

Erin Welsh

We want to start with a disclaimer that throughout this series we feature explanations and stories that include some heavy material, including early pregnancy loss, stillbirth, and other traumatic experiences of pregnancy, childbirth, and the postpartum period.

Sienna

I'm Sienna. I'm 28 years old and 28 weeks pregnant with my first child. It seems like a cliché but my most daunting pregnancy symptom has been morning sickness. I was aware that it was a misnomer and that it would not be restricted to the morning but my biggest surprise was how frequent, long, and intense morning sickness is. I didn't expect to lose weight during the first trimester or be woken up at 1 am because of the sudden urge to vomit. I'm not a stranger to vomiting. I've thrown up before with the flu, food poisoning, intense migraines, anxiety episodes, and of course after a night of having a little bit too much fun as they say.

But morning sickness is different. It feels similar to motion sickness, like you're on a boat all the time. When there's nothing in your stomach, the urge to throw up is so intense and you end up throwing up this thick, bright yellow fluid that looks honestly like lemon Gatorade. I had my iWatch give me sound warnings from my own vomiting, saying just 10 minutes at this level can cause temporary hearing loss. And in my experience the heaving has been so intense that even if I just went to the bathroom, I still end up peeing myself. It's just so aggressive. I actually have to wear diapers now just in the off chance that I happen to throw up and that's just something I've accepted as part of my life now with my pregnancy journey.

It has been a challenge, especially with working full time and having to commute 2.5 hours every day. You never know when morning sickness is going to strike, so I even have little bags in my car. My morning sickness started at week 5 and was pretty much all day, every day until week 22. I got a little bit of a break and then it started up again around week 26. Although it's no longer all day, it is truly just in the morning usually. And I've tried all the remedies that they tell you, ginger, B6, Unisom, pressure point bands, the list goes on. Zofran has worked the best for me but it's still very hit or miss on whether it'll work on any given day.

Anonymous

When I went in for my first ultrasound at 7 weeks, the doctor was able to see a gestational sack and a yolk sack but no fetal pole. My doctor tried to assure me that it was possible I wasn't as far along as I'd thought but I had been tracking my ovulation and I knew this wasn't a good sign. Since this was a deeply wanted pregnancy, my doctor suggested we wait a week and do another ultrasound. At 8 weeks the ultrasound showed some growth, a fetal pole and a heartbeat. At first I felt so relieved, certain that progress from the week before meant that maybe things would actually be okay.

But then my doctor explained that the embryo was measuring less than 6 weeks and the heartbeat was only 84. When I got home, I turned to Google and found a study that said first trimester heart rates under 90 had a quote "dismal" prognosis. The following week when I was 9 weeks into my pregnancy, I went in for my final ultrasound, which showed an embryo measuring only 6 weeks, 1 day, and no heartbeat. My doctor was able to schedule me for a D&C the next day.

My whole pregnancy I had no indication that anything was wrong. I had strong dark lines on my home pregnancy test and early blood tests showed my HCG doubling at an appropriate rate. I felt lucky that I was experiencing only mild nausea but I did have all the usual pregnancy symptoms. And I had no bleeding or spotting at all, no cramping, absolutely nothing that led me to think my pregnancy wasn't progressing exactly as it should. I knew miscarriage was common, especially for women in their late 30s like me, but I always assumed that there would be some kind of outward sign. Going through a missed miscarriage led to feelings of profound betrayal. My pregnancy wasn't viable and my body had no idea. I feel as though I am no longer able to trust the signals that my body is sending.

TPWKY

(This Podcast Will Kill You into theme)

Erin Welsh

Thank you all so much for sharing your story with us. And really a huge thank you to everyone who has written in with their experiences. We read each and every single one of the hundreds of firsthand accounts that people submitted and we're so grateful and truly honored that you felt like you could share those with us. And we tried to include as many of your stories as possible and you'll hear more firsthand accounts throughout the rest of this episode and the other episodes in this series.

Erin Allmann Updyke

Yeah, thank you again. It really was a huge privilege to be able to read all of your stories; listen to all of the stories that you guys sent in. I genuinely cried through most of them-

Erin Welsh

Oh my gosh, yeah.

Erin Allmann Updyke

Whether it was happy or sad tears. So really thank you again so much from the bottom of our hearts for sharing all of your stories with us.

Erin Welsh

Truly.

Erin Allmann Updyke

Yeah.

Erin Welsh

Hi, I'm Erin Welsh.

Erin Allmann Updyke

And I'm Erin Allmann Updyke.

Erin Welsh

And this is This Podcast Will Kill You.

Erin Allmann Updyke

Today is episode 2 of our four part series.

Erin Welsh

Four parts.

Erin Allmann Updyke

On pregnancy.

Erin Welsh

Yep, yeah.

Erin Allmann Updyke

Yet again, coming to you from the Exactly Right studios.

Erin Welsh

I know. I feel like I'm getting more used to it now.

Erin Allmann Updyke

Yeah?

Erin Welsh

It's good. Yeah.

Erin Allmann Updyke

It's going to be like this is the new normal.

Erin Welsh

This is the new normal. But before we get into this episode, we want to share a few words about what these four episodes will cover. And if you listened to our first episode this will sound familiar to you but in case this is your first time tuning in-

Erin Allmann Updyke

Welcome.

Erin Welsh

I just want to go everything over again. Yes, welcome. But we also want to get into the language that we'll be using and our goals with creating this series. So we decided early on to dedicate four episodes to cover pregnancy, one for each trimester.

Erin Allmann Updyke

Not enough we realized early on but alas.

Erin Welsh

I mean very, very much not enough.

Erin Allmann Updyke

Yep.

Erin Welsh

And yeah, so we did realize this and we're not going to be able to cover everything. And throughout the series we started to jot down like different ideas for future episodes and so do keep in mind that if you're listening in and you're like oh, I want to know more about that, hey, send us your idea.

Erin Allmann Updyke

Yeah.

Erin Welsh

Maybe we will cover it in a future episode.

Erin Allmann Updyke

I'm sure we will honestly.

Erin Welsh

I'm sure that we will.

Erin Allmann Updyke

So knowing that, this entire series will likely not answer all of your questions about pregnancy or cover every experience that a person can have during pregnancy. Pregnancy is an incredibly individual experience, as highlighted by all of our firsthand accounts. But what we aim to do with this whole series is take you through the broad changes that we see in the human body and that you might experience during pregnancy, childbirth, and the postpartum period, and then also explore the historical and today especially the evolutionary aspects of pregnancy and childbirth. So each episode very roughly corresponds to each trimester. So last week we covered the first trimester, how you even know whether or not you're pregnant, and what was happening in very early development.

Erin Welsh

Yep. Then today-

Erin Allmann Updyke

Today!

Erin Welsh

In our second episode, we're going to talk about the amazing organ that is the placenta and some of the physiological changes which really I'm so excited to learn more about what is happening. Okay.

Erin Allmann Updyke

I can't tell you how excited I am.

Erin Welsh

We have two more episodes to like briefly go through, so yeah. But we're going to talk today about the placenta and these physiological changes that someone will experience as they go through pregnancy, including some of the complications that might arise.

Erin Allmann Updyke

Right. And then next week in our third episode we'll talk about childbirth itself. We'll cover labor, all of the different modes of delivery, and then the history of Cesarean sections.

Erin Welsh: Yep.

Erin Allmann Updyke: It's going to be good.

Erin Welsh: It's going to be good. And then finally our fourth episode, which happens to be our season finale, will be about this concept of the 4th trimester, exploring the changes that happen after pregnancy. And we're also going to be talking big picture history about overall medicalization of pregnancy and childbirth and how the transition from home to hospital happened and some of the consequences of that.

Erin Allmann Updyke: We intend for all of these episodes to be inclusive of all families and we recognize that not everyone who experiences pregnancy identifies as a woman. So we try wherever we can to use gender neutral language such as pregnant person, while at the same time we recognize that a lot of what we're going to discuss when it comes to medical bias during pregnancy and childbirth both historically and today really is the result of gender discrimination as well as racism. And so in those contexts we will also be using the term 'woman' and 'women' and throughout these episodes we'll be using terms like 'mother' or 'maternal' and 'paternal', as these are terms that are very often used in the scientific and medical literature.

Erin Welsh: And we also want to acknowledge that there is no such thing as a normal pregnancy, right.

Erin Allmann Updyke: Yeah.

Erin Welsh: There is no textbook pregnancy.

Erin Allmann Updyke: There's plenty of textbooks about pregnancy.

Erin Welsh: Yes but when it comes to pregnancy, there's no textbook example.

Erin Allmann Updyke: Yeah, yeah.

Erin Welsh: But we do want to also provide a baseline of the expected physiologic and anatomic changes that occur during pregnancy because that can help us to understand where these complications are coming from and what we actually mean by complication.

Erin Allmann Updyke: Exactly, yeah. And so now, today, we enter the 2nd trimester.

Erin Welsh: The 2nd trimester. Shall we?

Erin Allmann Updyke: We shall. But first-

Erin Welsh: But first.

Erin Allmann Updyke: Quarantini time.

Erin Welsh: And we're drinking again Great Expectations.

Erin Allmann Updyke: Great Expectations.

Erin Welsh: Yeah.

Erin Allmann Updyke: I do have great expectations for this episode.

Erin Welsh: I have great expectations for this whole series.

Erin Allmann Updyke: Me too.

Erin Welsh: Yeah.

Erin Allmann Updyke: Remind us, Erin, what is in Great Expectations.

Erin Welsh: Of course. It is blackberries muddled with mint, some ginger ale and lemon. It's a placeborita.

Erin Allmann Updyke: It's a placeborita for a pregnancy series for obvious reasons.

Erin Welsh: Yeah. It's great.

Erin Allmann Updyke: And if you haven't already, please do check out YouTube-

Erin Welsh: Yeah.

Erin Allmann Updyke: Where you can find the Exactly Right network channel that now includes our content.

Erin Welsh: Yes.

Erin Allmann Updyke: Including a very special quarantini recipe by Georgia Hardstark.

Erin Welsh: Yeah!

Erin Allmann Updyke: Made just for this series. We're thrilled.

Erin Welsh: And we'll also be posting the recipes for this quarantini and placeborita set on our social media and as well as our website thispodcastwillkillyou.com.

Erin Allmann Updyke: Have you been there yet?

Erin Welsh: I get to shuttle it again to you.

Erin Allmann Updyke: It's me again. On our website thispodcastwillkillyou.com you can find so many incredible things. For example, you can find transcripts from each and every one of our episodes. You can find a Goodreads list from where Erin Welsh likes to read books mostly.

Erin Welsh: There's also a bookshop.org affiliate account.

Erin Allmann Updyke: Yeah, I was going to say that this time. I forgot last time.

Erin Welsh: Yeah.

Erin Allmann Updyke	We've also got merch, some pretty incredible merch that we're repping today if you're seeing this on video.
Erin Welsh	Yep.
Erin Allmann Updyke	What else do we have? We have sources from every single one of our episodes. We have links to Bloodmobile who provides the music for all of our episodes. We've got a contact us form, a firsthand account form. Have you been to our website yet?
Erin Welsh	No one is going to want to go. They're like I've seen it all, I've heard you talk about it all.
Erin Allmann Updyke	I know.
Erin Welsh	What else? What else do I need?
Erin Allmann Updyke	Nothing new.
Erin Welsh	Nothing new.
Erin Allmann Updyke	Okay.
Erin Welsh	Shall we?
Erin Allmann Updyke	I think we shall. I don't have any other business for today.
Erin Welsh	Same, same.
Erin Allmann Updyke	Tell me, Erin, all about the placenta.
Erin Welsh	I really can't wait.
Erin Allmann Updyke	Good.
Erin Welsh	Let's take a break though and then I'll get started.
Erin Allmann Updyke	Okay.
TPWKY	(transition theme)
Tracy	Hi, my name is Tracy and I was 30 years old and went off the birth control pill. I had been on it since I was 16. Hoping for the best, my husband and I went for it. Three months into being off the pill, I was late having my period. It was a Friday night and I would normally be having a nice gin and tonic to greet the weekend. So I went to the store and bought a pregnancy test and immediately took it. It was negative. Okay, I guess I will be having a G&T and went into the kitchen to mix up my favorite cocktail. Five days later on April 1st, I had a regular checkup at my OB. She and I talked about what my plan was and that I was officially off the pill. I did the normal things at the appointment, urine sample, etc. She was gone for a bit and when she came back into the room she said well this is no April Fool's joke but you're pregnant.

Whoa, okay. I went home to tell my husband and thought I'd have a little fun with the fact that it was April Fool's Day. So aside from being totally shocked, we were excited and a bit terrified. The next week I went into the doctor's office to have my HCG levels measured. My doctor said they weren't great but perhaps that is why I got a negative reading when I had taken the test. I would need to come back into the office a few days later to see if they had increased. But they had not increased. They should be doubling at this point. I figured this pregnancy might not make it but the good news was I had become pregnant and I could try again. A few days later I went back in. Nope, not having any luck with the numbers. I went back several times over a couple of weeks and it just didn't seem like this is going to happen.

Then a couple of weeks into the process I went in for yet another test and my doctor came into the exam room and said your numbers are all great. Everything had rebounded and I was exactly where I should be. So I thought I could get a little excited now. From then on out, aside from feeling very dizzy and sick for four months, she came bounding out a week early, a healthy baby girl and now she is about to start her third year of medical school. You never really know how things are going to play out. And yes, she is the one who got me hooked on TPWKY.

Sarah

Hi, my name is Sarah and I live in Oxfordshire, England with my husband Mike and our youngest son Ethan. Like many people I didn't actually know my blood group until I became pregnant. Thankfully being Rhesus negative made very little difference to either of my first two pregnancies. I had the routine anti-D injections and both boys were born full term and healthy. Sadly, my third pregnancy ended in early miscarriage. No reason was found and I was reassured that it wasn't connected to Rhesus disease. However when I became pregnant with Ethan the following year, signs of a rhesus reaction appeared very early. A blood test showed the presence of antibodies that were found to be resistant to anti-D. Thankfully the antibody levels remained low and regular scans reassured us that he was growing as expected. Each week that passed felt like a victory.

Unfortunately at about 5 months, the antibody levels rose sharply. Regular checkups continued as we monitored him for any sign of distress. The plan was to postpone any intervention for as long as we could. We made it to 7 months before the scans showed that he was developing fetal anemia. He needed a blood transfusion to limit the effects of the anemia and to give him more time before delivery became necessary. Despite signing all of the waivers, we really weren't prepared for the transfusion to fail and for an emergency C-section to be performed to save his life. I vividly remember the shock of seeing him for the first time, so small in his incubator, covered in wires with a machine breathing for him. It just didn't feel real. I was discharged a few days after Ethan was born and going home without him was one of the hardest moments in my life.

My husband's paternity leave was soon over and I then faced continuing to recover from surgery while caring for our older boys and trying to visit the hospital as often as possible. Slowly Ethan became stronger and he worked his way through the nurseries in the NICU and SCBU. Finally after 8 long weeks, we got to bring him home just a few days before his due date and without the need for any additional oxygen support. Our full perm preemie is now a happy, very tall 13 year old with a brilliant sense of humor. His difficult start in life has had no effect on his health and most people can't believe that he was premature. We can never do enough to thank the NHS and everyone at the John Radcliffe Hospital in Oxford. Our lives are richer with Ethan in them.

TPWKY

(transition theme)

Erin Welsh

Around the world and over centuries, the placenta has held and continues to hold deep meaning.

Erin Allmann Updyke

Okay.

Erin Welsh

Some cultures revere it, honoring it with a special burial. Mummified placentas have been found in Ancient Egyptian tombs. You know I would get back to ancient Egypt again, right?

Erin Allmann Updyke

Every one of these episode.

Erin Welsh

Every single time. Others consume it in recognition of its power. It's been used in beauty products, preserved in a jar to ensure good health. It is varyingly seen as an older sibling, a twin, part of the baby itself, a friend, the finest jacket. This reverence is not unwarranted. The placenta at its core represents the fundamental vital connection between a mother and developing fetus, a physical, metabolic, and immunologic bond. It's the first organ you make and the first you say goodbye to.

Erin Allmann Updyke

That feels so profound somehow.

Erin Welsh

Because it is.

Erin Allmann Updyke

Am I gonna cry about a placenta?

Erin Welsh

I know, I just teared up a little bit myself. I read over this a million times.

Erin Allmann Updyke

Yeah but wow, Erin.

Erin Welsh

Yeah.

Erin Allmann Updyke

Okay.

Erin Welsh

It's the only organ ever connected to another individual.

Erin Allmann Updyke

Oh my god, Erin.

Erin Welsh

It filters waste, it transfers vital nutrients, and acts as an important immunological barrier between mother and fetus. It's remarkable.

Erin Allmann Updyke

I also... I have shared before how much I love the uterus.

Erin Welsh

Yeah.

Erin Allmann Updyke

And I still feel that way. Like I feel so, I have my earrings on today. I love, love. Thank you, they're a gift from you.

Erin Welsh

Congrats to myself for the good gift.

Erin Allmann Updyke

I, especially doing this research-

Erin Welsh

Yeah.

Erin Allmann Updyke

And I haven't even learned what you're going to teach me yet but I love the placenta.

Erin Welsh: I know.

Erin Allmann Updyke: So much.

Erin Welsh: Yeah. And I think it had always been just a secondary character.

Erin Allmann Updyke: What, in your life story or just...?

Erin Welsh: In my life story, in the story that I imagined.

Erin Allmann Updyke: Yeah.

Erin Welsh: And I don't even know if I had a good idea of what a placenta looks like.

Erin Allmann Updyke: Yeah.

Erin Welsh: So Erin, would you mind?

Erin Allmann Updyke: Do you want to see?

Erin Welsh: Yeah, I would like to see.

Erin Allmann Updyke: Okay. I have one here today.

Erin Welsh: So Erin has with us here today-

Erin Allmann Updyke: A model of a placenta.

Erin Welsh: A model of a placenta.

Erin Allmann Updyke: It's not a real placenta.

Erin Welsh: Not a placenta.

Erin Allmann Updyke: Thank you to UCSD Family Medicine department for letting me borrow this. Shout out.

Erin Welsh: Yeah. I mean that's basically it.

Erin Allmann Updyke: It is round.

Erin Welsh: It's discoid.

Erin Allmann Updyke: It's discoid. It has vessels on one side that is connected to the baby by umbilical cord.

Erin Welsh: Yep.

Erin Allmann Updyke

And then on the other side where it was connected to the uterus, it usually is more rough and bumpy. That's why this one is like that.

Erin Welsh

Yeah. I think it's bigger than I think a lot of people think. It's bigger than I thought it would be.

Erin Allmann Updyke

Yeah. And some of them are hefty.

Erin Welsh

Oh yeah, I was looking at pictures and I was just blown away.

Erin Allmann Updyke

I don't know if i should leave this here or...

Erin Welsh

It's up to you.

Erin Allmann Updyke

Keep it here for the good vibes.

Erin Welsh

Keep it here. But yeah, the good vibes. Yeah, we can honor the placenta here.

Erin Allmann Updyke

Yeah.

Erin Welsh

But yeah, it is a remarkable organ.

Erin Allmann Updyke

It really is.

Erin Welsh

And I really want, if nothing else, just for us to think more about the placenta like going forward. Anyone who's listening. Yeah.

Erin Allmann Updyke

Okay.

Erin Welsh

Because the placenta deserves this recognition.

Erin Allmann Updyke

It does.

Erin Welsh

At the same time, the placenta is also at the root of some of the most common disorders of pregnancy such as preeclampsia. It can invade into the uterine wall too deeply, not deeply enough, or in a problematic spot. It can separate too early or not separate when it should. And the placenta acting in these unexpected ways can lead to potentially harmful or even deadly consequences for both fetus and pregnant person. As I'm always saying on this podcast, life is full of trade-offs, and the placenta is no exception. The intimacy formed by this connection is necessary for fetal growth and development but it can also leave both mother and fetus vulnerable when things go wrong. Despite this potentially high cost, the placenta is a widespread feature of mammals and it has evolved in many other classes of animals. The how and why of that evolutionary story is what I'm going to talk about today.

Erin Allmann Updyke

I'm so excited.

Erin Welsh

From the human placenta's ancient origins to the diversity we see in the placentas of present day mammals, from the role viruses may have played in its development to some of the trade-offs that we humans face when it comes to our invasive placentas.

Erin Allmann Updyke

Okay.

Erin Welsh: And also what I mean by invasive.

Erin Allmann Updyke: Right.

Erin Welsh: I'll get into it. My overall goal is to get us to think about why the placenta as opposed to other reproductive strategies like egg laying, and why the human placenta as opposed to other mammalian placentas. Like why these things? How did we get here?

Erin Allmann Updyke: Right, right.

Erin Welsh: Before I dig in, I want to mention a couple of things up front. The first is that I'll be talking about the placenta in terms of what it is expected to do throughout a pregnancy, which does not capture the incredible variation that can occur between individuals or even within one individual throughout pregnancy.

Erin Allmann Updyke: Right. And different pregnancy.

Erin Welsh: Yeah. Nor will I be exploring the multitude of things that can happen when the placenta acts outside of that. We could do an entire episode on each placental disorder. We really, really could.

Erin Allmann Updyke: Yeah.

Erin Welsh: The other thing is that this is not a comprehensive review of the placenta in all of its dimensions, like the cultural importance, the history of its study, its physiology, and so on. It's just a quick tour through one of the coolest organs. But fortunately there are many sources where you can get that more detailed info and we'll be posting those on our website. Okay.

Erin Allmann Updyke: Okay, give it to me.

Erin Welsh: You know that I love to start deep.

Erin Allmann Updyke: How deep are we going to go, Erin?

Erin Welsh: Pretty deep.

Erin Allmann Updyke: Before the dinosaurs or...?

Erin Welsh: Life on Earth began in the water.

Erin Allmann Updyke: I love it when you do this, Erin. I really do.

Erin Welsh: Oh my gosh.

Erin Allmann Updyke: Okay.

Erin Welsh: And there it remained for hundreds of millions of years. We're going pretty deep.

Erin Allmann Updyke: I love it.

Erin Welsh

Around 350-400 million years ago, a group of four-legged animals made their way onto land. This group is the ancestor of all vertebrates except for fish, so it includes humans, not fish.

Erin Allmann Updyke

Right.

Erin Welsh

These first land dwelling animals couldn't quite shake their aquatic roots and so they continued to keep laying their unfertilized eggs in water where a male would later come by and fertilize them. This water aspect of these eggs, it's not a preference, it was a necessity. Without it the eggs would dry out. But this reliance on water was limiting. So some of these animals evolved another strategy, eggs covered with a more protective coating which meant that they could last outside of water which then enabled these animals to further explore land and go out deeper and deeper into land.

Erin Allmann Updyke

Yeah.

Erin Welsh

But this coating made the eggs less permeable which meant that fertilization had to happen internally.

Erin Allmann Updyke

Okay.

Erin Welsh

Required a whole new set of things.

Erin Allmann Updyke

Okay.

Erin Welsh

Before the egg and the yolk had fully formed.

Erin Allmann Updyke

Okay, yeah.

Erin Welsh

Yep. And then that was in contrast to externally like the way that frogs will lay eggs.

Erin Allmann Updyke

Or like a lot of fish that spawn. Yeah.

Erin Welsh

A lot of fish. Right, exactly. And so then after fertilization internally and after the yolk and egg had formed, the female would then lay her eggs and wait for them to hatch like a crocodile.

Erin Allmann Updyke

Right.

Erin Welsh

Right.

Erin Allmann Updyke

It's not the first egg laying animal that I think of by the way but I love that that's the example.

Erin Welsh

What is the first one?

Erin Allmann Updyke

A bird.

Erin Welsh

Yeah but like yeah. I mean it's true. I think of crocodiles.

Erin Allmann Updyke

I love that.

Erin Welsh: Or turtles.

Erin Allmann Updyke: I don't often think about crocodile reproduction. I think that's what it is.

Erin Welsh: But you think often about bird reproduction?

Erin Allmann Updyke: Well I eat eggs.

Erin Welsh: Oh I see.

Erin Allmann Updyke: So like egg, that's my...

Erin Welsh: Yeah, I guess I don't eat crocodile eggs but I just... I don't know. Also that's so funny because when you said bird I pictured like robins, not chickens, which the most... Oh my god.

Erin Allmann Updyke: I love it.

Erin Welsh: Yeah.

Erin Allmann Updyke: Okay. So crocodiles lay eggs.

Erin Welsh: Crocodiles lay eggs, yeah. And so but the time window between internal fertilization and egg laying, so like when those eggs were fertilized and formed and then when they were actually deposited, right-

Erin Allmann Updyke: They actually deposited. Yeah.

Erin Welsh: Was variable. If you kept your eggs inside longer, it meant that you could more closely control the temperature and humidity that these eggs were exposed to which could increase the chances that your offspring survived.

Erin Allmann Updyke: Okay.

Erin Welsh: Eggs can be quite vulnerable to environmental threats, predators, weather extremes, fungal pathogens, and so some animals took this one step further, keeping the eggs inside until they were ready to hatch.

Erin Allmann Updyke: Okay.

Erin Welsh: One major transition remained though. How did the embryo get its nutrients? How did that embryo, inside the eggs?

Erin Allmann Updyke: Right.

Erin Welsh: So egg layers provided nutrients through the yolk, encased in that less permeable barrier.

Erin Allmann Updyke: Right.

Erin Welsh: But the thing is you were limited. So like when that egg was formed, that yolk, you're just going to deplete until that's all you have.

Erin Allmann Updyke: That's all you have. The embryo has to be able to survive and develop enough with just whatever is in that yolk.

Erin Welsh: Yeah.

Erin Allmann Updyke: Yeah.

Erin Welsh: It's like meal prepping essentially.

Erin Allmann Updyke: Yeah, it's exactly like meal prepping.

Erin Welsh: It's exactly like meal prepping.

Erin Allmann Updyke: I love it.

Erin Welsh: Okay, wow.

Erin Allmann Updyke: It really is.

Erin Welsh: Okay, there you go. See?

Erin Allmann Updyke: Yeah.

Erin Welsh: But then what if you didn't want to meal prep and you're like this is not enough food.

Erin Allmann Updyke: Right. I'm sick of it.

Erin Welsh: Yeah, end of the week and you're like I'm starving. I don't know what I'm doing.

Erin Allmann Updyke: I'm still hungry.

Erin Welsh: Yeah, yeah. So what if instead you could provide nutrients to the embryo directly and continuously throughout pregnancy?

Erin Allmann Updyke: Continuously. You could make your meals on the go.

Erin Welsh: Right.

Erin Allmann Updyke: Yeah.

Erin Welsh: You could always have like a resort, there's a little snack drawer.

Erin Allmann Updyke: Snack drawer.

Erin Welsh: Yeah. I don't... These metaphors might not work.

Erin Allmann Updyke

You're going a little bit off the rails but I really like it.

Erin Welsh

We can reel it back in. And so a subset of these egg-laying animals evolved the ability to pass nutrients directly to the developing embryo.

Erin Allmann Updyke

Okay.

Erin Welsh

Not via a yolk but through an organ that connected mother to embryo; an organ that we know as the placenta. So we went from laying unfertilized eggs in water to laying fertilized eggs on land to retaining those fertilized eggs for longer periods of time to then getting rid of this eggshell that didn't let nutrients in or out to directly connect with the fetus and remain in contact for the duration of pregnancy.

Erin Allmann Updyke

Okay.

Erin Welsh

That's how we got to the placenta.

Erin Allmann Updyke

Boom, boom, boom. Straightforward honestly.

Erin Welsh

Right? Okay, it's an oversimplification of course.

Erin Allmann Updyke

I know.

Erin Welsh

It's like covering hundreds of millions of years. And I also don't want to with this explanation give off the impression that the placenta or live birth is like the end all, be all reproductive strategy.

Erin Allmann Updyke

Right.

Erin Welsh

Or that it's one unique to mammals. Like I said earlier, it evolved independently in many classes of animals and the fact that we see so many different reproductive strategies today like laying unfertilized eggs, laying fertilized eggs, retaining eggs until they're ready to hatch, live birth, and so on, the variation is endless.

Erin Allmann Updyke

Yeah.

Erin Welsh

What was the one that I like texted you about? Gastric brooding frogs.

Erin Allmann Updyke

Frogs. Yeah.

Erin Welsh

Yeah.

Erin Allmann Updyke

And then I came back with the seahorses.

Erin Welsh

Yes.

Erin Allmann Updyke

Yeah.

Erin Welsh

I know. There are so many different ways.

Erin Allmann Updyke

So many reproductive strategies.

Erin Welsh

It's incredible. And this shows us that there are pros and cons for each and that what works for one species might not work for another. So sure, laying eggs might make them more susceptible to external threats but it frees you up. Outrunning or out flying a predator is more challenging when you're carrying around a load of offspring in your uterus.

Erin Allmann Updyke

Literally.

Erin Welsh

On the other hand, investment in offspring is generally higher in placental mammals which can translate into higher survival for those offspring. I mean we could spend hours discussing and arguing the trade-offs of different reproductive strategies but we're not going to do that.

Erin Allmann Updyke

We're not going to.

Erin Welsh

No. So I mentioned that the placenta evolved independently multiple times across the animal kingdom.

Erin Allmann Updyke

Yeah, what?

Erin Welsh

In mammals though it happened just once.

Erin Allmann Updyke

Okay.

Erin Welsh

We're going to talk about the mammals.

Erin Allmann Updyke

Right. And now I really want to know about the other ones though, just so you know.

Erin Welsh

I can send you some sources, Erin.

Erin Allmann Updyke

Okay, yeah.

Erin Welsh

Go to our website thispodcastwillkillyou.com. Go to the sources tab. But this means that the incredible placental diversity that we see in mammals today comes from just one origin.

Erin Allmann Updyke

Wow.

Erin Welsh

Around 250 million years ago, we still have to go far back, a group of animals called the therapsids split off from the rest.

Erin Allmann Updyke

Okay.

Erin Welsh

And these were reptile-like creatures and they differed from the rest in three key ways.

Erin Allmann Updyke

Okay.

Erin Welsh

First, they could generate their own body heat and maintain temperature, crucial. Second, they had body hair which helped provide insulation for heat maintenance. And third, they developed the ability to produce milk.

Erin Allmann Updyke

Oh. Interesting.

Erin Welsh

I know.

Erin Allmann Updyke

That early on.

Erin Welsh

I didn't know it went that far back.

Erin Allmann Updyke

Me neither.

Erin Welsh

Yeah.

Erin Allmann Updyke

Okay.

Erin Welsh

Over the next 100 million years or so, this group continued to diversify, splitting off into the three main groups that today make up modern mammals. We've got the monotremes, the egg laying mammals like the platypus and the echidna.

Erin Allmann Updyke

Okay. Love them.

Erin Welsh

We've got the marsupials, the one who use a pouch and birth teeny tiny young like the Tasmanian devil, kangaroo, koala, etc. Some of my faves. And then the eutherians or the placental mammals which includes all other mammals today, including humans.

Erin Allmann Updyke

Okay.

Erin Welsh

I have to throw in this 'well actually' because it just bothered me as I read this and it's probably old news to people who know more about the placenta but marsupials also possess structures resembling a placenta, they just play a slightly different role and are very different than our placentas. And so one key difference between marsupials and eutherians is when nutrient transfer takes place.

Erin Allmann Updyke

Okay.

Erin Welsh

So in marsupials it mostly takes place during lactation, while in eutherians most nutrient transfer happens during gestation.

Erin Allmann Updyke

Got it.

Erin Welsh

Right?

Erin Allmann Updyke

I think I understand.

Erin Welsh

Yeah, so it's like-

Erin Allmann Updyke

So you're saying they have something that's like a placenta-

Erin Welsh

Yeah.

Erin Allmann Updyke: But its main role is not providing nutrients.

Erin Welsh: It's not providing the nutrients. Yep, yeah.

Erin Allmann Updyke: Okay, makes sense.

Erin Welsh: But we still call the eutherian mammals the placentals.

Erin Allmann Updyke: Okay.

Erin Welsh: And I'm just like...

Erin Allmann Updyke: Well actually!

Erin Welsh: Yeah, I know. I can't resist. But what I wanted to say about lactation was that in monotremes they don't have nipples, they have like little pores.

Erin Allmann Updyke: Yes, I knew that.

Erin Welsh: And like the little babies lap up. I know.

Erin Allmann Updyke: So interesting.

Erin Welsh: It's amazing. I know.

Erin Allmann Updyke: I want to ask more about... I won't though.

Erin Welsh: You could ask me and I'll just say I don't know.

Erin Allmann Updyke: Well I don't know how to form my question is the problem.

Erin Welsh: Okay.

Erin Allmann Updyke: Because it's like going back to those early, early, early-

Erin Welsh: The therapsids?

Erin Allmann Updyke: The therapsids. Like you know Dimetrodon?

Erin Welsh: Yeah.

Erin Allmann Updyke: Was that a therapsid or was that something-?

Erin Welsh: No.

Erin Allmann Updyke: See? It's only because I'm thinking of like all of the dinosaur toys that we have at home. And I always go well this one's not a dinosaur.

Erin Welsh: Which ones are therapsids and which ones are synapsids? Yeah. Or something like that.

Erin Allmann Updyke: Yeah, I don't know synapsid, maybe. Yeah.

Erin Welsh: See and this is where my...

Erin Allmann Updyke: Anyways.

Erin Welsh: My deep evo bio is...

Erin Allmann Updyke: Off topic.

Erin Welsh: Off topic. We'll bring it back to the placenta.

Erin Allmann Updyke: Let's please.

Erin Welsh: Okay. So these earliest eutherian placenta-having mammals probably emerged around 110-125 million years ago.

Erin Allmann Updyke: Okay.

Erin Welsh: Yeah. And from there nature did its thing, evolution did its thing, the asteroid that caused a mass extinction event 66 million years ago did its thing and cleared the way for the age of mammals. Check out our blastomycosis episode for more.

Erin Allmann Updyke: So much more.

Erin Welsh: And the placenta diversified. When it comes to eutherian placentas, there's a whole lot of variation from size to shape to invasiveness. We held up the the human placenta which is like a discoid shape. They come in all different shapes. It's amazing. One book I read suggested that it is probably the most variable of all mammalian organs.

Erin Allmann Updyke: Really?

Erin Welsh: Yeah.

Erin Allmann Updyke: That's interesting.

Erin Welsh: I mean I wonder if every organ researcher says the same thing about their organ.

Erin Allmann Updyke: Like my organ is actually the most-

Erin Welsh: The gallbladder is the most diverse... No.

Erin Allmann Updyke: I'm sure it's not that one.

Erin Welsh: We'll do an episode on it.

Erin Allmann Updyke: Okay.

Erin Welsh But for today I'm only going to get into one dimension of this variation in mammalian placentas and that is in the invasiveness of the placenta.

Erin Allmann Updyke Right.

Erin Welsh So you can look at invasiveness in two ways. One is in the number of cell layers separating fetal and maternal bloodstreams and the second is in how physically deeply fetal tissue invades and restructures maternal tissue.

Erin Allmann Updyke Okay.

Erin Welsh So one is like how many layers are inbetween and the other is like how-

Erin Allmann Updyke How deep do those villi go?

Erin Welsh Exactly, yeah.

Erin Allmann Updyke Yeah.

Erin Welsh Researchers generally group the invasiveness of the placenta into three categories, sometimes there's a fourth one added depending on the number of cellular layers.

Erin Allmann Updyke Okay.

Erin Welsh So on the less invasive side of things we've got like pigs, sheep, dolphin, hippo. In the medium invasive we've got dogs, sloths, elephants, aardvarks, raccoons. And on the maximally invasive, yeah-

Erin Allmann Updyke That was like a really wide range.

Erin Welsh Well that's... Okay, yeah, yeah.

Erin Allmann Updyke Okay.

Erin Welsh In a second, yep.

Erin Allmann Updyke Okay.

Erin Welsh On the maximally invasive, as in the placental tissue is often referred to as being bathed in maternal blood-

Erin Allmann Updyke Right.

Erin Welsh We've got humans and other great apes, mice, rabbits, guinea pigs, nine-banded armadillos, hyenas, and others.

Erin Allmann Updyke Okay. That's also more than I realized.

Erin Welsh: Yeah.

Erin Allmann Updyke: That are considered that invasive.

Erin Welsh: Yeah. On the invasive side of things, yeah.

Erin Allmann Updyke: Interesting. Yeah, okay.

Erin Welsh: But like in terms of the cell layers, yeah.

Erin Allmann Updyke: Yeah.

Erin Welsh: And so unless I specify otherwise, when I'm talking about invasiveness I'm usually referring to this classification based on cell layers between fetal and maternal blood.

Erin Allmann Updyke: Okay.

Erin Welsh: Why is there such variation? Is there a benefit to one type of placenta over another?

Erin Allmann Updyke: Okay. I mean yes.

Erin Welsh: Well yes and no.

Erin Allmann Updyke: Or like trade-offs.

Erin Welsh: Trade-offs, yeah. I mean we don't fully know the answer.

Erin Allmann Updyke: Classic.

Erin Welsh: Classic. Yeah. And it doesn't seem to be driven solely by like how related... Like different animal groups.

Erin Allmann Updyke: Yeah.

Erin Welsh: And like oh well all of the... There are some broad trends.

Erin Allmann Updyke: Okay.

Erin Welsh: But for the most part it doesn't really seem that way.

Erin Allmann Updyke: So it's like a bunch of examples of convergent evolution essentially?

Erin Welsh: Kind of.

Erin Allmann Updyke: Okay.

Erin Welsh: Like what is driving in different species, we don't fully understand I think the drivers for that.

Erin Allmann Updyke

Okay, interesting.

Erin Welsh

Yeah. But one thing that we do know is that our invasive placenta, like the human invasive placenta is the type that probably evolved first and then it evolved to become less invasive.

Erin Allmann Updyke

Interesting.

Erin Welsh

Interesting indeed.

Erin Allmann Updyke

Okay.

Erin Welsh

It's possible that like... So we're talking about trade-offs, it's possible that certain molecules like iron have a slightly more difficult time getting to the fetus in mammals with less invasive placentas.

Erin Allmann Updyke

Okay.

Erin Welsh

But that's not entirely clear.

Erin Allmann Updyke

Okay.

Erin Welsh

And another hypothesis is that the more invasive the placenta, the better the signaling in all directions like mom to fetus, fetus to mom, placenta to mom, etc. I also read that placental transfer of certain antibodies, IgG if you're curious which is the most abundant in our blood, has only been observed in invasive placentas, possibly demonstrating active transport of this antibody to the fetus which could have then protective roles.

Erin Allmann Updyke

Right. Because then your fetus is basically your baby is being born with all of the antibodies that mom has had.

Erin Welsh

Yeah.

Erin Allmann Updyke

So like protection from all of these things at least passively, at least for those first few months.

Erin Welsh

Protection. Right, okay. Which, question mark, is not fully clear. Yeah.

Erin Allmann Updyke

Okay.

Erin Welsh

Why still? Why do we have this invasive placenta? One popular but now largely discarded hypothesis is that our invasive placentas were necessary to get enough nutrients to the developing human fetal brain. For one, our big brains came after this invasiveness.

Erin Allmann Updyke

Clearly if this was the first type of placenta.

Erin Welsh

Yeah. Well it wasn't always known that that was the case, right.

Erin Allmann Updyke

Of course, yeah, yeah, yeah. That makes sense.

Erin Welsh: But two, not all animals with invasive placentas have big brains and not all animals with big brains have invasive placentas, like dolphins which have among the least invasive type of placenta.

Erin Allmann Updyke: Yeah. Okay, okay.

Erin Welsh: And four, there is no evidence that transfer of nutrients is somehow greater or more efficient in more invasive placentas compared to less invasive ones.

Erin Allmann Updyke: Okay.

Erin Welsh: Okay. All right.

Erin Allmann Updyke: Interesting.

Erin Welsh: The idea that invasive placentas were necessary for our big brains was based on this arrogant assumption that whatever placenta we humans have must be the most advanced and the least primitive.

Erin Allmann Updyke: It's the best.

Erin Welsh: It's the best. But since that's not the case, we may have to consider instead two related questions. What are the potential downsides to an invasive placenta? And how have those of us with invasive placentas adapted to deal with those downsides?

Erin Allmann Updyke: Right.

Erin Welsh: So let's start with one of the major potential drawbacks. The fact that during pregnancy there is an alien thing growing inside you.

Erin Allmann Updyke: Yes.

Erin Welsh: Yes, it's 50% you.

Erin Allmann Updyke: But only 50%.

Erin Welsh: But only 50%. That other 50% is not you.

Erin Allmann Updyke: Not you.

Erin Welsh: Over the past 500 million years, which is when the first natural killer cells are thought to have evolved-

Erin Allmann Updyke: Oh my god, wow. Okay.

Erin Welsh: I know.

Erin Allmann Updyke: Wow.

Erin Welsh: I know. It shows how fundamental this idea is, yeah.

Erin Allmann Updyke: And like just immunology of needing to be able to find non-self.

Erin Welsh: Yeah. That is the whole point of the immune system is distinguishing self and non-self.

Erin Allmann Updyke: Yeah.

Erin Welsh: That is pretty much the point of any... I mean and that's an oversimplification.

Erin Allmann Updyke: Sure.

Erin Welsh: But pretty much at its core, self vs non-self.

Erin Allmann Updyke: Self vs non-self, yeah.

Erin Welsh: And so sometimes our immune system works a little better than we want it to like when we reject a transplanted organ, sometimes it's a little overzealous and it blurs the line between self and non-self as in the case of like autoimmune diseases.

Erin Allmann Updyke: Autoimmunity.

Erin Welsh: And sometimes it might need a little help. But overall, this ability is so crucial to our survival that it's a universal feature in all multicellular life on this planet and has been for quite some time.

Erin Allmann Updyke: Wow. Yeah.

Erin Welsh: And so pregnancy then should offer a pretty huge immunological challenge.

Erin Allmann Updyke: Right.

Erin Welsh: There's this non-self thing inside you.

Erin Allmann Updyke: That has to stay there for however many months depending on what species you are.

Erin Welsh: Right.

Erin Allmann Updyke: 266 days at least in ours.

Erin Welsh: There we are, yeah.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: Yeah.

Erin Welsh: And so from an immunological standpoint, our bodies should flag the newly implanted blastocyst and mount a defense against it. Sometimes this is what happens. And one potential downside of our invasive placentas is that the deeper the invasion, the higher the risk for triggering an immune response from the mother.

Erin Allmann Updyke: Right.

Erin Welsh: Many species that have similarly invasive placentas like ours tend to have much shorter gestations in part potentially to minimize this risk. But we seem to manage overall.

Erin Allmann Updyke: Right. This is why we see things like Rhesus disease, right.

Erin Welsh: Yes.

Erin Allmann Updyke: Where you have at least some fetal cells that are able to cross over this barrier and come onto the other side of our cells. And then we do see those and mount a defense against them in a future pregnancy potentially.

Erin Welsh: Right. And with potentially really, really-

Erin Allmann Updyke: Really disastrous consequences.

Erin Welsh: Exactly.

Erin Allmann Updyke: Exactly.

Erin Welsh: Yeah.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah. And so there is like this immune relationship that is really complex.

Erin Allmann Updyke: Yeah. It's a very tight rope that we are walking.

Erin Welsh: Yep.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah. So what? Like how? Why? What allows for tolerance over rejection?

Erin Allmann Updyke: Yeah.

Erin Welsh: One thing that helps is that a fetus is not the same as an organ transplant. A transplanted organ is connected to the recipient's blood supply.

Erin Allmann Updyke: Yeah.

Erin Welsh: Whereas during pregnancy the fetal and maternal blood are kept separate.

Erin Allmann Updyke

Right.

Erin Welsh

And they are kept separate by the outer layer of the placenta. And this outer layer consists of a bunch of cells that are fused together to make a tissue. So it's not like individual cells anymore, the membranes have been fused together to create like one giant cell with like multinucleated cell.

Erin Allmann Updyke

That's why they call it a syncytiotrophoblast, if you remember our RSV episode, that stands for respiratory syncytial virus. I'm going too nerdy, I'm so sorry. But syncytium, yeah, multinucleated cell.

Erin Welsh

Multinucleated cell. So it's this like one cell but it's a long giant cell.

Erin Allmann Updyke

It goes the whole entire outside of that blastocyst.

Erin Welsh

Yep, yep. And this tissue is pretty impenetrable because these cells are fused together, there are no more membranes between the cells which means there aren't any gaps to let in let's say, for example, mom's antibodies which might flag the fetus as non-self. So it just creates this like there are no gaps.

Erin Allmann Updyke

Right.

Erin Welsh

You can't even... No foot in the door.

Erin Allmann Updyke

Can't get in. No maternal stuff can get into the placenta at that point.

Erin Welsh

Yeah, yep. And this is a pretty crucial tissue and its role is not limited to barrier, right. It's also a hugely important regulator in the expression of hormones like upregulate that hormone, downregulate that hormone. And proteins and other molecules that are used in communication between placenta and mom. And we owe it all to an ancient virus.

Erin Allmann Updyke

Stop it.

Erin Welsh

Oh yeah.

Erin Allmann Updyke

What?

Erin Welsh

Oh yeah. At some point, one of our ancestors was infected with a retrovirus which inserted its genetic material into one of their sperm or egg cells.

Erin Allmann Updyke

Okay.

Erin Welsh

Okay.

Erin Allmann Updyke

What?

Erin Welsh

When those cells replicated, like when they formed an embryo and so on, so did the viral DNA, carried it with it.

Erin Allmann Updyke

Okay.

Erin Welsh: Which was then also passed down to subsequent generations.

Erin Allmann Updyke: Okay.

Erin Welsh: Because it would have been in all of the germ cells down the line.

Erin Allmann Updyke: Right.

Erin Welsh: Over time we lost bits of that viral DNA but some crucial parts remained. Genes that maybe we were like huh, this seems like it could be worth keeping around. We call these viral remnants in general endogenous retroviruses and our genome is chock full of them.

Erin Allmann Updyke: Okay.

Erin Welsh: I think I've talked about this before on the podcast.

Erin Allmann Updyke: I'm getting really excited.

Erin Welsh: About 5%-8% of the human genome is of viral origin. 5%-8%.

Erin Allmann Updyke: Erin.

Erin Welsh: That's a huge proportion of us that's not us.

Erin Allmann Updyke: Us.

Erin Welsh: It's a virus but I mean it is us.

Erin Allmann Updyke: It is us.

Erin Welsh: The genes Syncytin-1 and Syncytin-2 which help us to fuse these cells together to make that one layer and also help us escape detection from mom, they come from a couple of these ancient viruses.

Erin Allmann Updyke: Erin.

Erin Welsh: That's what allows for that that formation of that tissue.

Erin Allmann Updyke: That formation of that... What?

Erin Welsh: That barrier. Yeah.

Erin Allmann Updyke: Really?

Erin Welsh: Really.

Erin Allmann Updyke: These viral genes essentially, these genes that are viral in origin?

Erin Welsh: Yeah.

Erin Allmann Updyke: Wow!

Erin Welsh: Syncytin-1 and Syncytin-2. Without these ancient viral infections, we would not be able to form the super important tissue, we wouldn't be here.

Erin Allmann Updyke: Wow.

Erin Welsh: Yeah. Chills. And what's amazing about these endogenous retroviruses, these Syncytin genes, is that they appear across eutherian mammals but not from just one infection event. Mammals have been infected over and over again with different viruses that have found their way into our genomes and have been co-opted into helping us build this tissue layer.

Erin Allmann Updyke: Wow.

Erin Welsh: Wow. I know.

Erin Allmann Updyke: I'm being mind blown right now.

Erin Welsh: I'm the same. I'm re-being mind blown and I wrote this.

Erin Allmann Updyke: Like I wrote this and it's still blowing my mind.

Erin Welsh: But the immunological relationship between mother and fetus isn't just one of avoiding detection or building barriers.

Erin Allmann Updyke: Right.

Erin Welsh: The activation of the maternal immune system is actually a necessary part of pregnancy. And instead of that activation leading to a destructive response, it leads to a regulatory or protective one, one in which acceptance of the embryo is initiated. The portrayal of pregnancy as immunosuppressive isn't accurate.

Erin Allmann Updyke: Right.

Erin Welsh: In fact the mother is very aware, or the mother's immune system is very aware of this new non-self thing growing. And it's more that the maternal immunological self is modified, a change in immune tolerance. As a side note this shift in self might help to explain why some people with autoimmune diseases experience symptoms lessening during pregnancy.

Erin Allmann Updyke: Right. Yeah.

Erin Welsh: But there may be a cost to this tolerance.

Erin Allmann Updyke: Okay.

Erin Welsh: Recent research has investigated whether our invasive placentas, which require more immune tolerance than less invasive ones, may have made us more vulnerable to cancer as a species.

Erin Allmann Updyke Really?

Erin Welsh Really.

Erin Allmann Updyke I did not know this connection.

Erin Welsh Yeah.

Erin Allmann Updyke Okay.

Erin Welsh It's been like I think in the past 10-ish years or so there's been a lot more interest in this aspect of the immunological side of placentas and placentation, yeah.

Erin Allmann Updyke Interesting. Okay.

Erin Welsh In fact many researchers have noted the similarities between cancer and placentation, the formation of the placenta.

Erin Allmann Updyke Very interesting.

Erin Welsh There is immune evasion, proliferation, invasion into other tissue, and blood vessel remodeling.

Erin Allmann Updyke Wow.

Erin Welsh Yeah. I know.

Erin Allmann Updyke And it's like self but not.

Erin Welsh Yes.

Erin Allmann Updyke Because it's abnormal cell division.

Erin Welsh Right.

Erin Allmann Updyke Ooh interesting.

Erin Welsh Yep. And studies that have compared cancer rates across mammals have found that cancer tends to be higher in species that have more invasive placentas like humans compared to ones that don't like cows.

Erin Allmann Updyke Interesting.

Erin Welsh And I'm sure like that other things play a role.

Erin Allmann Updyke Of course.

Erin Welsh Life span, body size, it's never one thing.

Erin Allmann Updyke It's never one thing.

Erin Welsh

Yeah. But the pattern isn't cut and dry, nor is it clear how cancer and invasive placenation might be related mechanistically.

Erin Allmann Updyke

Okay. Right, right, right.

Erin Welsh

It's a fascinating area for future study though, especially what it might be able to tell us about our individual responses to invasive placenation.

Erin Allmann Updyke

Yeah.

Erin Welsh

Because wow, there is a range of responses.

Erin Allmann Updyke

Yeah.

Erin Welsh

So like we talked about, the placenta is more than just a gateway for communication between mother and fetus, it's also the place where we see maternal, fetal, and paternal needs expressed. From the fetus's perspective, more is better, more resources, more nutrients, more everything to help you grow.

Erin Allmann Updyke

Sometimes, and we'll get there, not always.

Erin Welsh

Not always. But also from mom's point of view, you also want fetus to grow but you can't give away all of your resources.

Erin Allmann Updyke

Right.

Erin Welsh

Since that would impact your ability to care for the fetus later in pregnancy, after birth, in future pregnancies, and also for existing offspring, right. And so these needs might be in immediate conflict but there seems to me to be an ultimate shared goal for the two, right, a healthy newborn while also not draining mom to the point where postpartum care is impossible.

Erin Allmann Updyke

Right. A little balance.

Erin Welsh

A little balance. It's like I think a lot of people refer to it as maternal-fetal conflict which is a whole separate thing and there are a lot of dimensions to that and there's also the sociology and political side and legal side of that.

Erin Allmann Updyke

Yeah.

Erin Welsh

But I have been thinking of it as like a maternal-fetal conversation.

Erin Allmann Updyke

Right.

Erin Welsh

Yeah.

Erin Allmann Updyke

It's a dance.

Erin Welsh

It's a balance.

Erin Allmann Updyke

A balance.

Erin Welsh

It's a dance; it's a balance.

Erin Allmann Updyke

Yeah.

Erin Welsh

And that balance is not always struck. Sometimes for instance the placenta invades too deeply into the uterine wall, past the decidua, which can cause hemorrhage or perforation of the uterus. Or sometimes it doesn't invade deeply enough and maybe this is because our immune system prevents it. This incomplete invasion is thought to be at the root of preeclampsia.

Erin Allmann Updyke

Right.

Erin Welsh

We don't know the precise mechanism or if preeclampsia has one root cause or multiple. Is it a syndrome or is it...? Yeah.

Erin Allmann Updyke

Right. Well also I'll talk more about like the different types of preeclampsia.

Erin Welsh

Right.

Erin Allmann Updyke

Whether it's early term, whether it's term, whether it's postpartum preeclampsia. Are they different? Are they the same?

Erin Welsh

Right.

Erin Allmann Updyke

We don't know.

Erin Welsh

Is it the same pathway that's getting us to these things or multiple pathways?

Erin Allmann Updyke

Exactly, exactly.

Erin Welsh

Yeah. But one idea for preeclampsia is that the placenta doesn't invade deeply enough which can limit the blood supply to the placenta and fetus. Initially in earlier in pregnancy that's not a problem since the fetus actually needs a low oxygen environment to develop. But as pregnancy progresses, oxygen demands increase and if that initial invasion wasn't deep enough, if those arteries weren't remodeled enough, that can mean that the fetus is getting low or intermittently low oxygen. And so then mom senses this or through the placenta is told this and then her blood pressure will spike to compensate. But that doesn't always solve the problem and so then things can kind of get increasingly out of balance and then there can be a lot of danger that happens.

Erin Allmann Updyke

Right, yeah.

Erin Welsh

Erin, I know that you'll get into more of the details later on but one of the things that I find fascinating about preeclampsia relates back to this idea that invasive placentas might be related to higher rates of cancer. If preeclampsia has an immunological component and if mother's immune system is preventing deep invasion of the placenta, might cancer rates be lower in people who have had preeclampsia? So first of all, now I'm like...

Erin Allmann Updyke

We are wondering. You are wondering this.

Erin Welsh: We are wondering. Yeah. I'm not saying like there's been reviews about this and meta-analyses. I did look up a few large studies and a meta-analysis that did suggest that people who have had preeclampsia are overall less likely to develop breast cancer.

Erin Allmann Updyke: Interesting.

Erin Welsh: But there's so much more to that story.

Erin Allmann Updyke: There's so much. Right, Erin.

Erin Welsh: There are so many factors. How protective might preeclampsia be? What's the mechanism of protection if there is one? Is this a causal connection or just a correlation?

Erin Allmann Updyke: Just happenstance, yeah.

Erin Welsh: And the same can be said for the placenta. Like there's so, so much more to this story. This was really just a brief or at least as brief as I could make it.

Erin Allmann Updyke: I could keep going, I could keep listening to you.

Erin Welsh: Just a brief tour through the evolutionary history of one of the most fascinating mammalian organs out there. And I hope that even if you don't remember any one thing from this story, you at least find yourself thinking more about the placenta.

Erin Allmann Updyke: The placenta that we all used to have.

Erin Welsh: That we all used to have.

Erin Allmann Updyke: I think that's the thing that's interesting that no one ever thinks about.

Erin Welsh: Yeah.

Erin Allmann Updyke: Like we all, because I think a lot about the uterus and how we all came from a uterus, whether you have one or not, you came from one.

Erin Welsh: Right.

Erin Allmann Updyke: Which is so interesting. But then like we all, I never thought about the fact that like we all had a placenta.

Erin Welsh: We all had a placenta.

Erin Allmann Updyke: And we all no longer do.

Erin Welsh: Yeah. Unless you kept yours.

Erin Allmann Updyke: Yeah but then that's not yours. That was your fetus's. That was your baby's placenta.

Erin Welsh: Right but if your parent kept your placenta.

Erin Allmann Updyke: Oh if you got it? Oh that's interesting, I never thought about that. Yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: So some people have theirs.

Erin Welsh: I mean yeah, it's no longer attached to us.

Erin Allmann Updyke: Yeah.

Erin Welsh: It's no longer-

Erin Allmann Updyke: It doesn't serve a function anymore.

Erin Welsh: Serving the function, yeah.

Erin Allmann Updyke: And right after birth it stops serving its function. I mean it's just so interesting.

Erin Welsh: I know. And it's huge.

Erin Allmann Updyke: Yeah. It is.

Erin Welsh: It's like that takes a lot of resources.

Erin Allmann Updyke: Oh my gosh, yes.

Erin Welsh: Yeah.

Erin Allmann Updyke: It's hefty.

Erin Welsh: It's a hefty organ.

Erin Allmann Updyke: And you can tell when they're not hefty.

Erin Welsh: Oh interesting.

Erin Allmann Updyke: Yeah, I mean you see a whole variety of placentas when you've been delivering babies.

Erin Welsh: Right.

Erin Allmann Updyke: Which I haven't done a lot of but I've seen a fair number and they range for sure.

Erin Welsh: Which is amazing in and of itself.

Erin Allmann Updyke: So interesting.

Erin Welsh	I know, I know. Okay, I mean we could keep talking.
Erin Allmann Updyke	I'm gonna stop. Yep.
Erin Welsh	Yeah.
Erin Allmann Updyke	Close my mouth.
Erin Welsh	But yeah, no, I mean and that basically is the placenta story.
Erin Allmann Updyke	I love it.
Erin Welsh	Let's think about viruses; let's think about what the placenta allows us to do from an immunological standpoint.
Erin Allmann Updyke	What a journey.
Erin Welsh	It's incredible.
Erin Allmann Updyke	Yeah.
Erin Welsh	So yeah, let's keep going with the journey, Erin.
Erin Allmann Updyke	Okay.
Erin Welsh	Tell me what's going on with your body in pregnancy.
Erin Allmann Updyke	Okay. I literally can't wait to.
Erin Welsh	Okay good.
Erin Allmann Updyke	We'll take a quick break and then we'll get into it.
TPWKY	(transition theme)
Anonymous	During both of my pregnancies, I experienced intrahepatic cholestasis of pregnancy. This is a rare complication where your liver cannot process bile salts and acids so those begin to accumulate in your blood. This causes itching which is mainly focused on the palms of your hands and soles of your feet. It was the worst itch I have ever experienced. It was not a dangerous complication for me as a pregnant person but it was extremely dangerous for the fetus. Mortality rate in utero is very high. That is why I had to be monitored very closely up until 37 weeks when I was induced both times. During both of my pregnancies, I had to go to the hospital every few days to have a CTG taken.

They did numerous ultrasounds and I was even hospitalized the first time around. They also prescribed ursodeoxycholic acid which helped a lot with lowering bile salts and acids. Itchiness also went away after that. The last 10 weeks of my pregnancies were very stressful and looking back I am amazed at how calm I managed to stay. Both of my kids were born healthy at 37 weeks after induction. Chances of getting intrahepatic cholestasis of pregnancy with every subsequent pregnancy are higher if you have had it before. Two was enough for me. That feeling of unbearable itchiness will always stay with me.

Sara

My name is Sara, she/her, 36 year old female, mother to an awesome daughter. I had a positive home pregnancy test on Christmas Day 2022. I was 34 years old at the time. We were very lucky to conceive on our very first try. We had our confirmation ultrasound at 8 weeks and as I progressed towards the 2nd trimester I felt my mental health spiraling. In addition to all of the other common pregnancy side effects like morning sickness and fatigue, my anxiety started to worsen to the point of panic attacks. My body was changing in a million ways and I had no control over any of it, let alone any peace of mind to assure me the baby was okay or how to judge what was normal. I started to feel like maybe my medical background was not an advantage in this situation because I knew too much. When I brought my fears up to my OB, I felt dismissed. Each visit was short, about 5 minutes. They checked the fetal heartbeat and sent me on my way even though this was my first pregnancy.

I took it upon myself to research pregnancy mental health and found mostly postpartum articles. I eventually talked to my PCP who started me on Lexapro and Buspar. I was referred to a mental health provider and over the remaining 6 months of my pregnancy I had weekly video calls with an LCSW. She helped me develop coping strategies for my anxiety and guided me in conversations with my OB and my husband. I made affirmation journals, mantras to recite, and fell asleep listening to guided hypnobirthing podcasts, all of which eventually helped me to overcome my anxieties about giving birth. I had to learn how to be the patient, not the provider, and to have faith in my husband, family, and healthcare team to take care of me. By all accounts, I had a very normal pregnancy and easy birth. At the pediatrician visits with my daughter, I filled out mood questionnaires at every visit to screen for postpartum depression which thankfully I didn't develop. But it did make me wonder why aren't these types of questionnaires available throughout the entire pregnancy?

TPWKY

(transition theme)

Erin Allmann Updyke

So I left off the biology last week, kind of at the start of the 2nd trimester. But in that episode I mostly was talking about the embryo and the invasion and the thing and etc. But in this episode I'm going to focus on the pregnancy and the pregnant person and not the fetus.

Erin Welsh

Okay.

Erin Allmann Updyke

Because as incredible and awesome as the process of fetal development is, like it only happens inside of a uterus and so the changes that are required in our bodies in order for a pregnancy to actually continue to term, like that's where the money is for me right now.

Erin Welsh

That's where the money is. Got it, okay.

Erin Allmann Updyke

Someday we'll do fetal development because it's really cool too.

Erin Welsh

Yeah.

Erin Allmann Updyke

Okay. So we're going to actually take steps backwards to the beginning of the pregnancy.

Erin Welsh: Okay.

Erin Allmann Updyke: Kind of.

Erin Welsh: Yeah, that makes sense.

Erin Allmann Updyke: We're going to go back to fertilization. Okay?

Erin Welsh: Sure, yeah.

Erin Allmann Updyke: So that we will recall from last week is about 2 weeks after your last menstrual cycle, right, is when you ovulate and then you get fertilized. Okay. And then about 6 days after that is when we have implantation that starts. So we're about day 21-ish of our menstrual cycle.

Erin Welsh: Okay.

Erin Allmann Updyke: By about this time and then like the next week after, when you may have missed a period and may have had that positive pregnancy test, already your own physiology has changed dramatically because of the way that embryo has embedded itself into the wall of your uterus, like you just walked us through, and started secreting hormones that are going to cause our body to change in ways that it really only changes in the context of pregnancy. I get really excited. And what I'm going to do for this episode is go through these changes, not week by week like you might see on all of the websites, like your body is doing this this week.

Erin Welsh: Right.

Erin Allmann Updyke: No, no. We're going to go body system by body system.

Erin Welsh: Great.

Erin Allmann Updyke: And explain why we see maybe some of the weird or uncomfortable symptoms that you might experience.

Erin Welsh: Okay.

Erin Allmann Updyke: And why we are susceptible to some of the complications that then arise because of these changes in our physiology. Okay?

Erin Welsh: Yeah.

Erin Allmann Updyke: I'm on a rapid fire through it but stop me at any time.

Erin Welsh: Okay.

Erin Allmann Updyke: Okay. We're going to start with our cardiovascular system because it's one of the most important and one of my favorites. One of the first changes that we see is in our blood vessels. So because of the increased levels of progesterone and other hormones like estrogen and prostaglandins, we see a dilation or a widening of our blood vessels. And what this does is decrease the resistance to flow of fluid because of physics.

Erin Welsh: Yeah.

Erin Allmann Updyke: And so right away you can start to see weird symptoms because this vasodilation can cause edema or swelling as these blood vessels, as they get wider, become a little bit more leaky. So then you get fluid that can go out through the blood vessels and into places like our ankles.

Erin Welsh: And this is like your whole body.

Erin Allmann Updyke: Anywhere. It could have, yeah, not like extreme but a little bit.

Erin Welsh: No but I mean like the blood vessel widening is everywhere.

Erin Allmann Updyke: Yes, everywhere in your whole body which also means you might get things like nasal congestion or nosebleeds.

Erin Welsh: Oh my gosh.

Erin Allmann Updyke: Now this vasodilation will also cause a decrease in your blood pressure usually early in pregnancy, which is very interesting to then contrast with what we'll see in preeclampsia.

Erin Welsh: Yeah.

Erin Allmann Updyke: Which is when we have higher blood pressures. Now on top of this change of the width of our blood vessels, we also have an increase in our blood volume. By how much you might ask?

Erin Welsh: I would ask.

Erin Allmann Updyke: By 40%-50%.

Erin Welsh: What? Okay, tell me more about what that means.

Erin Allmann Updyke: It means that if you have... I actually meant to look up what your normal blood volume is, however many liters, I don't remember.

Erin Welsh: Yeah.

Erin Allmann Updyke: But it is now 50% higher within a number of weeks.

Erin Welsh: Okay. And it's just...

Erin Allmann Updyke: You literally just make more blood volume. It means your plasma... Okay, we're going to get even more into it.

Erin Welsh: Okay, yeah, yeah, yeah.

Erin Allmann Updyke: Because it's your plasma volume that's primarily increasing.

Erin Welsh: Okay.

Erin Allmann Updyke: And this means a few things. Number one, it means your heart has to be able to keep up with this increased amount of flow. And so to do that we actually see structural changes to your heart to allow for an increase in cardiac output.

Erin Welsh: What kind of structural changes?

Erin Allmann Updyke: We see thickening of the walls of the left ventricle. Did you bring over the heart? Oh my gosh. If you have a diagram of a heart, your left ventricle is over here, right, and the aorta is going to come out here. And this is where your blood goes to the rest of your body from.

Erin Welsh: Okay. Yeah.

Erin Allmann Updyke: So yeah, the left ventricle of your heart is going to get a little bit thicker. Your overall heart is going to get a little bit bigger. And then as we'll talk about later, because of the changes in your diaphragm and the size of your thoracic cavity, it also gets shifted up and to the left.

Erin Welsh: Interesting.

Erin Allmann Updyke: I know. Now also-

Erin Welsh: Thank you.

Erin Allmann Updyke: Give that back to you. Now also we will see a compensatory increase as well in our heart rate because your overall cardiac output is a function of both the volume and also the rate.

Erin Welsh: Okay.

Erin Allmann Updyke: So we see an increase in heart rate which I remember seeing on my smartwatch where it was like you have a new normal.

Erin Welsh: Oh how interesting.

Erin Allmann Updyke: When I was pregnant.

Erin Welsh: How soon does that happen?

Erin Allmann Updyke: So a lot of these changes are kind of gradual.

Erin Welsh: Okay.

Erin Allmann Updyke: Where they start really early but then it just continues to change all the way till the 3rd trimester until term. For the most part.

Erin Welsh: Okay, okay. And it's just sort of an up; it's just sort of this is a linear, well not linear but I mean-

Erin Allmann Updyke: Yeah, not linear. But yes, it's a kind of continual-

Erin Welsh: Unidirectional.

Erin Allmann Updyke: For the most part.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah. There's probably nuance there that I'm skipping. Now I said your blood volume increases by 50%.

Erin Welsh: Yeah.

Erin Allmann Updyke: However your red blood cell volume, and remember red blood cells are the ones that actually carry oxygen to our tissues, so they're like kind of pretty important, they also increase but only by about 20%-30%.

Erin Welsh: What does this then difference in rate increase, how does that manifest in other part...? How does that...? Like what are the implications of that?

Erin Allmann Updyke: Okay, let me tell you.

Erin Welsh: Why aren't your red blood cells also increasing?

Erin Allmann Updyke: They are increasing.

Erin Welsh: Not to the same degree.

Erin Allmann Updyke: Just not to the same degree. So what is this? What does it mean? What are the implications?

Erin Welsh: Yeah.

Erin Allmann Updyke: It means that you have during pregnancy a physiologic anemia and your blood, it has less viscosity, so it can flow-

Erin Welsh: Less viscosity.

Erin Allmann Updyke: Right. Because you have less particle.

Erin Welsh: That's probably a good thing, yeah.

Erin Allmann Updyke: Yeah, it can flow a little bit more easily.

Erin Welsh: Yeah, okay.

Erin Allmann Updyke: It also though means that of course you can carry a little bit less oxygen, relatively speaking, like on the whole you're carrying more because everything is increased.

Erin Welsh: Yeah.

Erin Allmann Updyke

But you have this physiologic anemia. You also then have this fetus that is going to be relying on the oxygen that you are giving to them. So that means that you have to become very efficient with your oxygen transport, which is a thing I could go really too deep on but I won't. But what we then see during pregnancy is an increase in this production of this compound on our red blood cells called 2,3-DPG. It basically means that when you are pregnant, your body is better at giving away that oxygen.

Erin Welsh

Right.

Erin Allmann Updyke

So your red blood cells are more efficient at offloading oxygen so that the fetus can get access to that oxygen.

Erin Welsh

Okay. It's just easier to drop off.

Erin Allmann Updyke

Exactly.

Erin Welsh

Okay.

Erin Allmann Updyke

Exactly. Yeah. It's so interesting. There's also like fetal hemoglobin things that are interesting too.

Erin Welsh

Oh fetal hemoglobin-

Erin Allmann Updyke

I know.

Erin Welsh

I know.

Erin Allmann Updyke

It's cool. Okay, so. But it also means, you said another implication, another implication is that in order for our bodies to keep up with this demand, iron requirements are significantly higher in pregnancy compared to outside of pregnancy. And that's for two reasons. One, to support the growth of the fetus who needs iron to grow, but also to keep up with this increased red blood cell production. And so iron deficiency anemia can develop on top of this physiologic anemia.

Erin Welsh

Okay.

Erin Allmann Updyke

And so during pregnancy, people are at pretty high risk of anemia in general because you already have this physiologic anemia and now you have this increased iron requirement. So if you're not getting enough iron in your diet, then you're not able to make enough red blood cells.

Erin Welsh

Okay.

Erin Allmann Updyke

Does that make sense?

Erin Welsh

And so, right.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so then what, if anemia or if this one-two punch happens, then what are some of the downstream effects?

Erin Allmann Updyke I mean it can be really problematic when we get then into delivery because in delivery you are going to lose some degree of blood most likely.

Erin Welsh Yeah.

Erin Allmann Updyke And so that can put people at higher risk of complications from hemorrhage or just from blood loss in general.

Erin Welsh Okay.

Erin Allmann Updyke Yeah.

Erin Welsh Okay.

Erin Allmann Updyke I mean it can cause problems for the fetus as well too if you were like severely deficient.

Erin Welsh And so I'm sure there's a range of physiologic anemia like outside of iron deficient anemia.

Erin Allmann Updyke Right.

Erin Welsh And so is there a point at which just like physiologic anemia is where it needs some-

Erin Allmann Updyke Problematic?

Erin Welsh Yeah, exactly.

Erin Allmann Updyke I don't think so.

Erin Welsh Okay.

Erin Allmann Updyke Yeah. Because it is what is expected during pregnancy.

Erin Welsh Right. Okay.

Erin Allmann Updyke Right? You expect that to happen. Okay, so if we move on from our blood vessels in our cardiovascular system, we'll move to another vessel that's being affected kind of. It's not really a vessel, it's your kidneys. They're connected by tubes.

Erin Welsh Okay.

Erin Allmann Updyke It's like a vessel. You have all this extra blood, right?

Erin Welsh Yeah, yeah.

Erin Allmann Updyke

Your kidneys are responsible for filtering all of your blood, that's what they do. And so your kidneys have to work a heck of a lot harder. And during pregnancy your kidneys enlarge and increase their filtration rate by 50%, which is so impressive and means that you're making a crap ton of urine and you have to pee all the time, even before there is a fetus literally crushing your bladder.

Erin Welsh

That's something I had never thought about.

Erin Allmann Updyke

I know. And that's why even early in pregnancy people would be like I'm peeing all the time and it's not because of the fetus because that thing is like a couple of cells big.

Erin Welsh

Right. Yeah.

Erin Allmann Updyke

It's because you're making so much more blood and so your kidneys are filtering all that blood and so you're peeing all the time.

Erin Welsh

Okay.

Erin Allmann Updyke

And then eventually of course this fetus is going to grow large enough to crush your bladder. And when they do, you also can get compression of some of the tubes that lead from your kidneys to your bladder. And then that along with the fact that progesterone, which I talked about already that causes that vasodilation, progesterone also causes like a slowdown of everything. Everything's just like moving more slowly and so your bladder has a little bit more stasis, it's not like squeezing out as much. So you can be more prone to UTIs or urinary tract infections during pregnancy.

Erin Welsh

Interesting.

Erin Allmann Updyke

Because, yeah, even though you're making so much pee and peeing all the time-

Erin Welsh

Yeah, yeah.

Erin Allmann Updyke

It also just can kind of sit there a little bit longer. And then because of all of these things that are happening with like compression and blah, blah, blah, you have a higher risk of those UTIs getting up into your kidneys and causing a kidney infection.

Erin Welsh

Okay.

Erin Allmann Updyke

Okay?

Erin Welsh

And does that is that risk consistent throughout pregnancy?

Erin Allmann Updyke

I don't have an answer to that question.

Erin Welsh

Okay.

Erin Allmann Updyke

It's a good question. And it's not like it's major. Like that's not like oh my god.

Erin Welsh

Right, right.

Erin Allmann Updyke: It's just like you're at a little bit higher risk.

Erin Welsh: These than some of the things that happen.

Erin Allmann Updyke: Yeah, some of the things that can happen. So that was a lot, so I'm gonna take a big breath.

Erin Welsh: Okay.

Erin Allmann Updyke: Just kidding, you can't take a deep breath during pregnancy.

Erin Welsh: Good one! Did you have that written out?

Erin Allmann Updyke: I did. It was a joke I wrote.

Erin Welsh: I love when your jokes are written out.

Erin Allmann Updyke: Thank you.

Erin Welsh: Still felt natural.

Erin Allmann Updyke: Thank you. It was my segue into the respiratory system.

Erin Welsh: It was a good segue.

Erin Allmann Updyke: Thank you. So the changes that happen in your respiratory system, they actually start really early in pregnancy. I think we think about the changes later in pregnancy when you have just a large volume that's compressing things, and we'll get there. But the hormonal changes actually cause an increase in ventilation called hyperventilation of pregnancy. And that starts really early, so your respiratory rate actually increases hormonally.

Erin Welsh: Okay, okay. Hormonally.

Erin Allmann Updyke: Yeah.

Erin Welsh: What hormones?

Erin Allmann Updyke: Progesterone mostly.

Erin Welsh: Progesterone. How does that work?

Erin Allmann Updyke: We're not going to go deep into mechanism here, Erin, because I've got too many other body systems to talk about.

Erin Welsh: What makes you breathe more?

Erin Allmann Updyke: I don't know.

Erin Welsh: Okay.

Erin Allmann Updyke

I don't have any answer to that in what I wrote so far. But I got plenty of papers that you can read about.

Erin Welsh

Okay, okay, okay.

Erin Allmann Updyke

Because it does, yeah.

Erin Welsh

Just, yeah, amazing.

Erin Allmann Updyke

It's so cool. And then as I have alluded to many times now, as pregnancy progresses and this uterus increases in size significantly, it displaces every single other organ in your abdomen. It moves from being a pelvic organ to an abdominal organ. And in doing so, it elevates your diaphragm which is that muscle between your chest and your belly, and your diaphragm is what allows for your lungs to expand. It has to move down for you to take a deep breath in.

Erin Welsh

Right.

Erin Allmann Updyke

During pregnancy, this gets shoved about 4 centimeters upward so your lungs cannot expand as fully as they could previously.

Erin Welsh

Right.

Erin Allmann Updyke

That's what also causes that displacement of the heart which gets pushed up and a little bit to the left.

Erin Welsh

Okay.

Erin Allmann Updyke

And now some of this is compensated for, this displacement is compensated for by the same hormones like progesterone and also other ones like relaxin and things that cause ligamentous laxity.

Erin Welsh

There's a hormone called relaxin?

Erin Allmann Updyke

Relaxin.

Erin Welsh

Stop.

Erin Allmann Updyke

Just relaxin.

Erin Welsh

I want to know who named that.

Erin Allmann Updyke

I have no idea. That's a you question.

Erin Welsh

Amazing. Relaxin.

Erin Allmann Updyke

Yeah. So it's what allows all of your ligaments to expand and relax so that you can fit a baby through your pelvis.

Erin Welsh

Yeah, yeah, yeah.

Erin Allmann Updyke

And then also so that the bottom part of your ribcage can flail out and actually expand in diameter this way, like front to back, about 5-7 centimeters you get change here.

Erin Welsh

Yeah. Wow.

Erin Allmann Updyke

Just the bottom part of your ribs.

Erin Welsh

All thanks to relaxin.

Erin Allmann Updyke

Well relaxin, progesterone, all of these hormones. Yeah.

Erin Welsh

Oh progesterone, sorry. Not to just throw a spotlight on relaxin.

Erin Allmann Updyke

We can spotlight it. Give it some cred. But with all of these changes combined, by the end of pregnancy your total lung capacity decreases by about 5%. Which isn't huge.

Erin Welsh

Right.

Erin Allmann Updyke

However because of increased demand, both because the fetus has increased demand, right, you have to share with the fetus, and because your own basal metabolic rate during pregnancy increases by about 15%, your total oxygen consumption and need goes up by 20%-30%.

Erin Welsh

Okay. So you've got, first of all, you're breathing more because progesterone is telling you to breathe more.

Erin Allmann Updyke

Yep.

Erin Welsh

Presumably.

Erin Allmann Updyke

That's how it goes somehow.

Erin Welsh

We're not gonna dig deeper into that. You've got less room for your lungs to expand and you need to breathe more.

Erin Allmann Updyke

You need more oxygen.

Erin Welsh

And so you're just like panting basically.

Erin Allmann Updyke

You feel a little bit short of breath.

Erin Welsh

Short of breath, okay.

Erin Allmann Updyke

Yes, yeah. You're not panting but you feel short of breath.

Erin Welsh

Okay. And then also the metabolic, yeah.

Erin Allmann Updyke

Metabolic, yeah.

Erin Welsh

Okay. There's a lot of things happening.

Erin Allmann Updyke: So there's a lot of reasons to feel a little bit short of breath, especially towards the end of pregnancy.

Erin Welsh: Yeah.

Erin Allmann Updyke: Now you also have, because of everything going on in your abdomen, right, you also have just a lot of pressure inside of your abdomen. And what this can do, especially if somebody ends up lying down flat on their back, is it can put pressure on the blood vessel that sends blood back to your heart called the inferior vena cava.

Erin Welsh: Okay.

Erin Allmann Updyke: And that, because it's a vein it has floppy walls, so it can actually become compressed later in pregnancy by the weight of the fetus and the uterus and everything else in there. And that can potentially be problematic mostly for the fetus because it can kind of reduce the blood flow back to the heart, thus reducing your cardiac output, and then you can have this drop in blood pressure that affects the perfusion to the fetus.

Erin Welsh: Right. Okay.

Erin Allmann Updyke: So that's why a lot of times late in pregnancy people are told like don't lay flat on your back.

Erin Welsh: Yeah.

Erin Allmann Updyke: That's the reason why.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah. We have so many more body systems. Okay, ready? Blood in general, going back a little bit, I guess. Blood clotting factors completely change during pregnancy.

Erin Welsh: Yeah.

Erin Allmann Updyke: Nearly all of our clotting factors increase except for our platelet count. And we think this is helpful in terms of preventing postpartum hemorrhage but it also means that people are at higher risk of a thrombotic event, of a blood clot forming when it shouldn't.

Erin Welsh: But I thought that our blood was less viscous.

Erin Allmann Updyke: Oh my gosh, it is. But our clotting factors are higher.

Erin Welsh: Okay, so we're just sort of compensating for that decrease in viscosity.

Erin Allmann Updyke: All in different ways.

Erin Welsh: And then it's like the clotting factors, I mean really we're getting to the same end result.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah. More clots potential.

Erin Allmann Updyke: Potential for more clots.

Erin Welsh: Okay.

Erin Allmann Updyke: And the mechanism there, don't ask me exactly, it's probably related to estrogen because same reason if you're on estrogen birth control, you're at higher risk.

Erin Welsh: Yeah, which-

Erin Allmann Updyke: But not as high risk as when you're pregnant.

Erin Welsh: How have we not talked about that? Okay.

Erin Allmann Updyke: We did I thought, during our birth control episode.

Erin Welsh: Oh yeah, we did.

Erin Allmann Updyke: We did. Okay but all of this I've talked about so far, which was a lot, and I've already skipped over what is a lot of people's first indication symptom-wise that they might be pregnant and that is the changes to our GI tract.

Erin Welsh: Yeah.

Erin Allmann Updyke: So from the very beginning of pregnancy, hormones again like progesterone and others are causing smooth muscle relaxation. That's how we get dilation of our blood vessels.

Erin Welsh: Okay.

Erin Allmann Updyke: That's why we get the stasis in our bladder, all these things. And this results in a decrease in tone of our esophageal sphincter which goes from our esophagus into our stomach. And that can mean that you get an increase of things like acid reflux.

Erin Welsh: Okay.

Erin Allmann Updyke: And we think that it's also related to nausea. Right? You have just like slowdown of your GI tract and opening of your esophagus and going in, so it just makes you feel more nauseous.

Erin Welsh: Yeah. Why does the slowdown happen?

Erin Allmann Updyke: Because of progesterone.

Erin Welsh: Yeah but-

Erin Allmann Updyke: Why?

Erin Welsh: Yeah.

Erin Allmann Updyke: Is it just a consequence of the fact that like progesterone is causing this overall relaxation? Probably. Like does it have a purpose? I don't know.

Erin Welsh: Okay. Okay. And then why does that lead to nausea? Like what is nausea?

Erin Allmann Updyke: Oh my god.

Erin Welsh: Sorry.

Erin Allmann Updyke: I can't believe the questions you're asking me right now.

Erin Welsh: I'm sorry.

Erin Allmann Updyke: It's like what is itch? Oh my gosh.

Erin Welsh: I still want to know what itch is.

Erin Allmann Updyke: Yeah, I mean-

Erin Welsh: I mean I know what nausea is.

Erin Allmann Updyke: Right. You know what it feels like.

Erin Welsh: Right.

Erin Allmann Updyke: But why does having... I mean you can think about it too as like your food is not able to move through as quickly so it's going to be sitting there for longer. You have things that are supposed to be staying in your stomach coming up into your esophagus more readily.

Erin Welsh: Okay.

Erin Allmann Updyke: I don't know a better answer than that and there's probably a better answer out there. Like a GI doc is like rolling their eyes at me right now. Sorry.

Erin Welsh: No, I'm sorry.

Erin Allmann Updyke: No, don't be sorry. But yes, so this happens. And what's interesting is that mild nausea and vomiting early in pregnancy is actually associated with a lower risk of miscarriage or early pregnancy loss in the first trimester.

Erin Welsh: Yes, I have heard that.

Erin Allmann Updyke: Yes. And so we think that is a big part of the reason that we think it's very progesterone-mediated, right, is that when you have adequate levels of progesterone, then your pregnancy is able to continue. And so if you have lesser, then you might have less nausea but then it also might mean... You know what I'm saying?

Erin Welsh: Yeah, I do know what you're saying.

Erin Allmann Updyke: But it's not cut and dry.

Erin Welsh: Right, right.

Erin Allmann Updyke: It's just like a slight association.

Erin Welsh: Okay.

Erin Allmann Updyke: But as you can also hear in several of our firsthand accounts, sometimes this nausea and vomiting can become very severe and that's called hyperemesis gravidarum. We do not fully understand the cause of hyperemesis. We think that it's probably in part these changes to the gastrointestinal tract and the mobility of our gastrointestinal tract. But also like some contribution of is it maybe other hormones like independent of their effect on the GI tract? There's probably some degree of genetic susceptibility. We don't know, in short.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah. We don't fully understand that one at all.

Erin Welsh: Yeah.

Erin Allmann Updyke: But this slowdown of the GI tract can also, especially later in pregnancy, end up affecting the liver and the gallbladder.

Erin Welsh: Okay.

Erin Allmann Updyke: And that is what can result in intrahepatic cholestasis of pregnancy or cholestasis.

Erin Welsh: Yes, I want to know more about this. This is I had only heard... Yeah, yeah, yeah.

Erin Allmann Updyke: Yeah. So this is more rare than some of the other complications like maybe anemia or something like that. It's estimated at 0.2%-2% of pregnancies, depending on which studies you're looking at.

Erin Welsh: Okay.

Erin Allmann Updyke: But cholestasis is when we see a buildup of bile acids because bile acids are supposed to be, they're made in the liver and then they have to be transported through a duct into the gallbladder where they're stored. And then from the gallbladder they have to be squeezed out and then squirted into our small intestine.

Erin Welsh: Okay.

Erin Allmann Updyke: And so we see a buildup of these bile acid because they're not being squirted out and excreted by the gallbladder.

Erin Welsh: They're stuck in the gallbladder.

Erin Allmann Updyke: Their stuck.

Erin Welsh Gallbladder is the source of so much issue.

Erin Allmann Updyke Right.

Erin Welsh Yeah.

Erin Allmann Updyke And so also they're building up in general. So it's like the liver, the gallbladder, the whole situation, they're not going down the track like they're supposed to.

Erin Welsh Okay. And so the salts are stuck in the liver, stuck in the gall. It's just sort of like again the slowdown.

Erin Allmann Updyke Slowdown. It's a slowdown. Yeah.

Erin Welsh Traffic jam in the gallbladder.

Erin Allmann Updyke A traffic jam. And so then this bile acid accumulation will then be essentially transported out of just the liver-gallbladder situation and can potentially end up in our bloodstream. So then we see an increase in bile salts in our bloodstream. The symptoms of that end up being really, really severe itching and it's usually like whole body itching.

Erin Welsh Whole body.

Erin Allmann Updyke Don't ask me why it causes itching.

Erin Welsh What is itch? How does it get in the bloodstream?

Erin Allmann Updyke Because it's not able to be transported out, so then there's just too much of it and it's just like ah!

Erin Welsh Okay.

Erin Allmann Updyke Okay? Because your liver has so much blood supply.

Erin Welsh Yes.

Erin Allmann Updyke And so if it's just backed up into your liver, then it's going to be kicked out.

Erin Welsh It's going go back.

Erin Allmann Updyke Yeah. And so yeah. And that does not pose a problem to the pregnant person but those bile salts can pass through the placenta and be toxic to the fetus because these are cytotoxic compounds.

Erin Welsh Right.

Erin Allmann Updyke That's why they're usually stored in our gallbladder where they're not causing problems usually. Okay. I've gone through a lot of physiologic changes so far.

Erin Welsh: Trying to think of other-

Erin Allmann Updyke: Don't ask me more questions. I'm going to keep going.

Erin Welsh: I'm trying to think of other body parts or what other systems.

Erin Allmann Updyke: They're not the ones you would think of necessarily.

Erin Welsh: Brain.

Erin Allmann Updyke: Yeah, brain is interesting. Your brain definitely changes during pregnancy and there are like fetal cells that make it all the way into your brain.

Erin Welsh: Yeah.

Erin Allmann Updyke: But I don't have data on like what are the changes, we have no idea.

Erin Welsh: But the fetal cell...

Erin Allmann Updyke: Okay. But here's what I'm going to do is now focus more on the two other major complications that we see-

Erin Welsh: Okay.

Erin Allmann Updyke: And the body systems that they're involved in. So diabetes. Okay. This is our endocrine system. And we already know that our endocrine system, which is our hormone system, you defined it last episode-

Erin Welsh: Could be either.

Erin Allmann Updyke: At some point.

Erin Welsh: Oh yeah, it was last episode because we talked about HCG.

Erin Allmann Updyke: Yeah, HCG. So our entire hormonal milieu is changed during pregnancy.

Erin Welsh: Yeah.

Erin Allmann Updyke: And people end up susceptible to diabetes during pregnancy in large part because of a hormone that the placenta is secreting that's called human placental lactogen. There's other stuff that it's involved as well but this is what I'm going to focus on.

Erin Welsh: Okay.

Erin Allmann Updyke: Because what this does is it makes our pregnant bodies less sensitive to insulin. We have an increased insulin resistance.

Erin Welsh: Okay.

Erin Allmann Updyke: Why do we need an increased insulin resistance? If we remember back to our diabetes episode, insulin's job, what it does in our body, is when we have high glucose, like we eat something, right-

Erin Welsh: Yeah.

Erin Allmann Updyke: And we have high glucose in our bloodstream, insulin is secreted and it tells the glucose like get away from here, pack yourself away so that we can store you and use you later. Okay? So insulin puts glucose into our cells. But a fetus needs glucose and they get it from our bloodstream.

Erin Welsh: Oh. Got it.

Erin Allmann Updyke: So by making our insulin less effective, you can have more glucose to be available for the developing fetus. But if this process goes too far, like if our pancreas... Because we're going to have this insulin resistance, right, so our cells are going to recognize hey, glucose is too high, we need to make more insulin.

Erin Welsh: Yeah.

Erin Allmann Updyke: If your pancreas can't keep up with that increased demand, then you end up with gestational diabetes where we see too much glucose in our bloodstream.

Erin Welsh: Okay.

Erin Allmann Updyke: Levels get too high. And that has a couple of big consequences. One is it can cause increased growth of the fetus, right. Because the fetus is just like getting a glucose pipeline.

Erin Welsh: Yeah, yeah.

Erin Allmann Updyke: Okay? And that is called macrosomia. So it ends up being large, babies are large for gestational age babies and that can make delivery very risky.

Erin Welsh: Yes.

Erin Allmann Updyke: Okay. But the second complication that I don't think people talk about as much is that while our glucose that's in our bloodstream passes through the placenta and into the fetus, our insulin does not. So if our glucose levels get really, really high, fetus inside of us has to make more and more insulin because their body is also like whoa, this is a lot of glucose.

Erin Welsh: Yeah.

Erin Allmann Updyke: So they're having an increased amount of fetal insulin that they're making. And then after they're born, that sugar syrup bloodstream pipeline is cut off and now they can get severely hypoglycemic because of how much insulin they've made in their bodies.

Erin Welsh: And so then what does that look like?

Erin Allmann Updyke: That can end up with seizures or coma or death to the fetus, to the baby.

Erin Welsh: And that is like immediately following birth or when?

Erin Allmann Updyke: Right, exactly.

Erin Welsh: Okay.

Erin Allmann Updyke: So in the neonate, in the newborn.

Erin Welsh: Wow.

Erin Allmann Updyke: They can have really severe hypoglycemia. And so that's why babies that are born when the mom has had gestational diabetes have to be monitored really closely especially in the first 24-48 hours.

Erin Welsh: Okay.

Erin Allmann Updyke: So interesting.

Erin Welsh: Can I ask some questions?

Erin Allmann Updyke: You can try, yeah.

Erin Welsh: Okay, okay, okay. When typically do we see gestational diabetes appear?

Erin Allmann Updyke: Okay. We usually test for it around weeks 24-28.

Erin Welsh: Okay.

Erin Allmann Updyke: It doesn't mean it can't happen before that or after that but that's usually in most places that's the timeline that we test for it.

Erin Welsh: Okay. My second question is then what do you do about it?

Erin Allmann Updyke: Yeah, great question.

Erin Welsh: Okay.

Erin Allmann Updyke: Do you have more that you want to keep going?

Erin Welsh: Yeah, no, no, but you answer then I'll...

Erin Allmann Updyke: Okay.

Erin Welsh: Yeah.

Erin Allmann Updyke: There's a few different things. A lot of times it can be managed with just dietary changes alone.

Erin Welsh: Okay.

Erin Allmann Updyke: And so figuring out like what are you eating that's maybe causing really big glucose spikes and can you just modify your diet to be able to not have that and then you're good. Otherwise it's usually insulin, so we manage it with insulin.

Erin Welsh: My third question, and maybe I should just let you finish talking about the other complication.

Erin Allmann Updyke: No, give it to me.

Erin Welsh: What are the differences between first pregnancies and subsequent pregnancies? This is a big picture question.

Erin Allmann Updyke: Okay, yeah, okay.

Erin Welsh: Because I would imagine that like okay, first pregnancy your body's like responding and doing all these things that it's doing for the first time.

Erin Allmann Updyke: Right. Your body hasn't done it.

Erin Welsh: Right. And the second time it's like are those pathways carved out? How different are the hormone levels?

Erin Allmann Updyke: Yeah.

Erin Welsh: How likely are the same complications to occur between one pregnancy and subsequent pregnancies?

Erin Allmann Updyke: That's interesting. So we'll talk definitely more about that with preeclampsia which is what I'm going to do next.

Erin Welsh: Yeah.

Erin Allmann Updyke: But I don't know when it comes to gestational diabetes. Certainly if you've had gestational diabetes in one pregnancy, you are at higher risk for having it in another pregnancy.

Erin Welsh: Okay.

Erin Allmann Updyke: Gestational diabetes is also associated with an increased risk of type 2 diabetes later in life.

Erin Welsh: Okay.

Erin Allmann Updyke: So it's thought to be kind of like a marker.

Erin Welsh: Yeah.

Erin Allmann Updyke: There's a lot of things that happen in pregnancy that are thought to kind of be markers. And we don't know are they like causal or are they just like kind of a snapshot in time where we're like oh maybe you are at higher risk for these complications later in life but it's not like because you had it during pregnancy. Does that make sense?

Erin Welsh: Yes.

Erin Allmann Updyke

But yeah, I don't know data on like what are the rates first pregnancy, second, third. It also is going to vary with age as well too. So yeah, I don't know, that's an interesting question though when it comes to diabetes.

Erin Welsh

Yeah.

Erin Allmann Updyke

I don't know. Overall though the estimates of like how many pregnancies are complicated by diabetes are like all over the map from 1%-30% depending on your study. So it's like who knows?

Erin Welsh

Right. What's the threshold? Like how do you-

Erin Allmann Updyke

How do you diagnose it?

Erin Welsh

how do you diagnose?

Erin Allmann Updyke

I really wanted to bring in a glucoala for you but I couldn't get my hands on one, so I'm sorry. And it does differ, different countries and different guidelines are a little bit different in terms of how exactly you diagnose it. But most of the time it's by doing a glucose tolerance test. And so you give somebody a fixed volume of glucose, 50 g, 75 g, whatever, and then you test their blood at intervals, either 1 hour, 2 hours, 3 hours, or multiple times.

Erin Welsh

Okay.

Erin Allmann Updyke

And then see what their numbers are.

Erin Welsh

Got it.

Erin Allmann Updyke

What their glucose level is.

Erin Welsh

Okay.

Erin Allmann Updyke

And there's different cutoffs and that part's boring, so let's move on, shall we?

Erin Welsh

Yeah. Preeclampsia.

Erin Allmann Updyke

Preeclampsia. Yes.

Erin Welsh

Yeah, big one.

Erin Allmann Updyke

So it is the biggest. It is a doozy and it can be for sure probably the most severe complication of pregnancy. That might not be true but it's a big one.

Erin Welsh

It's a big one.

Erin Allmann Updyke

So this is really truly not just, it doesn't fit as neatly in a single organ system because it is, like you mentioned, Erin, the result of a kind of dysfunctional relationship really between the placenta and our own cardiovascular system. And it can result in a whole spectrum of disorders that we call hypertensive disorders of pregnancy. So it's not just preeclampsia. It also includes gestational hypertension, so just high blood pressure.

Erin Welsh

Okay.

Erin Allmann Updyke

Preeclampsia and eclampsia and then also HELLP which is hemolysis elevated liver enzymes and low platelets. But often we think about and focus on preeclampsia because that is a kind of point at which if this kicks in, if it's officially preeclampsia, then that's when the risks to both fetus and mom become pretty significant.

Erin Welsh

Okay.

Erin Allmann Updyke

Preeclampsia overall is estimated to complicate between 4%-5% of all pregnancies worldwide.

Erin Welsh

It's such a high rate.

Erin Allmann Updyke

It's pretty high.

Erin Welsh

Yeah.

Erin Allmann Updyke

And it's estimated, and estimates on this really did vary in several papers that I read, but most reliably the papers that I read said it's estimated to result in 70,000 maternal deaths every year. 70,000 maternal deaths every year. And 500,000 stillbirths or neonatal deaths.

Erin Welsh

Oh my gosh.

Erin Allmann Updyke

Which is just like heartbreakingly massive numbers.

Erin Welsh

Yeah, yeah.

Erin Allmann Updyke

On top of that, for every maternal death that's related to preeclampsia it's estimated that 50-100 women are having significant morbidity as a result of it. So it's affecting a huge number of people.

Erin Welsh

Yeah.

Erin Allmann Updyke

And I'm sorry that that started off so heavy but preeclampsia can get really scary.

Erin Welsh

Yeah, absolutely.

Erin Allmann Updyke

So in terms of when I say preeclampsia, what does that mean?

Erin Welsh

Right.

Erin Allmann Updyke

It's defined as hypertension, so elevated blood pressures and at least one of a few other features, symptoms that we see. One big one is protein in the urine because that's a sign that your kidney is being affected.

Erin Welsh: Okay.

Erin Allmann Updyke: Or sometimes other signs, other lab values that we see that tell us that your kidney is having kidney dysfunction.

Erin Welsh: And that's like it's not filtering well?

Erin Allmann Updyke: Exactly, exactly.

Erin Welsh: Okay.

Erin Allmann Updyke: Or liver dysfunction.

Erin Welsh: All right.

Erin Allmann Updyke: And all of those we do like laboratory values to see what those numbers are. Or sometimes it's diagnosed by neurologic complications, which can be severe persistent headaches, visual changes, stroke, or abnormal reflexes. Or sometimes it's hematologic complications, especially platelet abnormalities.

Erin Welsh: Okay. So there are a multitude of ways to diagnose-

Erin Allmann Updyke: A multitude of criteria that you kind of like check the boxes and if you're meeting these, then it's called preeclampsia rather than just hypertension.

Erin Welsh: Yeah. Interesting.

Erin Allmann Updyke: Yeah.

Erin Welsh: So it would have to be like these neurological changes in addition to high blood pressure.

Erin Allmann Updyke: Exactly.

Erin Welsh: And you would also have to have protein in the urine.

Erin Allmann Updyke: Exactly.

Erin Welsh: Or other liver enzyme elevation. Okay.

Erin Allmann Updyke: And what it can cause is a number of different things. From the fetal perspective it can cause fetal growth restriction because of abnormal blood flow into the placenta.

Erin Welsh: Yeah.

Erin Allmann Updyke: But when preeclampsia, especially if it goes untreated or unchecked, it can result in a number of really severe complications including eclampsia which is preeclampsia but with seizures. So that's the line at which it becomes eclampsia rather than preeclampsia.

Erin Welsh: Right. Downton Abbey.

Erin Allmann Updyke: Downton Abbey.

Erin Welsh: Yeah.

Erin Allmann Updyke: I know, I think of that too. And then it also can sometimes cause stroke, especially a hemorrhagic stroke which would be a very severe complication of preeclampsia.

Erin Welsh: Okay.

Erin Allmann Updyke: Sometimes it's not the nervous system but it's a different organ that gets mainly affected, so it can cause severe liver damage and that often results in that HELLP syndrome.

Erin Welsh: Okay.

Erin Allmann Updyke: Because it's causing damage to the liver.

Erin Welsh: Yeah. So HELLP is-

Erin Allmann Updyke: It's on the spectrum.

Erin Welsh: It's on the spectrum. Okay, so what is that spectrum? I know there's hypertension.

Erin Allmann Updyke: Yeah, gestational hypertension, preeclampsia, eclampsia, HELLP.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah. That's like the main spectrum.

Erin Welsh: Okay.

Erin Allmann Updyke: But then with preeclampsia we can also see these other... And they're not discrete events necessarily. Like it's not like HELLP or this.

Erin Welsh: Sure, right, okay.

Erin Allmann Updyke: Yeah. And preeclampsia also it doesn't discriminate. It can cause severe complications to your kidneys and end up causing renal failure. It can cause flash pulmonary edema, meaning fluid onto the lungs, largely from just such high blood pressures because that's something we see with severely elevated blood pressures outside of pregnancy as well. And then like I said, for the fetus it can cause placental abruption as well which is where the placenta detaches spontaneously before the baby has been delivered and that can be potentially catastrophic. And then also premature delivery or stillbirth. And we don't fully understand the mechanisms of preeclampsia.

But you talked a lot, Erin, about what we know about the placenta and this relationship between abnormal or whether it's inadequate, like not deep enough or too deep placentation. And what we think is that that process results in these anti-angiogenic factors that float around in our maternal bloodstream and end up causing damage to our blood vessels. And that causes us to have this increase in blood pressure and that is what ultimately leads to preeclampsia. So it's like inflammation and these like anti-angiogenics, so like not making enough blood vessels, not getting enough remodeling in the uterus.

Erin Welsh

Right.

Erin Allmann Updyke

And this whole kind of perfect storm almost.

Erin Welsh

Signaling like hey, there's not enough going on here, send more, send more.

Erin Allmann Updyke

Exactly, exactly. And there is of course a lot of interest in understanding like are there biomarkers? Are there things that we can identify in your blood to say either you definitely have preeclampsia or you are at higher risk of developing preeclampsia?

Erin Welsh

Yeah.

Erin Allmann Updyke

And in several countries they actually Do use a few different blood tests-

Erin Welsh

Okay.

Erin Allmann Updyke

That test for a few different specific things. And I think I forgot to write down their names but they're like PIF, blah, blah, blah.

Erin Welsh

Some biomarkers, yeah.

Erin Allmann Updyke

Exactly, biomarkers. So far as of 2024, we don't use those yet in the United States.

Erin Welsh

Okay.

Erin Allmann Updyke

So what we mostly look at in terms of trying to identify who is at risk for developing preeclampsia is what we know from the epidemiological data. And we know a lot about what the risk factors are that make someone higher risk for developing preeclampsia. We know that one of the biggest ones is having a previous pregnancy with preeclampsia.

Erin Welsh

Right.

Erin Allmann Updyke

The other huge one is having a first pregnancy. So you asked about the difference between first pregnancies and subsequent pregnancies.

Erin Welsh

Yeah.

Erin Allmann Updyke

First pregnancies are generally higher risk for preeclampsia compared to second, third, fourth pregnancies, unless you had preeclampsia in your first one.

Erin Welsh

Right.

Erin Allmann Updyke

And then you're at higher risk during the other ones as well too. And we don't fully understand that but we think that it's related again to this immune tolerance thing.

Erin Welsh

Yeah.

Erin Allmann Updyke

Where your body has never seen these cells from this fetus floating around and you develop this immune response to it. Whereas if you've had a pregnancy before and your immune system tolerated it, you are at lower risk of having an abnormal reaction to that in the future pregnancies.

Erin Welsh

Yeah.

Erin Allmann Updyke

If they're with the same paternal DNA.

Erin Welsh

So that I find fascinating and I didn't get into this but there is a lot about paternal DNA-

Erin Allmann Updyke

Yes.

Erin Welsh

And like pre-exposure to paternal DNA before pregnancy.

Erin Allmann Updyke

Yes, yes, yes.

Erin Welsh

Yeah.

Erin Allmann Updyke

So like IVF pregnancies, especially those with donor sperm, are also a little bit higher risk than non-IVF pregnancies or IVF without donor sperm. So really that's part of what lends support to this idea that there's like an immune tolerance spectrum kind of a thing.

Erin Welsh

Yes, yeah. Well it also makes sense then why subsequent pregnancies where the first pregnancy, there's preeclampsia, would have preeclampsia.

Erin Allmann Updyke

Exactly, exactly.

Erin Welsh

Because it's almost sensitized, like oh I've seen this before.

Erin Allmann Updyke

Right.

Erin Welsh

Yeah.

Erin Allmann Updyke

And I know what to do.

Erin Welsh

Yeah.

Erin Allmann Updyke

Right, exactly. There's a lot of other risk factors though. Having chronic hypertension prior to pregnancy; maternal age, so increasing age increases our risk. Why? We do not know. And then a lot of other like medical complications that might affect the functioning of your organs prior to pregnancy like kidney disease, things like lupus which can affect blood clotting factors and things like that, having a family history of preeclampsia. And then this part's really important, especially in the United States race is a risk factor for preeclampsia, specifically Black people who are pregnant are at significantly higher risk of pre-eclampsia compared to white people who are pregnant. But that is not a biologic difference.

Erin Welsh

Right.

Erin Allmann Updyke

And this is specified in the ACOG guidelines, this is due to systemic racism.

Erin Welsh

Yeah.

Erin Allmann Updyke

Because we also see that low income regardless of race which causes increase in life stressors is also associated with an increased risk of preeclampsia. And so these are the kinds of differences that are really important to understand because by recognizing who is at risk, we can, can we?, hopefully prevent preeclampsia.

Erin Welsh

How would one prevent preeclampsia?

Erin Allmann Updyke

I'm so glad that you asked, Erin. Right now the only thing that we have to help prevent preeclampsia is low dose aspirin of all things.

Erin Welsh

Okay.

Erin Allmann Updyke

So taking aspirin, which we did a whole episode on and you might remember-

Erin Welsh

Yeah.

Erin Allmann Updyke

Is an anti-inflammatory agent that also irreversibly inhibits platelets from aggregating. So it stops your platelets from forming clots and we think that these microthrombotic events are involved in the pathogenesis of preeclampsia. And so by irreversibly inhibiting this platelet aggregation, we've shown through a lot of epidemiological studies that's what we think the mechanism is.

Erin Welsh

Yeah.

Erin Allmann Updyke

But we know that starting low dose aspirin early in pregnancy, usually 1st or early 2nd trimester, and continuing it until term can significantly reduce someone's risk of developing preeclampsia. Not make it zero. And the risks are different for whether it's term preeclampsia, pre-term preeclampsia, or postpartum preeclampsia.

Erin Welsh

So what are those?

Erin Allmann Updyke

I don't have like-

Erin Welsh

I mean they are what they sound like I guess.

Erin Allmann Updyke

They are what they sound like. It's like when in pregnancy does it develop?

Erin Welsh: Yeah.

Erin Allmann Updyke: Most of the time this is something that does not develop or at least we don't see it, can't recognize it clinically until after 20 weeks of pregnancy.

Erin Welsh: Okay.

Erin Allmann Updyke: But it can potentially develop anytime, you might just not see the signs. It might be... That's part of why people are looking for biomarkers. Can we find it? Can we find evidence of this super early on?

Erin Welsh: Right. Yeah.

Erin Allmann Updyke: But usually it's after 20 weeks. The earlier that you start to see preeclampsia, usually the worse the outcomes are which makes sense.

Erin Welsh: Yeah.

Erin Allmann Updyke: Because you're just going to have a bigger effect on the fetus and you're going to have a longer time that you're having potentially complications to the mother as well.

Erin Welsh: And postpartum?

Erin Allmann Updyke: And postpartum we really do not understand. But you can develop preeclampsia for the first time postpartum even if you did not have high blood pressure during pregnancy.

Erin Welsh: We have no idea?

Erin Allmann Updyke: No. And it is thought that because some people also don't develop preeclampsia until like right at the end, right, they're after term, you're after 37 weeks and you now all of a sudden have high blood pressure and then potentially preeclampsia. And we think that maybe those two entities are slightly different and less related to inadequate placentation early on but maybe some other mechanism but we don't know what that mechanism is yet.

Erin Welsh: Is that the same... Is it related to any bits of the placenta remaining or getting stuck to-

Erin Allmann Updyke: Sometimes yes.

Erin Welsh: Okay.

Erin Allmann Updyke: It can be from the placenta not fully detaching or something like that but not always.

Erin Welsh: Yeah.

Erin Allmann Updyke: So it's not as clear cut as that.

Erin Welsh: Right, okay.

Erin Allmann Updyke: Yeah.

Erin Welsh: There's still something that's sending the signal of there's not enough oxygen.

Erin Allmann Updyke: Exactly.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah. But we don't know exactly how it works.

Erin Welsh: Yeah.

Erin Allmann Updyke: And how is it different or is it not different and that kind of a thing. In terms of other ways that we have to reduce the risk of preeclampsia, there's some evidence that maybe calcium supplementation might help but it's not as clear cut as aspirin. And then in terms of if someone has preeclampsia, how can we prevent it from getting severe or how do we cure it? Magnesium sulfate is given to prevent seizures, so specifically to prevent eclampsia. We don't know the mechanism or why it works but it does. But the only cure for preeclampsia is delivery of the fetus and the placenta.

Erin Welsh: Yeah.

Erin Allmann Updyke: But that is not only something that you have to balance getting to a gestational age where the fetus can survive and hopefully thrive.

Erin Welsh: Yeah.

Erin Allmann Updyke: And also ensuring the health of the pregnant person.

Erin Welsh: Right.

Erin Allmann Updyke: And of course that's not always the case because postpartum preeclampsia does still exist.

Erin Welsh: Yeah.

Erin Allmann Updyke: So it's a little bit complicated and we don't fully understand it.

Erin Welsh: Do you have a breakdown for the percentages of each of those?

Erin Allmann Updyke: No.

Erin Welsh: Okay.

Erin Allmann Updyke: And I really tried to find that but I don't have a good breakdown of that.

Erin Welsh: Yeah. Okay.

Erin Allmann Updyke: Yeah. So that's preeclampsia. And really like the overall physiology of pregnancy.

Erin Welsh: Yeah. What about breasts?

Erin Allmann Updyke: I wasn't going to talk about breasts until two episodes from now.

Erin Welsh: Oh, we can talk about it then.

Erin Allmann Updyke: They do start to change early on in pregnancy.

Erin Welsh: Yeah.

Erin Allmann Updyke: Yeah. You actually start to make colostrum in the 2nd trimester which is the first stuff that you secrete right after that the newborn usually eats for the first couple of days before your actual milk comes in.

Erin Welsh: Food aversions, food cravings.

Erin Allmann Updyke: Dunno.

Erin Welsh: Okay.

Erin Allmann Updyke: There's a lot of talk about like the evolutionary significance of nausea and vomiting and food cravings and is it so that we-

Erin Welsh: Yeah. How it peaks at the time that the fetus is vulnerable to toxins crossing the placental barrier.

Erin Allmann Updyke: Right, right, right. But I don't know.

Erin Welsh: I mean there seems to be some basis to that. It's like Darwinian medicine or whatever.

Erin Allmann Updyke: Sure. But I don't know more about it than that.

Erin Welsh: Yeah.

Erin Allmann Updyke: But what I think is so interesting and part of the reason that I am so astounded by and fascinated by the physiology of pregnancy is that despite all of these changes to literally every organ system in our body and despite all of the possible complications, some of which might be minor and not result in severe harm and some of which can be very severe-

Erin Welsh: Yeah.

Erin Allmann Updyke: Despite all of that, the majority of pregnancies progress all the way to term and delivery without major complication.

Erin Welsh: Yeah.

Erin Allmann Updyke: Which is just astounding.

Erin Welsh: It is mind blowing.

Erin Allmann Updyke That our bodies can change so dramatically.

Erin Welsh I have a question about that.

Erin Allmann Updyke Okay.

Erin Welsh Permanent changes. What are there and then how... You can tell whether someone has been pregnant before like looking at organ changes.

Erin Allmann Updyke A lot of times. I mean-

Erin Welsh Not all the time.

Erin Allmann Updyke Yeah, not all the time. Yeah.

Erin Welsh But what are those things that signal that?

Erin Allmann Updyke We'll talk more about that in the fourth episode when we talk about postpartum stuff.

Erin Welsh Okay.

Erin Allmann Updyke So yeah, I don't have an easy answer to that question.

Erin Welsh Okay.

Erin Allmann Updyke But yeah, I mean things change like in terms of cervix changes and things like that that you can maybe see on physical exam. There is evidence that fetal cells remain in our tissues for potentially the rest of our lives which is crazy to think about.

Erin Welsh I mean again, it kind of is that relationship with cancer where it's like...

Erin Allmann Updyke Yeah, yeah.

Erin Welsh Yeah, it's interesting.

Erin Allmann Updyke It's really, really interesting. But yeah, that's pregnancy, Erin.

Erin Welsh In a short 1.5-2 hours, yeah.

Erin Allmann Updyke In a short 40 million years that I took to explain all of that.

Erin Welsh We went from deep time. We really crossed hundreds of millions of years this episode.

Erin Allmann Updyke We went from deep time all the way until delivery which is next week.

Erin Welsh Deep time to delivery. Yeah.

Erin Allmann Updyke So.

Erin Welsh: So.

Erin Allmann Updyke: If you'd like to learn more.

Erin Welsh: Sources.

Erin Allmann Updyke: Boy howdy.

Erin Welsh: Boy howdy. Okay. I have some sources here.

Erin Allmann Updyke: Oh I bet.

Erin Welsh: There are two books that I read. One is called 'The Evolution of the Human Placenta' which is what it sounds like by Michael Power and Jay Schulkin.

Erin Allmann Updyke: Okay.

Erin Welsh: And then there's 'Life's Vital Link: The Astonishing Role of the Placenta' by Yung Loke. Then those are the books. I think they were pretty good overviews of what's going on. It is an overwhelming amount of information. If you want to learn more about retroviruses, there are a few papers that I have posted. One is by Chuong from 2013 called 'Retroviruses Facilitate the Rapid Evolution of the Mammalian Placenta'.

Erin Allmann Updyke: Love it.

Erin Welsh: There are some other ones too about retroviruses that are good. Then there's Kshitiz et al from 2019, 'Evolution of placental invasion and cancer metastasis are causally linked'.

Erin Allmann Updyke: Ooh.

Erin Welsh: Yeah.

Erin Allmann Updyke: Interesting.

Erin Welsh: Interesting.

Erin Allmann Updyke: Bold statement.

Erin Welsh: Bold statement. Then from 2013 by Crosley, 'Placental invasion, preeclampsia risk, and adaptive molecular evolution at the origin of the great apes: evidence from genome-wide analyses.'

Erin Allmann Updyke: Wow.

Erin Welsh: Because humans are not the only species to get preeclampsia. Yeah, which we thought for the longest time that we were.

Erin Allmann Updyke: That we were.

Erin Welsh: But no, I think there was a gorilla at the Houston Zoo last year, the year before or something, that had preeclampsia.

Erin Allmann Updyke: Aw, poor baby.

Erin Welsh: I know.

Erin Allmann Updyke: Is she okay?

Erin Welsh: I think so.

Erin Allmann Updyke: Okay, good. I have a number of sources for this, some of which focused more on just the basic physiology of pregnancy. One that I liked that was easy to read was called 'Physiology of Pregnancy' from Anesthesia and Intensive Care Medicine from 2019. I had a few others that were more focused on the cardiovascular physiology of pregnancy too that were great. A review paper on gestational diabetes called 'Gestational Diabetes Mellitus'.

Erin Welsh: There you go.

Erin Allmann Updyke: Really creative title from Nature Reviews Disease Primers 2019. And another from Nature Reviews Disease Primers on preeclampsia called 'Preeclampsia'. It's not really creative titling.

Erin Welsh: I mean I feel like it's pretty easy to understand what the paper's about.

Erin Allmann Updyke: Exactly, you know what you're getting. It's a review.

Erin Welsh: There's no puns, we don't need puns in this.

Erin Allmann Updyke: And then there was a bunch more.

Erin Welsh: Okay.

Erin Allmann Updyke: So listen, check out our website thispodcastwillkillyou.com under the EPISODES tab where you can find the list of all of the sources that we used from this episode and every single one of our episodes.

Erin Welsh: Every single one. A huge thank you again to everyone who sent in their firsthand account and shared them with us. We really can't thank you enough.

Erin Allmann Updyke: No.

Erin Welsh: Thank you, thank you.

Erin Allmann Updyke: Thank you, thank you.

Erin Welsh: We'll try though.

Erin Allmann Updyke: Thank you again to everybody here at Exactly Right studios for having us, we're super excited about it.

Erin Welsh	Yay!
Erin Allmann Updyke	Thank you, Tom. Thank you, Lianna. Thank you, Jessica. Thank you, Brent. Thank you, Craig. Everyone.
Erin Welsh	Thank you everyone.
Erin Allmann Updyke	There's so many other people.
Erin Welsh	This has been so much fun.
Erin Allmann Updyke	It has.
Erin Welsh	Yeah. Thank you to Bloodmobile for providing the music for this episode and all of our episodes.
Erin Allmann Updyke	And thank you to all of you for listening and watching.
Erin Welsh	Yes.
Erin Allmann Updyke	And we hope that you enjoyed this episode and that you're ready for two more.
Erin Welsh	Two more. I know we still have so much to cover. Wow.
Erin Allmann Updyke	I know, yeah.
Erin Welsh	And thank you to our patrons. You really, you mean a lot to us. We really appreciate you.
Erin Allmann Updyke	Yeah, thank you.
Erin Welsh	Yeah. Well until next time, wash your hands.
Erin Allmann Updyke	You filthy animals.