in what phase?
A: metaphase II

If you're having any trouble with these concepts, just use it as an informative experience that shows you where you can improve.

You can just go back and give the last few episodes a listen for a helpful review.

Okay, back to the egg.

The egg has been swept up by the fimbriae and now is in the fallopian tube, minding its own business hanging out in the ampulla, which is the widest part of the fallopian tube, and a common spot for fertilization.

And along comes this sperm.

Now egg cells are about 10,000 times larger than the sperm. So there is a very large size difference. And this is where the real magic happens. And my real magic, I mean science

Do you remember that part of the sperm that I called the beanie? It's on the top of the sperm head? The acrosome. When the acrosome binds to the oocyte it releases some special enzymes that allow it to penetrate the corona radiata and zona pellucida. This first sperm to the

egg creates a special tube called the acrosomal apparatus which penetrates the cell membrane so that the pronucleus can enter the oocyte once the oocyte has completed meiosis II.

So basically, it needs a tunnel. To deliver its special genetic material. Let's be honest, right here I imagine the sperm is basically using its penis to put its genetic material into the egg. After you have sex, the egg and sperm basically have to do the same song and dance. So, the penis, in this case is this acrosomal apparatus.

After the sperm has penetrated the membrane, a cortical reaction happens. Now, a few more root words for you here, cause you know that I love root words.

Corico - actually means bark like the bark of a tree or shell in Latin. So, the cortical reaction is what happens when the sperm is able to get through the shell of the egg which would be what 2 layers from the external to the internal?

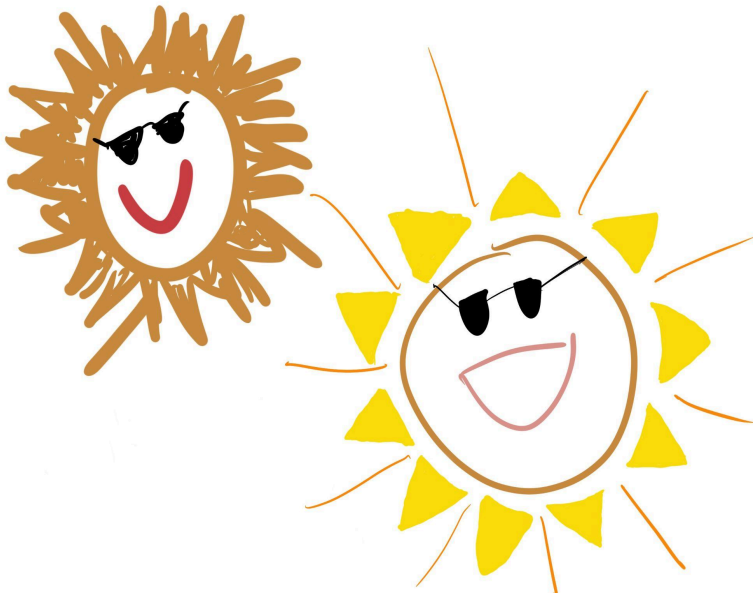
A: corona radiata, zona pellucida.

There are other layers but these seem to be the ones we need to be familiar with for the general anatomy and physiology on the MCAT.

I don't know if you've seen the illustrated images of the egg cell, but to me, the egg cell always kinda looked like the sun drawings I did in elementary school—with all the rays coming off, wearing sunglasses, and smiling.

The rays that are sticking out are the corona radiata. The radiata means spoke and/or ray in Latin. And it is really just the cell's crown. So the name really paints an image in my brain.

So when you hear corona radiata think of those elementary school kid drawings of suns. This image will also help you keep the layer straight since those rays are on the outside. And the corona radiata is the outside layer.



Back to the cortical reaction -

The cortical reaction is actually pretty cool; a bunch of calcium is released, which depolarizes the membrane of the ovum.

A quick reminder that depolarization is when there is an electrical shift within the cell. So basically all of this calcium, which has a positive charge is released from these pockets and the cell becomes less negative because all of this positive calcium was released. This reaction prevents polyspermy, which just means fertilization by multiple sperm.

The increased calcium also increases the metabolic rate of this new little zygote.

And now this zygote needs to implant in the uterus—or baby box, if you will. But a few things happen to the zygote as it travels from the ampulla to the uterus.
The zygote will start undergoing rapid mitotic division, without growth, which is known as cleavage. Once this cleavage starts. The zygote can now officially be called an embryo!!

Cleavage is splitting without growth this happens in the embryo because it has to divide so fast, it doesn't have time to grow. So the embryo it’s doing all of these quick cleavages.

There are 2 types of cleavage: indeterminate cleavage and determinate cleavage. This difference is completely contained in the names. Determinate cleavage means, essentially that the cells fates are set. These cells differentiate into already determined types of cells. Indeterminate cleavage means that the cells can still develop into complete organisms. In fact, this is how you can get monozygotic twins. Monozygotic means 1 zygote is formed and then it is split so there are gonna be identical twins. So monozygotic twins are 1 egg fertilized by 1 sperm that then splits and implants. Get it, monozygotic, one --- zygote

Does anyone know what another type of twins?
A: I know a smart alek out there said non-identical twins, which is correct but doctors call this dizygotic or fraternal twins. Dizygotic because 2 different eggs are fertilized by 2 different sperm, thus 2 zygotes. So if you are a dizygotic twin you share no more genetic information than regular siblings share.

Back to the embryo,

Once the embryo has divided 16 times it really starts to look like a mulberry, and it's called a morula; I'm gonna be honest here, I know that this stage is called a morula because it looks like a mulberry but I didn't know what a mulberry looked like, so I googled it. A mulberry looks like a mix between a raspberry and blackberry, t it was kinda freakishly long. But even with these pinky-length berries I now want to try something with mulberry in it. So if any of you have a good mulberry recommendation, shoot it my way. But really send me some recipes.

Pic taken from
https://www.froghollow.com/products/2020-mulberry-madness-organic-fruit-club-4-shipments

So after a morula is formed the little berry now goes through what is called blastulation to form a blastula. So for me, I think of a blastula like one of that old-school gumball that is hollow on the inside. So a blastula is a hollow ball of cells with fluid on the inside. The inner cavity is called a blasteocoel

Coel C-O-E-L means hollow in greek. So a blastocoel means hollow bud. Which is exactly what this little guy is a hollow bud. Also, you could just think of it as a blasted-out cell.

Really quick, we're gonna run down the list of stages and names from zygote to blastula.

Zygote - embryo - morula - blastula after blastual we have the blastocyst.

The blastula is the hollow ball and the blastocyst is what is called once a few different layers have formed: **trophoblasts** and **inner cell mass**. The trophoblasts are on the outside, and the cluster of cells on the inside is the inner cell mass.

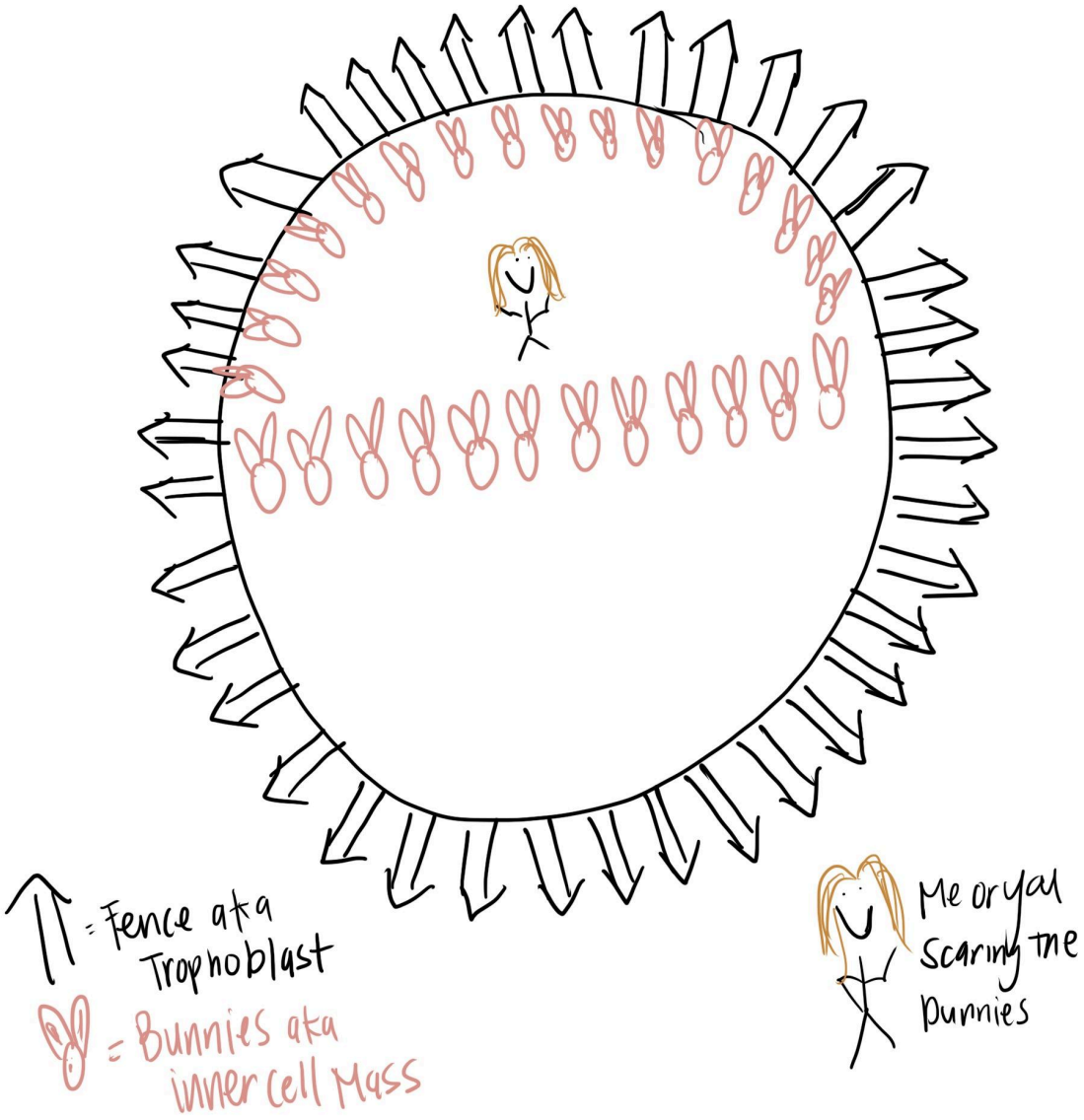
**pic of trophoblast

One more time, the cells that make up the outside, or the gum part, if we are sticking with the gumball analogy, it's the outside layer, It's called the trophoblast. The trophoblast is the outside layer that surrounds the blastocoel.

Tropho means to nourish, like food, nourish in Greek, which makes sense because this outer layer will become part of the placenta, which is needed to nourish the growing fetus. Also, tropho kinda sounds like a trough—the things that you use to feed the animals. That should help you remember this outer layer.

In blastocysts.
There is another important small clump of cells on the inside called the inner cell mass. The inner cell mass cells have clustered so tight together that they leave a cavity on the other end. It's like when you are trying to catch baby animals and they all cluster away from you. We're gonna use puppies in this scenario. Actually puppies might not be a good example my dog banana joe always wants to be touched and held and just walked right up to us as a puppy ummmm. Let's go with bunnies. Imagine this. You walk into a circular enclosure, the fence on the outside is the trophoblasts, and the bunnies that are huddling on the other side, cowering from you, are the inner cell mass and you are hanging out in the hollow area which is called the blastocoel. So now this is no longer looking like a mulberry and is no longer just a hollow shell of cells so it has graduated from a blastula to a blastocyst. I put a stick figure drawing of this in the notes, if you need an extra visual and/or want to see how terrible my stick figure drawings are.

I forgot to mention at the beginning that the script notes can be found on the website cellfielife.com



So now you walk towards the bunnies and they fan out and now there's a layer of bunnies in front of you, to the sides of you, and behind you. They have formed a new cavity with you in the middle of this new cavity. This new cavity is called the amniotic cavity.

Does this make sense, I might have run this bunny scenario into the ground.

Okay. imagine this. You have a circle, there is a line that cuts half way across the circle and lines the inside of half this circle. The inner cell mass has hollowed out so now there are two hollow areas. The one that is lined by the inner cell mass, is now called the amniotic caviety and the other cavity is still called the blastocoel. The inner cell mass differentiates even more and the cells closest to the blastocoel side are called hypoblasts and the cells right above it are called epiblasts.

That's kind of a lot, so lets run though that one more time. You have a ball of cells and we are going to look at a cross section of it. So we are looking at a circle. Let's draw this circle in black. You split the circle in half with a red line and outline the inside of the top half of that circle in pink. Underneath your pink line that splits the diameter of the circle is that red line you drew. The red line is called the hypoblast and the pink line on top of the redline is called the epiblast. So we have two hollow areas inside our circle. The bottom hollow area that is cut in half by a red line is the blastoceol with that red line being the hypoblast layer. The other hollow area is on top and it is outlined with pink. This is the amneotic caviety.

You guys, super boiled down, its a circle that has two layers down the middle. The hypoblast and epiblast. The hypoblast and epiblast layers came from the inner cell mass.

The hypoblast and epiblast also called the the bilaminar disk because this is what will give rise to the 3 germ layers, which will form the entire tiny human.

Top layer, epiblast - epi- over
Bottom layer hypoblast - hypo - under.

This is the bilaminar disk. The bilaminar disk is like a stack of 2 pancakes that are permastuck together. And then you pour 1 line of maple syrup on the top pancake. You start just before the midpoint and draw the line to the edge. So the line is not quite half the diameter of your

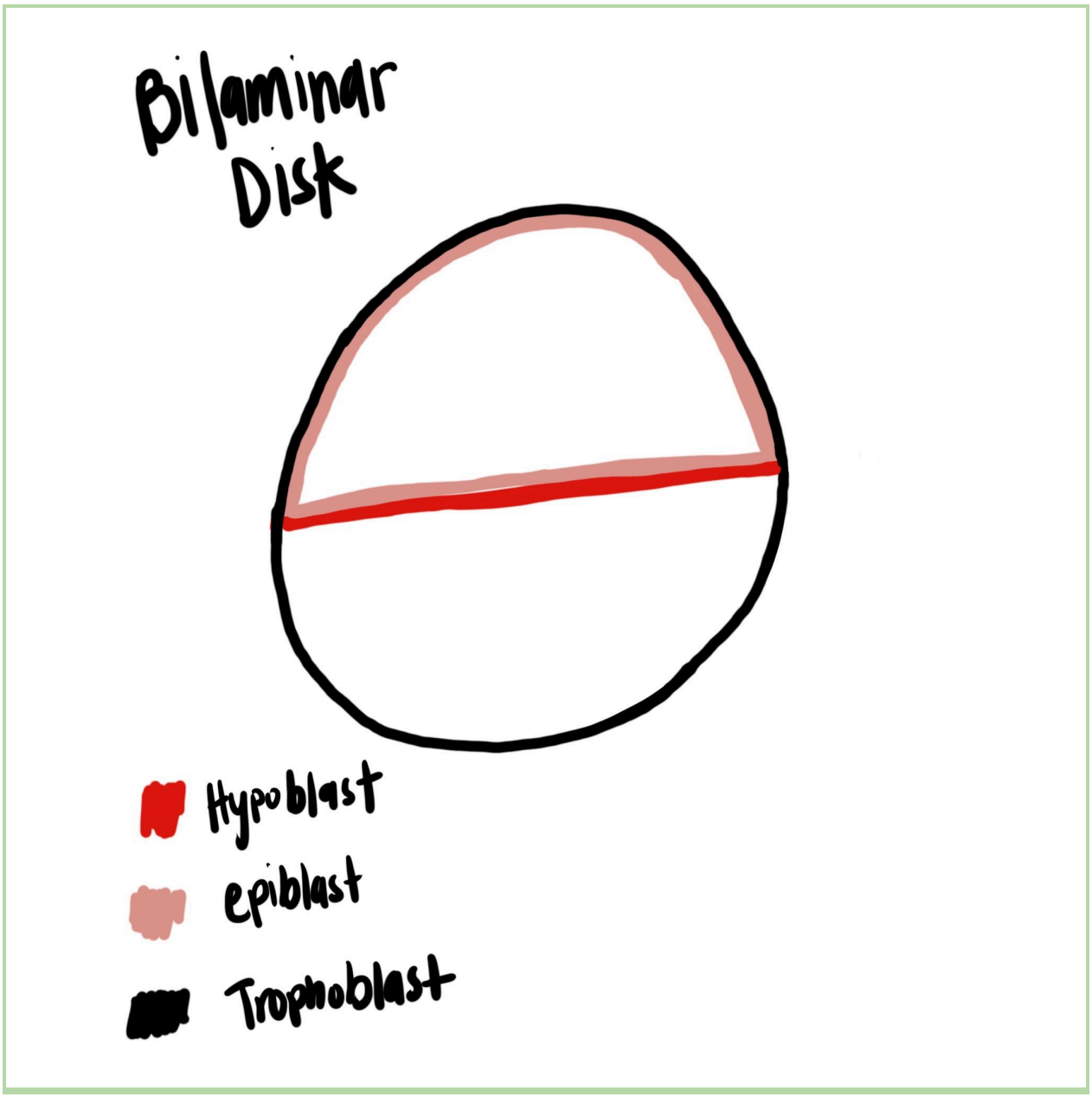
pancakes. This weird little streak thing happens along the middle of the epiblast layer. This is called the primitive streak. Which, come on is kinda a great name. A primitive streak. It's not in latin or greek. Its basic and one of the primary steps in developement.

***pic primative streak

Okay here's what I'm going to do, I'm going to do a quick outline of gastrulation, and neurulation, just so you can get a big picture, don't worry I will go into more depth. But I think a general outline here is helpful because embryogenesis can be a little dense.

This primitive streak marks the beginning of gastrulation.

The primitive streak marks the area where the epiblast cells start moving. The cells along the primitive streak burrow down between the epiblast and hypoblast layers, differentiating until there are three layers. This formation of three layers is called gastrulation. Now that there are three layers, these three layers are called germ layers.



Okay we had 2 layers that were the bilaminar disk and now we have 3 layers, the trilaminar disk, the germ layers, the top is the ectoderm, the middle is the mesoderm and the bottom is the endoderm.

Knowing these 3 layers is important they always seems to pop up on the practice mcat questions. And doctors need to know this So these will be important to know, again right now we are just doing a general overview.

After gastrulation we have neurulation. So we are going to start with our 3 layers. What are the 3 layers, do you remember? I know i said them like 4 seconds ago. But lets name them from the top to the bottom. Just for the review.

Ectoderm is the top
Mesoderm- is the middle
Endoderm - is the bottom layer

To me they always looked like a hamburger when the professors were drawing them out. The top bun is the ectoderm, the mesoderm is the patty, and the endoderm is the bottom bun.

Neurulation starts in the middle of the hamburger patty. So in the middle of the middle aka the middle of the mesoderm, there starts to be some differentiation of these cells; this little knot of cells is called the notochord.

So lets remember that the notochord happens in the very middle of the middle. The notochord forms in the center of the mesoderm.

The formation of the notochord is important because it causes a change in the ectoderm. Which ultimately results in the neural tube.

In the notes, I have a link for a YouTube video I foud helpful.

https://www.youtube.com/watch?v=dAOWQC-OBv0

I wanted to introduce you to neurulation but we are going to pause there, we will come back to though.

Because

all of this is great, but none of these layer differentiations can happen if the embryo doesn't implant into the endometrial lining of the uterus.

Do you know at what stage the embryo is in when implantation occurs?
A: a blastocyst is implanted into the endometrial lining.

Let’s go into some detail about this.

So the endometrial lining is proliferating and building up in preparation for implantation of an embryo. So, the embryo is bouncing around and ends up in a valley in the endometrial lining. Where it burrows in. Kinda like at the end of a really long day (aka my yesterday), and you climb in bed and burrow into the blankets, and it is just the best feeling. Ever. This is how I picture the little blastocyst. Just really trying to burrow in and find the comfiest spot.

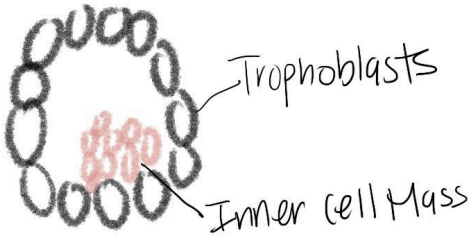
Now, do you remember what was the outermost layer of the blastocyst is called?
A: the trophoblast.

The blastocyst has shed the zona pellucida before it implants.

the trophoblast cells give rise to the chorion which develops into the placenta.

Now this next part I've always thought is really cool the trophoblasts form these finger-like projections called the chorionic villi. These chorionic villi are projections into the endometrium. I always think of it as clawing with like really long crooked witches fingers.

The chronic villi, aren't actual witches' fingers but they're really digging into the endometrium and these microscopic projects are what will support the maternal-fetal gas exchange. So these fingers are in the endometrial lining and they are finding uterine blood and are joining up with them. **There is no direct exchange; the fetal blood will be separated by a thin layer of trophoblasts from maternal blood.**



So the trophoblast implant and sends out these finger like projections that will support the maternal-fetal gas exchange. It will continue to grow until it takes up most of the uterus and it is called the placenta. But while the placenta is still growing the embryo is supported by the yolk sac.

But let's rewind a little and talk about mama. What's going on with mama right now? What are her hormones up to…?

Now if you will remember in the female reproductive episode we talked about the corpus luteum, which is what the ova's house is called after the ova has been ovulated. Its what left behind after the egg has left the ovary

remember the corpus luteum releases a bunch of hormones.

I was going to tell you what these hormones are but I feel like this is a great pop quiz question. What are the 3 hormones the corpus luteum releases?
A: progesterone, Inhibin, and estrogen.

Follow-up question. What does each of these hormones do? And I know one of you is like, they do a plethora of things but what do these hormones do in relation to the uterus?

A: progesterone - progesterone is the pro- gestation hormone so it maintains the uterus for implantation. Progesterone is really hoping for a little embryo. The high levels of progesterone also cause a negative feedback loop with the brain's hormones.

Inhibin: Inhibin inhibits FSH so that the body is investing in the egg it has in production, not getting ahead of itself, and working on multiple eggs at once. It's not like a factory conveyor belt.

I think of that “I love lucy’ episode. The one where she is shoving the chocolate in her face and can’t keep up with the conveyor belt. No, this system is quality over quantity. It wants to give all the attention to one egg at a time. (there are exceptions, aka multiple births, but you get what i’m saying) basically, what I'm getting at is that inhibin is one of the hormones that make this possible. If Inhibin were to talk it would say, “Hey, let's focus on finishing this one project before we move on to another project.”

Estrogen. Estrogen helps regenerate the uterus after menses.

But, in this case, the egg was fertilized and the blastocyst is going to implant into the uterus so what needs to happen with mom's hormones?

The blastocyst will implant and secrete human chorionic gonadotropin hCG - that chorionic sound a little familiar? It should remember how the chorionic villi stretch out their fingers and weave their way in, to set up the placenta. This chronic development is one of the first things that the newly implanted embryo does, so it makes sense that it also releases human chorionic gonadotropin. HCG

See it's not too bad, it all fits together.

hCG is actually a very chemical similar to LH. It's so similar that it can stimulate the LH receptors, and the corpus luteum is maintained. So instead of dying off and the levels of hormones decreasing until the GnRH once again starts the FSH and LH cycle over again, the corpus luteum is maintained by the hCG.

So once you get pregnant, the corpus luteum hangs out for a little bit because the embryo is like,

Hey, hey you. You should stick around for minute. I'll give you this hCG and the corpus luteum is like, might as well.

And since the corpus luteum is sticking around it does its thing. The thing is releasing hormones.

The corpus luteum keeps releasing estrogen and progesterone. So the hcg is critical because it keeps the corpus luteum around and the corpus luteum releases progesterone and estrogen which maintain the uterine lining so that it is not sloughed off. Aka no period.

By the second trimester, the placenta is large enough that it can take over the progesterone and estrogen so the HCG levels decline.

These high levels of estrogen and progesterone that are being secreted by the placenta now are high enough to take care of the negative feedback loop so that Gonadotropin-releasing hormone GnRH is still inhibited. Also, please note that the placenta is releasing hormones, which makes it an endocrine organ.

Side note: have you guys heard of the hcg diet? People take hcg and then are on a super low-calorie diet. I've heard that if f they take a pregnancy test while on a diet, the pregnancy test will come back positive because a lot of pregnancy tests are looking for the presence of hcg.

Quiz question: By the time that the blastocyst is ready to implant the endometrial lining will be under the influence of what hormone?
A: progesterone.

Follow-up question:
What is producing the progesterone?
A: the corpus luteum.

What phase is the endometrium in? Remember the endometrium has those 3 stages?
A: if progesterone is the main hormone we know that we are in the secretory phase.

You guys are freaking brilliant. If you were stuck, it's all good. Go give the female reproductive podcast another listen for a refresher.

Okay, now let's go back to the embryo before I took us down that hormonal memory lane. We were talking about how, until the placenta is up and producing enough estrogen and progesterone, the yolk sac supports the embryo. The placenta is the most important extra-embryonic structure, but there are other important structures, especially in the early phases when the placenta has not yet fully developed.

So, what are these extraembryonic membranes? And what do they do?

Also, they are called EXTRA embryonic membranes, so other than the embryo, what else is there?

So lets put our embryo in the middle, the first layer that surrounds it is called the amnion and it contains the amniotic fluid.

Amnion is the extraembryonic membrane that surrounds the developing embryo. The amnion is filled with fluid and its main job is to serve as a shock absorber. It also helps regulate temperature. It really is just a protective layer. Think bubble boy. The baby can inhale and exhale this fluid but it does not get any oxygen from it. Here's a thought for you. The waste products from little embryo are also excreted into the fluid. so the fluid is really just circulating around…..

So, this amnion layer starts out in early development and surrounds the embryo. The embryo right now is more of a bean shape with the indent being about at the embryo's belly button. Okay so picture this. You have a bean, from the bean's belly button, there is a sac that completely surrounds and envelops the embryo, but there are also 2 other structures that stick out and at this early stage in the drawings, they kinda look like bunny ears. are the yolk sac and the Allantois
A - lan -to -is

One more time, you have a bean that is surrounded by a bubble that meets at the bean's belly button, at the belly button, you also have 2 bunny ears sticking out. These "bunny ears are the yolk sac and the allantois.

The yolk sac doesn't have a huge role, but a really cool fact about it—that I really don't think we need to know for the MCAT, but you'll need it in med school—is that the yolk sac will form the embryo's first red blood cells. Actually, it's the yolk sac, then the liver, then the bone marrow.

The other structure is the allantois

The allantois and yolk sac will form the umbilical cord

The allantois is involved in early fluid exchange between the yolk sac and the embryo

The 4th and final of the extraembryonic membrane is the chorion, which surrounds the entire system and has some folds, or vili, which result in extra surface area. These villi ultimately absorb nutrients from the endometrium. Can you guys remember what villi we mentioned earlier? So one side, we have the chorionic villi, which are gonna be the embryonic portion of the placenta, and the other side is just called the chorion.

Okay, let's go over that one more time, from the embryo out. Surrounding the embryo is the amnion, then we have the yolk sac and allantois. Ultimately, remnants of the yolk sac and allantois will form the umbilical cord, but mostly the allantois. Then, surrounding the entire thing is the chorion. The choric villi form the embryonic portion of the placenta.

So how do I remember the allantois? It kinda sounds like Atlantis. You know Plato's lost island, the one that sank in a day and a night around 9,600 BCE. Nobody really knows if it was real or a metaphor. Anyway, that island, Atlantis, is wasted.

The Allantois will remove waste from the embryo, such as waste like c02, and it does this through the umbilical cord, which was formed by the Allantois.

Okay, so this episode is getting longer than I wanted. So I'm going to split it in two. I'll call this episode early embryogenesis, and in the next episode we will finish up the embryogenesis review.

In this episode, we talked about fertilization, cortical reactions, and the types of twins. The zygote, morula, blastula, blastocoel. We also reviewed the development of the bilaminar disk and outlined what will be covered in gastrulation and neurulation.

Friends, Thanks for listening. Please rate, review, and subscribe, and tell your fellow want-to-be doctor friends about this podcast.

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do me a favor and practice some self-love and schedule a nap in the near future. And when you are getting all snuggled in. just be like. I am a blastocyst getting all sorts of cozy.

Study Hard Friends
Byeeeeee-----

Hit me, baby one more time