Dominique	Hi, my name is Dominique and a few years ago I went through IVF. I had been married for a while, my partner had testicular cancer so we figured that even though we've been trying for a long time, it might have been that previous illness and resulting surgery that was getting in the way. Now we actually ended up splitting up for other reasons but after I had kind of set myself up on my own, I just figured mid 30s, I wanted to get on with it. So I consulted with my GP and started the process of IVF. There were a lot of hormone injections and other things, pelvic scans, ultrasounds, oral medications. And everything went pretty well for the first little while. But then it started to become a little bit more of a rollercoaster.
	So my first egg collection day, I had a scan and it said I had 13 really nice follicles, that was what the OB/GYN said. I went into surgery, when I woke up they told me all of the follicles had been empty. Now I didn't know that this was a thing but there is a syndrome called empty follicle syndrome where you have a lot of follicles but they don't actually have any eggs in them. I was really devastated. I had to go another round with different medications, different dosages. And I went in for my next surgery, egg collection surgery with 11 follicles ready to go. And they were able to obtain three eggs from those. One of those was a dud, two of them successfully fertilized. Out of those two, the first transfer didn't stick. And by this point I was actually getting pretty broke. I had sold stuff, my motorcycle and things to cover these expenses and I had the final transfer about a month later.
	And now I have a four year old. People ask me if I'm gonna have another one. I don't have any more embryos, follicles are probably not actually making many eggs and this is actually probably the biggest reason why I wasn't able to get pregnant beforehand and I just didn't even know. I also found out I had a retroverted uterus throughout the process which was another surprise. So there's a lot of things that can come up during IVF that you don't necessarily expect and it can happen at just about any stage. Yeah, I don't think that people ask if I'm going to have a second one if they know my journey. Everybody's IVF journey is really, really different, but they're all roller coasters I think, they all have ups and downs whether those are big or small.
Anonymous	As a gestational carrier, my view on IVF widened broadly throughout that process. So just a quick comparison, for my own child I went off birth control and that first month I got pregnant with her. And it was very quick to conceive and that was it. I didn't have to think about it, I didn't have to do anything. And so fast forward to when my daughter was 12 and I decided to work with a surrogacy agency to become a gestational carrier for a family. I didn't fully realize that process, I just wanted to help m mainly a member of the LGBTQ become a family because I knew that that's a struggle for a lot of gay men to have children. And so I wanted to do that. That was my choice I made.
	And so when I went into that process, I guess I didn't think about like the full, what all has to happen, right. My husband and I, we decided to have a baby. Boom, we had a baby. Whereas especially from the gestational carrier standpoint, I had to go through a psychological exam, my husband and I had to go through counseling, and we had to be like check boxed that we were okay to do this. Which I am 100% understand why. But I didn't have to do that to have my own child, right? And then they had to make sure I was like compatible with the family that I worked with. And so it was such a different experience obviously.

	But then when you get into having to have your uterus, your ovaries, your fallopian tubes, everything examined very thoroughly to make sure they're all functional, I didn't know mine were functional prior to that. I mean I remember the doctor giving me the compliment that I had like very nice eggs and I could have donated them, that kind of comment, and I had no clue about that kind of thing prior to this experience. And in like talking to people who I now know who have struggled with IVF, because I think my gestational carrier experience has caused people in my life to come and talk to me about their own struggles with it, has really made me empathetic and really made me realize how hard it is because like I went through this for somebody else.
	But I can't imagine just like going through that. I had to go through two cycles because I had one miscarriage and then I was pregnant and I carried that baby to term. But to go through that month after month after month, like the psychological toll it must take on a person. And I just like... Like I was on hormone suppressants and then I was on estrogen and progesterone and I had to do shots, which I hate needles. I can't imagine having to do that. I think if it had been me in a situation of having my own child, I might have gone down a different path because it's a lot to put on a person and it's so like... They're so brave for doing it.
TPWKY	(This Podcast Will Kill You intro theme)
Erin Welsh	Thank you again, so much to the providers of all of these firsthand accounts. It really is, it's just... Thank you. I don't have the words.
Erin Allmann Updyke	Yes, seriously. Thank you so much. It's... Yeah. We can't thank you enough.
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	Welcome to part two of our three part series on infertility and IVF.
Erin Welsh	Yep, part two. This is where, so if you didn't tune in to our first episode in this series, then in that episode we talked a lot about infertility basically, concepts of infertility, how you can define it, how it has changed throughout time, different perceptions of infertility. And then what happens if you go in for like fertility testing. What are the type of tests? What are they going to be looking for? How can we categorize infertility in the broadest and most non broad way possibles... Like non broad way, that's a very confusing thing to say. And like broad and narrow definitions, how about that? Really just like the full gamut of things. And then in today's episode we are going to be talking about IVF. And so of course infertility is just one of the things that IVF is used for often as a treatment. But it's not the only thing. And so really we're just going to approach this from like hey, how did it get developed? How does it work? What does a typical cycle of IVF entail? And so on.
Erin Allmann Updyke	If you haven't listened to our first part, you don't have to to get through this episode-
Erin Welsh	Yeah.
Erin Allmann Updyke	But you should, it's a really great episode.
Erin Welsh	Yeah.

Erin Allmann Updyke	And if you're looking for context and you're really like where's the context? It's there. It's in that episode.
Erin Welsh	Yeah. It is, it is. And also in that first episode is where we shared the quarantini for this three parter.
Erin Allmann Updyke	We sure did.
Erin Welsh	Which was A Work of Art. It's such a great name. And so if you want to know the recipe for that, check our socials or tune into that first episode or check our website, which is also where you can find all kinds of stuff. Erin, take us through it.
Erin Allmann Updyke	You can find the sources from all of our episodes, you can find a link to our Goodreads list, you can find Bloodmobile who does our music, you can find our bookshop.org affiliate account, you can find our incredible merch. Do you have it yet? Can you get your hands on it?
Erin Welsh	Oh yes!
Erin Allmann Updyke	It's so good. You can find transcripts from all of our episodes which are apparently also now available on Apple podcasts. That's so exciting. There's a lot there. Thispodcastwillkillyou.com. Check it out.
Erin Welsh	Check it out. Should we just start again?
Erin Allmann Updyke	I really feel like we should-
Erin Welsh	Okay.
Erin Allmann Updyke	Because I'm super excited to learn about the history of how IVF was developed because I know nothing, Erin.
Erin Welsh	I mean I know a little bit more than nothing. So let me tell you-
Erin Allmann Updyke	Give yourself credit!
Erin Welsh	We'll see. Right after this break I will get into it.
TPWKY	(transition theme)
Anonymous	We were a little older than I would say many people are when they decide they want to start trying for a baby. And I had done one of those at home fertility tests a couple years prior and found out that my ovarian reserves were lower than average for my age. So when my husband and I started trying to get pregnant, I figured it would take a couple of months and we'd nail it eventually. I was also very fortunate that at the time I was working at a company that offered significant fertility treatment benefits. So after six months and no pregnancy, I was able to schedule an appointment with our preferred fertility clinic where they ordered a barrage of tests for me and my husband. We found out at that time that not only are my ovarian reserves low but that my husband's sperm count and sperm motility are really low as well. Essentially doctors gave us a 1% chance of conceiving naturally.

	The first IVF round we did, the doctors put me on the Cadillac of treatment. They gave me a strict schedule of a high dose of drugs, trying as hard as they could to get my ovaries to produce enough mature eggs for retrieval, fertilization, and implantation. Unfortunately even with all that medication, my ovaries produced only three eggs for retrieval and only two of them were mature enough to be fertilized and only one of those embryos made it to day three after fertilization. So they scheduled my embryo implantation that day to give the fertilized egg the best shot at growing and attaching in my uterus since we had no backup eggs or embryos that could be frozen. That embryo resulted in a chemical pregnancy. Where it had attached, I got a positive early pregnancy test and then it was lost.
	We tried another round of IVF a couple months later, this time with far less medication since the doctors figured I'd only produce three eggs regardless. And this time my ovaries produced only one egg, resulting in a canceled retrieval and a failed IVF cycle. My husband and I decided to stop IVF at that time and are now determining if we want to go any other routes to grow our family. The whole time I knew our chances were maybe slim but going through the process ourselves and seeing the actual stats, percentages, and chances to get pregnant, keep a pregnancy, and then deliver a baby were wild. In a world that told me how easy it was to get pregnant, turns out it is actually pretty difficult for some people.
Adrienne	Hi, I'm Adrienne. One thing that needs more discourse is the complex miasma of emotions IVF creates. For example, I felt torn about sending this in because so many people struggle with IVF and my husband and I were incredibly lucky. We had six genetically normal embryos and went two for two with successful transfers. It's a miracle. But I don't feel comfortable talking to other people who did IVF because so many times their experience was so much harder than mine that I feel I should just shut up. But at the same time I can't talk to anyone who conceived naturally because they do not understand the stress and darkness that comes with IVF, the pain of watching everyone around you get pregnant, the oppressive anxiety of 'will it work this time?', the constant needles, doctors, meds, and having to juggle work at the same time.
	I'm a wildly successful example of IVF and it was still one of the most difficult times in my life, not to mention the special hell it is trying to get pregnant by committee. I had a transfer canceled and postponed indefinitely because of a hurricane and I had to go to a different clinic. This meant months went by, more paperwork, and I had to do all the medical tests again. That's not something people who conceive naturally have to give a second thought about. In short, IVF sucks. And it's a miracle that I'm thankful for every day.
TPWKY	(transition theme)
Erin Welsh	In part one of this series I explored infertility throughout history, how people wrote about it, who wrote about it, what explanations did people come up with? And I ended up just like summarizing the entire 20th century by saying like as our scientific and medical understanding of infertility and fertility grew, infertility began to be increasingly seen as a thing for science to overcome. First with surgeries, hormonal regulation, especially as our understanding of endocrinology grew in the early 20th century, artificial insemination, and ultimately leading to IVF and the first IVF babies born in 1978. Today I want to get into that journey to IVF by talking about how this technology was developed, the foundational research that made it possible, and what happened when this pie in the sky idea became reality.
Erin Allmann Updyke	Yes.
Erin Welsh	Framing it that way makes it kind of sound like developing IVF to treat infertility was the goal all along, like all roads lead IVF. But that really wasn't the case.
Erin Allmann Updyke	Huh.

Erin Welsh	Much of this research came out of a desire to understand how human reproduction worked, including IVF and the applications including using IVF for reasons other than infertility which is a big part of IVF. These applications kind of arose later on. And it's just something I want to put out there because I feel like we tend to think of IVF as like 'and this has been the end goal' and 'this is the thing that IVF is used for' and that is really an oversimplification, it's leaving a lot of the story out.
Erin Allmann Updyke	Interesting.
Erin Welsh	Yeah. It's because we're doing this episode out of our usual order, I don't get to benefit from having the biology of IVF already so thoroughly explained by you, Erin. And so I know that we'll get there later on in the episode. But for the purposes of the history section today, I'm gonna lay out the steps of IVF in the most basic way that I could think of. At the core of it, IVF, in vitro fertilization; in vitro meaning 'in glass outside of the organism', it consists of four basic steps. Number one, retrieving an egg or multiple eggs. Number two, fertilizing that egg with sperm. Number three, culturing the fertilized egg for a while until it turns into a cluster of cells called a blastocyst. And number four, transferring the blastocyst or blastocysts into a uterus where it will hopefully implant and develop into an embryo, a fetus, and then ultimately a baby.
Erin Allmann Updyke	Yeah. 100%. We'll get into so much more detail later on. But that's a good basic.
Erin Welsh	So these are the basic steps that scientists and clinicians had to figure out in order to get to 1978. Which makes it sound like a whole lot simpler than it actually is because it is so complex.
Erin Allmann Updyke	I also feel like it sounds so hard.
Erin Welsh	I know it does. But it's like here are these four basic steps, just figure this out.
Erin Allmann Updyke	Right.
Erin Welsh	Just retrieve an egg.
Erin Allmann Updyke	How do you do that?
Erin Welsh	Fertilize the egg with sperm. That took a lot. Culturing, all of these things took a long time to figure out. And it was really decades, decades of work, of trial and error, of collaboration between scientists and physicians, and of really courageous participation by so many volunteers and patients to get all of these kinks worked out in this process, which like also they're not fully worked out but even still, even in 1978, or especially in 1978, there was no certainty that this would become a standard treatment and an industry or this industry that it has grown into.
Erin Allmann Updyke	Yeah.
Erin Welsh	And it also took a detailed and thorough understanding of human reproduction, not just the role of major organs like the uterus or ovaries but also at the cellular level, at the hormonal level, at the genetic level, and how these things work together to lead to the development of embryos into fetuses into infants. It's incredible.
Erin Allmann Updyke	It's really cool.

Erin Welsh	By the middle of the 19th century, studies in anatomy and physiology started to shed light on how the reproductive system worked. But this was mostly at the organ level with things visible to the naked eye. Scientists had known about eggs and sperm since the 1670s but it took another 150 years for people to understand how the two work together. Was the sperm just food for the egg? Was the egg passive? That was actually thought at one point which is kind of cool.
Erin Allmann Updyke	Fascinating.
Erin Welsh	Yeah.
Erin Allmann Updyke	Munch, munch, munch. Like a little Pac-Man.
Erin Welsh	Yes, yes. Was the egg just passive, fertile soil in which the seed is planted? The 19th century clarified things in part with Gregor Mendel and others showing that parents contribute equal heritable material to offspring.
Erin Allmann Updyke	Wow. I don't think that I ever thought about people knowing that eggs and sperm exist before they knew about DNA and chromosomes. Oh wow, that is so interesting!
Erin Welsh	Right? Because it's like how are these things put together?
Erin Allmann Updyke	Oh that is so incredibly fascinating to think about, Erin.
Erin Welsh	It's amazing. But even still the nitty gritty of mammalian reproduction was largely a mystery since fertilization and implantation and development all happened internally, out of sight.
Erin Allmann Updyke	Yeah. You can't watch it.
Erin Welsh	Whereas a lot of the other research was done with reptiles, for instance.
Erin Allmann Updyke	Yeah.
Erin Welsh	Researchers like Walter Heep and Albert Brachet didn't let that stop them though. In 1891 Heep transferred rabbit embryos from one rabbit to another and that rabbit became pregnant and delivered baby rabbits or kits, as I learned that they're called.
Erin Allmann Updyke	How cute. It's very cute.
Erin Welsh	Very cute. Cool but not in vitro fertilization. A few decades later in 1913, Albert Brachet was the first to successfully culture mammalian blastocysts before implantation. Also cool. Still not in vitro fertilization. Things were moving steadily but slowly. In the first few decades of the 20th century, the field of reproductive biology seemed to attract more interest from science fiction enthusiasts than it did from biologists. The public seemed particularly interested in the idea of ectogenesis, so fertilization and just station completely outside the body.
Erin Allmann Updyke	Brave New World'.

Erin Welsh	Exactly. That's my next line. In 1932 Aldous Huxley published 'Brave New World' and this book opens with a description of the Central London Hatchery and Conditioning Center, which is basically a baby factory complete with artificial wombs. And I know, like I'm sure how many times have you seen 'Brave New World' mentioned in papers about IVF?
Erin Allmann Updyke	Yeah, yeah.
Erin Welsh	Every single one.
Erin Allmann Updyke	Right.
Erin Welsh	You can't...
Erin Allmann Updyke	Well not every one that I read but I could see it.
Erin Welsh	Okay. Yes. It is persistent. And Aldous Huxley probably got this idea from conversations with his brother Julian, who was a scientist, and Gregory Pincus, who was an endocrinologist that helped to create the first oral contraceptive pill and also did a lot of work, really important work on IVF and rabbits.
Erin Allmann Updyke	Wow.
Erin Welsh	I'll talk a little bit more about him. Yeah. The popularity of 'Brave New World' reflected this growing sense of disillusionment with technology. People no longer believed as they had at the turn of the century that technology would solve all of life's woes. War and economic downturn had tipped the scales from assisted reproductive technologies being perceived as part of like a utopian future to these technologies being a sign of our ultimate downfall. And maybe that's dramatic but maybe not because consider what happened to Gregory Pincus. So Pincus was appointed Assistant Professor of Biology at Harvard in 1931 where he did research on in vitro fertilization in rabbits and studied the hormonal changes that lead to one mature egg being released each month. In 1936, his work and his claim that he and colleague E. V. Enzmann were the first to successfully demonstrate IVF and rabbits, that claim was later challenged by people who couldn't replicate it. I'm not sure, it's.... Yeah. There's a lot of claims and a lot of skepticism throughout this whole history.
	But his work, Pincus's work drew the attention of the popular press, mostly falling somewhere between speculative and negative reaction-wise. Some journalists imagined a world where human children would be brought into the world by a host mother, not related by blood to the child. Eventually leading down the slippery slope of eugenics where quote "advocates of race betterment might urge such procedures for men and women of special aptitudes, physical, mental, or spiritual." End quote. Others warned what would happen to the men if the science were applied to humans. Quote: "In the resulting world, man's value would shrink. It is conceivable that the process would not even produce males. The mythical land of the Amazons would then come to life, a world where women would be self sufficient. Man's value, precisely zero." End quote.
Erin Allmann Updyke	That is so telling, Erin. Wow.
Erin Welsh	Isn't it?
Erin Allmann Updyke	That is so telling. Wow.

Erin Welsh	Yeah.
Erin Allmann Updyke	IVF will create the world of the Amazons.
Erin Welsh	Where women are self sufficient and so men's value is zero. It's I mean-
Erin Allmann Updyke	Again, there's so many layers here, so many layers.
Erin Welsh	So many layers. So many. And Pincus himself wasn't interested in these broader implications of the research that he was conducting. He just wanted to do his experiments and like learn more. But that didn't matter, the negative press was enough to get him denied tenure at Harvard and let go.
Erin Allmann Updyke	Wow.
Erin Welsh	And that wasn't the end for IVF or for Gregory Pincus who would go on to help create the birth control pill along with the next name in our IVF story, John Rock, a gynecologist at the Free Hospital for Women Boston and Harvard Medical School. Rock had come across the rabbit IVF paper by Pincus and became fascinated, so much so that he decided to work on IVF. He teamed up with Miriam Menkin who had been a research assistant working on hormones with Pincus at Harvard before he was kicked out.
Erin Allmann Updyke	Okay.
Erin Welsh	And I just kind of love that. And also her story is really interesting and definitely at least go to her Wikipedia page and check it out. But the third member of their team was pathologist Arthur Hertig. And together these three performed groundbreaking research in reproductive biology in three big areas. The first area was capturing the timing of ovulation, which would prove to be super helpful in IVF later on for egg retrieval but also for artificial insemination which began to be more popular around this time. And the second area was in describing the early stages of human embryonic development, which they did at a time when really no one knew how anything worked, before even the development of the ultrasound.
Erin Allmann Updyke	Wow.
Erin Welsh	Which is wild. And the third was in the fertilization of human eggs outside of the body. And so to do this they enlisted the help of women who were set to undergo hysterectomies and they performed the surgeries just before the volunteers ovulated so that they could extract as many eggs as possible. And after getting the donated tissue, Menkin would run, like literally run up and down flights of stairs over to the lab where she would begin trying to fertilize these eggs outside of the body in vitro. But after years and over 130 eggs exposed to sperm out of the 800 they collected, nothing seemed to work. And then one day in 1944, exhausted from staying up late with her baby, Menkin only washed the sperm once as opposed to the usual three times. And later she returned to see that the egg had divided into two cells.
	And they repeated this a couple more times with the revised protocol with fewer washes and took pictures. And I feel obligated to include this, like this is a 'well actually' that I'm going to throw in here, there does seem to be some debate on whether that actually represented fertilization since people later realized that freshly ejaculated sperm actually needs to spend a period of time in the genital tract before they're ready for fertilization in a process called capacitation. I'm not really clear on this but some people have been like okay, maybe the egg just divided without being fertilized, which also has been known to happen or seen to happen. But yeah.

Erin Allmann Updyke	Okay.
Erin Welsh	I don't know. That's like my little pedantic 'well actually'.
Erin Allmann Updyke	We all have them.
Erin Welsh	Yeah. We do, we do. But in any case, this was huge news all over the news outlets, just like global headlines. Rock immediately saw the potential application of IVF for treatment of infertility and as did all of these news outlets. And he and Menkin received dozens of letters from women all over hopeful that they could use this new technology to help them have children. Rock personally replied to many of these letters with cautious optimism and was like maybe someday, we're not quite there yet. But he also like took the time to explain the science and I just appreciate that. I don't know. And by and large, the public response to this announcement seemed positive. The war had just ended, and this is also like primarily US-specific but like the war had just ended, the economy was booming, pronatalism was in full force, and IVF was going to solve the problem of involuntary childlessness. Over the next couple of decades, things were kind of quiet on the human side of IVF. But some researchers were exploring the technique in other animals. And in 1959 Dr. Min Chueh Chang successfully used IVF in a rabbit to produce kits.
Erin Allmann Updyke	1959!
Erin Welsh	1959. The enthusiasm for IVF in humans began to die down by the end of the 1960s in part due to a lack of progress, in part due to rejection of technology sort of across the board, and in part due to a decline in prenatalism. But that happens to be when significant progress on the technique began to be made. In 1973 and 1975, researchers reported the first IVF pregnancies, although they only lasted a few days. And the first IVF babies were just around the corner. Robert Edwards, Patrick Steptoe, and Jean Purdy formed a powerful IVF team in England that had spent a good deal of the 1970s working on this technique, leading to a chemical pregnancy in 1975 that turned out to be ectopic. But this heartbreaking result did show them that they were on the right path. And a few years and a few tweaks to the protocol later and they tried out their new method on a few people at their clinic. Nine months later on July 25th, 1978, the second person they tried this out on, Lesley Brown, gave birth to Louise Brown.
Erin Allmann Updyke	Wow.
Erin Welsh	The world's first IVF baby.
Erin Allmann Updyke	That is very cool.
Erin Welsh	It's amazing.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah. And Louise's birth was like a total media circus.
Erin Allmann Updyke	Oh I bet.
Erin Welsh	I mean Lesley had to constantly move houses and hospitals, there was a bomb scare to the hospital to try to get a picture of her. People would dress up as window cleaners to try to find out which room she was in and get a picture for the papers.

Erin Allmann Updyke	Oh my god.
Erin Welsh	And the cesarean was filmed to show that Lesley had no fallopian tubes in anticipation of people doubting that it was actually IVF.
Erin Allmann Updyke	Wow.
Erin Welsh	Wow.
Erin Allmann Updyke	Also did they do a cesarean just because of that? That might be more detail.
Erin Welsh	I don't know.
Erin Allmann Updyke	That's fascinating.
Erin Welsh	I don't know. Yeah. Amazing though.
Erin Allmann Updyke	Wow.
Erin Welsh	And in 2010, Robert Edwards was awarded a Nobel Prize for his work, Steptoe and Purdy had both died and it's not awarded posthumously. Only 10 weeks after Louise Brown was born, Kanupriya Agarwal was born in India. The second "test tube baby" quote unquote as they began to be called. Led by a team consisting of Subhash Mukherjee, Sunit Mukherji, and Saroj Kanti Bhattacharya. Whereas Steptoe, Edwards, and Purdy relied on natural cycles of ovulation, the team in India used drugs to induce ovulation and then froze the embryo before implanting it.
Erin Allmann Updyke	Wow.
Erin Welsh	Which I think is so interesting to see these different methodologies-
Erin Allmann Updyke	Yeah.
Erin Welsh	And how like which clinic uses what? And I don't know, I guess you'll talk about sort of what are the different pros and cons but many different ways to get a result I think.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah. So you don't always see this birth mentioned in histories of IVF because almost immediately after it was met with skepticism. It was described as a fluke, as experimental, and likely to be a standalone. And this reaction might have been because the Indian team allegedly carried out the work somewhat secretively and without formal approval. But it wasn't a fluke or fraudulent. That didn't matter though to the institutions where Subhash Mukherjee, who was the team leader, worked. Mukherjee was sent to an ophthalmology institute where he couldn't do any work. But it was just as a way to be like we're preventing you from doing any of the work that you actually want to do.
Erin Allmann Updyke	Wow.

Erin Welsh

He was forbidden to present his IVF research or participate in conferences. And in July of 1981 he took his own life.

Erin Allmann Updyke

Oh my god.

Erin Welsh

Yeah. Isn't that awful?

Erin Allmann Updyke

It's awful.

Erin Welsh

Awful. The 1978 birth of Kanupriya Agarwal was really only recognized in 1997, I read, and so it's still sort of making its way into these global histories of IVF. After these two 1978 births, several more followed. The first Australian IVF birth was in 1980 and the next year, 1981, the first American IVF baby was born. But even with these births, IVF was by no means a sure thing technologically speaking, financially speaking, and in terms of regulation. The news of these first IVF babies was met with a lot of feelings, some very pro, some very anti, but rarely indifferent. The potential that IVF held good, bad, other, was and is tremendous. And we'll get into some of these things next week. But I want to wrap up today's history section with a brief look at when IVF came to the US and how that set a precedent for IVF becoming a mostly private, pay for services institution, a market driven enterprise for better or worse.

After the birth of Louise Brown and the other early IVF babies, the US realized that IVF might be here to stay. And so they began to call for congressional hearings to discuss the implications of IVF and policies for how treatment and research should be regulated. Should IVF research or research involving embryos be allowed to receive federal funds? That question has been debated for years and there is currently a ban on federal funding for research involving embryos in the US. But for quite a long period of time it was anticipated that it would be allowed. And to clarify, the research is still allowed to be conducted, it's just that it can't be federally funded, the funding has to come from other sources. Just throwing that out there.

In the late 1970s when it was looking like federal funds would be approved, two researchers/clinicians and married couple Georgeanna Seegar Jones and Howard Jones left Johns Hopkins University for Eastern Virginia Medical School where they could pursue IVF research. Their story is actually really cute and it goes back like really far and there are like cute letters during the war. Anyway, Georgeanna was a pioneering, highly accomplished reproductive endocrinologist and her husband Howard trained as a general surgeon and then specialized in gynecology so that he could work closely with his wife. And for years they worked together sharing a lab, an office, even a desk. And Robert Edwards from the England IVF team actually trained with them for a while. But not being willing to wait for federal funding for IVF to be approved, they would still have been waiting, they decided that this technique was enough in demand that they could seek private funds and charge for services.

In 1981 the first IVF baby in the US was born from their clinic. Each couple had to meet the following criteria: youth under 35, good health, bad fallopian tubes, a husband, and the unspoken one was that you had to have money. Each couple had to shell out around $4000 in 1980 dollars or $15,000 in today's dollars. But the cost didn't keep people from flocking to the clinic. Other IVF programs in the US followed shortly, the first primarily at medical schools then in community hospitals in partnership with private infertility practices and finally in independent centers. Despite urging from the American Fertility Society to come up with federal guidelines and oversight for these clinics, progress was slow. The most they could do, like the society, was establish a subgroup, the Society for Assisted Reproductive Technology and require clinics to follow particular standards if they wanted to be SART members.

But there is no way to enforce these guidelines and the number of clinics grew steadily, in part because of the appeal of no strict regulation or really no regulation. The introduction of the vaginal ultrasound probe made things easier for IVF, which required only local anesthesia and meant a surgeon and operating room were no longer required. And this marked the end of many relationships between private IVF clinics and academic medical centers in the US. And it enabled even more growth which led to, among other things, improvements in technique and application for IVF. So people not just with tubal factor infertility but also endometriosis, unexplained infertility, male factor infertility, genetic conditions, same sex couples, single parents, and so much more.

Age restrictions began to be raised, intracytoplasmic sperm injection was introduced, ICSI, as was egg and embryo freezing. And many clinics began to incorporate donor eggs and embryos and gestational and traditional surrogacy. IVF was bringing more and more people the children they had always wanted. And as the number of clinics grew globally, as technological advancements were made, more questions were being asked about the financials of IVF, about access, about ethics, about transparency from clinics, about what the future could hold. And that's what we'll be getting into next week. But for now, Erin, I'll hand it over to you to tell us all about how IVF works.

Erin Allmann Updyke

Excellent. I can't wait to kind of go over what it looks like today just after this break.

TPWKY

(transition theme)

Johanna

Hi, my name is Johanna and in February of 2023 I gave birth to our daughter who was conceived with intrauterine insemination using donor sperm. When my partner and I first talked about getting pregnant, we had to do a lot of Googling, a lot of reading, and a lot of talking to our fertility specialist to figure out what our options are for a same sex couple and how the logistics of it all work, the ins and outs of getting the sperm, genetic testing, and the different ways of getting the sperms inside of my uterus. So we wound up going with intrauterine insemination which is really just inserting the sperm through the cervix with a long needle directly into the uterus. The chances of pregnancy are slightly higher than with just intercourse but not super high. So that's usually the first step. And then if that doesn't work after a few cycles, the next step would be using medication to boost fertility. And then after that is IVF, in vitro fertilization.

So we did all of the prep stuff. We did genetic testing, we bought sperm off a sperm bank and we also did genetic counseling which is required because they just want to kind of gauge how you would deal with having a donor-conceived child, how you would talk about that with friends and family, and of course most importantly how you would talk about that with your child. So after all of that prep work was done, I've been charting my cycles and tracking my ovulation and then once it was regular, I alerted the fertility clinic when I was ovulating. And we got the sperm transported from the storage facility to the fertility clinic and I went in for my first insemination. The first one didn't take. So we did a second one, the next cycle. And that one did take and I became pregnant.

So the first few weeks they monitored my pregnancy at the fertility clinic, they did a couple of tests to confirm, they did the first ultrasound there. And then I was released into regular prenatal care with my regular OB/GYN. And I wound up having a great pregnancy and giving birth to an amazing baby. Our daughter is 15 months now and she is absolutely the best. And I am so glad and so grateful for all of the support that we had and for the fact that we have that option and that that was something that we were able to do to have our baby. And to live in a state where most people are supportive and understanding and where we didn't have to fight very hard to make this a reality for us. It's been a really amazing experience and I'm really proud to be part of the IUI community of having used assistive reproductive technology and having had the chance to have that in my life to help bring our child.

Lillian	My name is Lillian and I'm an IVF long hauler. My husband and I started trying to conceive in 2017 soon after I turned 32. After two miscarriages, we began IVF treatment in 2018 after I was diagnosed with diminished ovarian reserve. We've done 11 IVF retrieval cycles to bank embryos, four retrievals in 2019, three in 2020, and four in 2022; and two frozen embryo transfers, one in 2019 and one in 2023. We've experienced a total of seven pregnancy losses through unassisted spontaneous conceptions and frozen embryo transfers including the 17 week fetal demise of our daughter conceived through IVF tank in March 2020 have had no live births.
	Throughout the years of IVF treatments and multiple surgeries, I was diagnosed with endometriosis, suspected adenomyosis, gestational trophoblastic disease, autoimmune disease that attacks my reproductive organs and pregnancies, and Asherman syndrome following multiple miscarriages. We've completed IVF with three different clinics, two conventional clinics and one specialty clinic that uses mini IVF, both in and out of state; worked with a reproductive immunologist out of state and consulted with almost a dozen reproductive endocrinologists specializing in recurrent pregnancy loss and endometriosis across the country. However despite pursuing every evidence-based treatment and a few not so evidence-based, my body is unable to sustain a pregnancy to term and live birth, even with the perceived quote "guarantee" of IVF resulting in a live baby.
	A critical factor in our pursuit of IVF was having insurance coverage, which made a huge difference in our treatment options because we weren't limited to what we could afford at the time. Since most of our IVF was covered by insurance, we didn't deplete our savings then which allows us to now pursue gestational surrogacy following the suggestions of our physicians and the limits my husband and I agreed we'd reached, which we called our heartbreak tolerance. We are grateful for the opportunity to try to have a biological child through IVF with gestational surrogacy and we grieve everything we've been through. There aren't many stories from long haulers who've suffered multiple miscarriages like myself for whom IVF doesn't end with a live baby because our stories are sad. But we do exist.
TPWKY	(transition theme)
Erin Allmann Updyke	So you walked us through, Erin, four main steps of IVF or at least four main things that had to be figured out to be able to do IVF. So I'm going to break it down into five. Just to make it a little bit more confusing.
Erin Welsh	Just a little more extra.
Erin Allmann Updyke	Honestly some of the sources that I read broke it up into nine steps and I'm like that's not wrong, it's just like let's chill with the detail. Okay?
Erin Welsh	I mean it's all a balance, right?
Erin Allmann Updyke	It's all... We're going to conflate some. Okay. Well let's keep going, shall we? This is going to be kind of the main procedure of ART in general, ART in general. And again, I mentioned this in the last episode, but ART is anything where eggs and embryos are being handled outside of the human bod. So this includes IVF, it includes IVF with ICSI or that intracytoplasmic sperm injection. It also even includes things like egg and embryo freezing, even without the in vitro fertilization part of it. And again, those other less common procedures that people don't do as much anymore today. So how do the steps of this work? Because the steps for all of these different procedures start out in many cases the same. And I caveat this as of course each cycle of IVF is going to be very individualized, so these are just like broad overview steps. But step one, and this is the step, Erin, that didn't happen in your cycle I guess; in your description.

Erin Welsh	Oh okay.
Erin Allmann Updyke	And that's because it didn't always happen, though it pretty much always happens today. But step one is to overstimulate your ovaries to produce a whole ton of eggs.
Erin Welsh	Right.
Erin Allmann Updyke	So typically we produce and ovulate only one egg per menstrual cycle, sometimes two. And multiple eggs do start to develop during each menstrual cycle but typically only one kind of comes all the way to the point of being ovulated. But for IVF to have a real chance at being successful, you have to boost this number in large part because there is attrition at every step in this cycle. So that process of overstimulation involves often a lot of needles but definitely a lot of hormones. This is one of the first places where there's going to be a huge variety of variation in what the specifics of each algorithm are going to be, like the specific drugs that are going to be used is going to be very person and patient and doctor specific. So I'm not going to get into all of that.
	But all of these are doing the same basic thing, all of these various hormones, and there's a number of different options that you can use, trick your body into readying for ovulation a whole bunch of eggs at once. And this process often starts the month before in order to get your body ready to next month start this process of inducing a whole bunch of eggs to be ready for ovulation. That whole process often takes about two weeks but again, it starts before, like the month before. So we're talking already like a multiple week process. And then we get to step two and that is taking the eggs out.
Erin Welsh	Yeah.
Erin Allmann Updyke	So egg removal usually starts with yet another hormone injection the day or so before the egg removal process. And that's to help the eggs mature at the correct rate to be ready for aspiration. And the aspiration process takes place in usually a doctor's office or at a hospital under ultrasound guidance, which you mentioned, Erin, where they take an ultrasound and a very long needle, hopefully under mild IV sedation though not always. And they use that to-
Erin Welsh	Not always?
Erin Allmann Updyke	Not always. It is standard practice to do IV sedation but I think in some cases either for patient preference or for a number of reasons they might not and they might use a regional anesthesia or something like that.
Erin Welsh	Okay.
Erin Allmann Updyke	Yeah. But they use this really long needle to, through the back of the vaginal wall, aspirate out as many of those ripe and ready eggs as possible. While this is happening, step three potentially, your sperm donor or your partner is leaving their sperm sample or it is being defrosted from the freezer. These sperm have to then be washed and checked to pick the healthiest sperm; to pick the ones most likely to be able to fertilize the egg. And then comes the in vitro part, step four. The eggs and the sperm unite. And this process can go one of two ways. So traditional IVF throws all of the sperm in with all of the eggs and the sperm are going to fertilize the eggs in a similar way that they would in the reproductive tract. Or there's ICSI, intracytoplasmic sperm injection, which is fascinating and exactly what it sounds like. It's injecting, using a very, very, very tiny needle, one single sperm directly into the egg.

	And then that fertilized egg is grown in culture for between 3-5 days until it reaches either the cleavage stage or the blastocyst stage. And the final step, step five, is that this blastocyst is transferred back into the uterus via a long catheter tube that goes up through the cervix towards the top of the uterus and is deposited there, either one or a number of blastocysts. Most people then still need to keep taking some form of hormone, either injections or oral medications for the first few days or weeks of that potential pregnancy to try and get it to stick. This is especially true in using frozen embryo cycles because you haven't just ovulated and so you have no corpus luteum of which to speak, which is the hormone producing part of your ovary. That's IVF in a very small nutshell. And shout out to Penn Medicine's patient facing website because I thought that that was the most comprehensive but detailed breakdown of IVF that I found on a patient facing website.
Erin Welsh	I have a couple questions, if I may.
Erin Allmann Updyke	Okay, give it to me.
Erin Welsh	Okay. Picking the sperm. What differentiates one sperm from another? Like you said pick the good sperm or whatever you said, the highest quality.
Erin Allmann Updyke	Yeah. So that's a good question. It's mostly based on morphology. And so it's looking at the sperm under very high powered microscopes. And there are other techniques, like more advanced techniques that people might be piloting or that can be used in some cases. But in general it's looking at the morphology of the sperm and that's how you make your decision.
Erin Welsh	Okay.
Erin Allmann Updyke	On which sperm to pick.
Erin Welsh	Okay. All right. So let's timeline this. So you go in for fertility testing, you decide IVF is the next step, IVF either with or without ICSI. You get seen by someone, hopefully not like six months later, although I know that-
Erin Allmann Updyke	Probably six months later but anyways.
Erin Welsh	Anyways. You get seen by someone who starts this process, you start taking hormones. So you mentioned that it's like a few weeks of hormones for stimulation and then egg retrieval and then what is the time like? What is a typical cycle timeline?
Erin Allmann Updyke	Yeah. A lot of times it's cited that a typical cycle length of IVF is about six weeks.
Erin Welsh	Okay.
Erin Allmann Updyke	But like you just mentioned, that doesn't account for all of the other time. But that is typically about the length of one typical cycle. And again, it might vary depending on what protocol you're using, there's like longer protocols and there's shorter protocols. Because it all depends on what the side effects and things that you're trying to manage really are.
Erin Welsh	How many blastocysts?
Erin Allmann Updyke	How many blastocysts at what stage?

Erin Welsh	Okay, good question. The transfer stage.
Erin Allmann Updyke	Yeah. That is a loaded question. So historically multiple blastocysts were transferred almost always with IVF. And that's because I mentioned that there is attrition at every stage of the IVF process. And there really is. In fact, about 10% of IVF cycles are stopped before you even get to egg retrieval. And then you'll get X number of eggs, some percent of those eggs won't be fertilized for one reason or another. And then some percentage of those fertilized eggs won't make it all the way to the blastocyst stage especially. And some of those blastocysts won't manage to implant or therefore won't cause a pregnancy. So to kind of help counteract that, especially historically, kind of actually before we got to blastocyst stage culture because it used to be more common that IVF happened at day three which is when you're still in what's called the cleavage stage. Then multiple blastocysts would be transferred during that IVF process.
	Today what's called single embryo transfer is actually a lot more common. And in some places it's like the recommended if not required thing to do. And that's because the risk of multiple pregnancies is significantly higher than the risk of a singleton pregnancy, that is twin or triplet pregnancies are significantly higher risk than a singleton pregnancy. So in some cases, single embryo transfer has become the kind of norm in most places. But it all just depends on the situation because you can also imagine especially in maybe an older couple who only has either a certain amount of money left to be able to do more transfers because each transfer costs money or who only has a certain amount of time or a certain number of embryos that are left, then they might opt for a multiple embryo transfer. So there's kind of a lot, there's a lot that goes into that decision of how many embryos to transfer. The lowest risk in terms of birth risk and risk of the pregnancy is going to be a single embryo transfer. But with multiple embryos, you might have a greater chance at a live birth.
Erin Welsh	Okay.
Erin Allmann Updyke	I also just wanna... This is a little bit pedantic but I mean we're us.
Erin Welsh	There's a lot of that going around, it's okay.
Erin Allmann Updyke	Yeah. IVF terminology pretty much universally refers to this process as embryo transfer and that's fine, that has become the kind of norm. It's not accurate though. And I do feel like especially as politicians start making decisions about what they think constitutes a person and who does not constitute a person, it's kind of important to point out that in this process, what we are talking about is a clump of cells that has been growing for 5-6 days in culture media. This particular stage of development is fascinating. It's one cell layer thick that forms about a ball that has a fluid-filled portion and then one section of it that's about 3-4 cell layers thick. So in total, we're talking about 200 or so cells. And this little part of the blastocyst that's 3-4 cell layers thick, that is what will become an embryo upon implantation in the uterus. There's a number of steps that have to happen, usually around days 9-10 is when it is then becoming an embryo which will then eventually develop into a fetus and then eventually a baby. And so I do think that these terms are kind of important because they help us conceptualize what we're really talking about.
Erin Welsh	Absolutely.
Erin Allmann Updyke	So I just want to point that out. But I'll probably say embryo transfer because that's what literally all the literature says.

Erin Welsh	It's what all the literature says. But I think I was surprised, and I'm going to talk about this a little bit next episode but not very much, but that globally the definition of embryo varies quite a bit.
Erin Allmann Updyke	That's interesting.
Erin Welsh	Right? So I believe it is Spain that an embryo, it's only an embryo if it is implanted in the uterus. The uterus is an essential part of that terminology. Whereas I think that's not necessarily the case in a lot of other places or at least in casual usage. Yeah.
Erin Allmann Updyke	Interesting. Right. Yeah. It's kind of that difference in casual uses vs strict scientific usage. But I just feel like it's important to point out. So yeah. So that's the main process of IVF. And I think you can lay it out and make it sound like well it's not that big of a deal. It's a huge deal.
Erin Welsh	It's a huge deal.
Erin Allmann Updyke	It's a huge process, it's a long process, and there are so many steps in which it can go poorly. And there are some really important risks that I think that we have to talk about with IVF, not just with IVF the process but also with an IVF pregnancy. So there are risks associated with the surgical procedures involved in IVF, like the aspiration and potentially the embryo transfer as well. These risks are the kinds of risks associated with any surgical procedure, things like bleeding or infection or injury. These risks exist, they tend to be very small. The other major risk of IVF as a process is something called ovarian hyperstimulation syndrome or OHSS. The risk I see cited usually as between 1-5% but it really can vary. But this is a life threatening complication of that initial process of stimulating the ovaries to make a whole bunch of eggs all at once.
Erin Welsh	What happens?
Erin Allmann Updyke	What happens? Yeah.
Erin Welsh	Yeah.
Erin Allmann Updyke	So symptom-wise what happens is significant abdominal bloating, ovarian enlargement, ascites which means fluid in the abdomen. And all of these things can result in significant electrolyte imbalances that can then also lead to decreased urine output, kidney failure, and hypercoagulability, respiratory distress. This can be very severe and life threatening. We don't fully understand the exact causes and mechanisms of this. But it's thought that it's a result of the ovary responding to this supraphysiologic doses of hormones signaling ovulation, that what it results in is really large scale vasodilation. So all of your blood vessels dilating and that causes this increased capillary permeability. So basically all your vessels get really wide and then permeable so that fluid can shift from inside of your blood vessels to the outside of your blood vessels. And these fluid shifts are things that happen during pregnancy but in a much different and slower fashion. And so this is something that's happening at a very fast and supraphysiologic rate.
Erin Welsh	Did this happen before IVF or before like stimulating with hormones?
Erin Allmann Updyke	So it's something that is specific to the process of ovarian stimulation.
Erin Welsh	Okay.

Erin Allmann Updyke	So it can happen in other ways but it's totally like an iatrogenic, like we do this to someone by stimulating the ovaries.
Erin Welsh	We do this.
Erin Allmann Updyke	Yeah.
Erin Welsh	Right. It's the 20th century and beyond thing condition.
Erin Allmann Updyke	100%, yeah.
Erin Welsh	Okay, okay, okay. Interesting.
Erin Allmann Updyke	Yeah, 100%. It can be prevented and in some cases some tests can kind of try and help predict who might be at higher risk for ovarian hyperstimulation by looking at things like ovarian reserve and seeing if someone is likely to be a really good responder vs a poor responder. So you can try and predict that and then pick a protocol that puts you at lower risk of hyperstimulation syndrome.
Erin Welsh	And so what happens if you develop this? Like how do you manage it?
Erin Allmann Updyke	Often people have to be hospitalized especially if it's severe, to be really closely monitored, have their fluid balance checked and regulated and things like that. But it kind of just depends on the severity. Almost always what it means is it could mean a cessation of the protocol, so having to stop the IVF at the point that you're at. But almost always what it does mean is that if you were planning on a fresh embryo transfer, so we talked about that whole process of IVF kind of assuming that at the end of it you take those embryos and put them directly into the uterus. But the other option is to freeze them. And so if someone develops ovarian hyperstimulation, then almost certainly they're going to have to have those embryos frozen because they have to have that condition managed before you can go on to then complete the steps of IVF.
Erin Welsh	Okay. Is it too early to ask about rates of all of this or breakdown of rates? I don't even know how to begin to ask these questions.
Erin Allmann Updyke	It's such a good question. And it's funny because I kind of put a lot of that initially in our next episode.
Erin Welsh	Okay.
Erin Allmann Updyke	But I would be happy to talk about it at this episode as well too. But first I want to talk about the risks of IVF pregnancies.
Erin Welsh	Yes, that's right. Sorry.
Erin Allmann Updyke	Because I think that this is something that isn't widely known, is that there are risks inherent to a pregnancy that's conceived with ART or IVF. And we don't fully understand the mechanisms behind this risk. And some of these are still a little bit controversial. So at the outset, pregnancy, and we're going to do a whole series on pregnancy, don't worry. Pregnancy is a very risky state of being.

Erin Welsh	Yes.
Erin Allmann Updyke	It is physiologically incredibly demanding. It's associated with significant morbidity and mortality. It is not a riskless condition. But what's interesting is that it seems that IVF pregnancies are also a bit riskier than spontaneous conception pregnancies as well. Specifically we see in some studies an up to 50% increased risk of hypertensive disorders including preeclampsia and an up to 50% increased risk of gestational diabetes. And these risks seem to differ between frozen embryo transfers compared to fresh embryo transfers. Again, we don't fully understand the mechanisms behind this and it might have something to do with whether or not there is a corpus luteum, like I mentioned, that's in the ovary.
Erin Welsh	Okay.
Erin Allmann Updyke	But we don't really know. There also seems to be an increased risk of abnormal placentation. And that's especially true in fresh embryo cycles. So that means that the placenta is either implanting in a place that's a little bit more risky in the uterus, like overlying the cervix or something like that, or in some cases invading a little bit too far into the uterus than is typical. And those kinds of abnormal placentations can put somebody at higher risk of hemorrhage during delivery or after delivery. And then there also seems to be an increased risk of severe outcomes like stroke or blood clots or ICU admission kind of in the postpartum period, which seemed to be higher in IVF or ART pregnancies compared to spontaneous conception. And that does include after controlling for things like maternal age or comorbidities that might affect those risks.
Erin Welsh	And is it the same for like gestational carriers vs not?
Erin Allmann Updyke	That's a very good question. I didn't see data on that specifically.
Erin Welsh	Okay.
Erin Allmann Updyke	But I would think so because all of the data just looks at IVF in general. But that's a really good question. Just I don't know that we have enough data on that specific subset of IVF.
Erin Welsh	Okay. I have a few more questions about this.
Erin Allmann Updyke	Okay, give it to me.
Erin Welsh	So what is... I'm not asking for specific numbers on all this but like higher risk is relative. Like what is the degree? Is it substantially, twice? Yeah.
Erin Allmann Updyke	It's a good question. I didn't see numbers for especially the later maternal outcomes. I didn't find exact numbers on those. They just say a slightly increased risk.
Erin Welsh	Okay.
Erin Allmann Updyke	For hypertensive disorders and gestational diabetes, we see an up to 50% risk in some of the meta analyses that I looked at. But a lot of the others, they just say like a slightly increased risk. I don't have a good number on it.
Erin Welsh	Okay.

Erin Allmann Updyke	Which is disappointing.
Erin Welsh	One of the things that I'm wondering about is IVF pregnancies I would assume are more closely monitored throughout every step of the way. Does that mean that the likelihood of capturing some of these things is much higher? And so is that accounting possibly for some of these differences in risk?
Erin Allmann Updyke	It's an interesting question. I don't expect so.
Erin Welsh	Okay.
Erin Allmann Updyke	Because these are things that you're going to probably catch at delivery.
Erin Welsh	Okay.
Erin Allmann Updyke	Maybe hopefully you would catch it sooner in the cases of things like hypertensive disorders or gestational diabetes. But yeah, it's an interesting question. They definitely are monitored a lot more closely. But I don't know that that would necessarily result in an increased, like a perceived increased risk that isn't a real risk I guess, if that makes sense.
Erin Welsh	Okay.
Erin Allmann Updyke	And we talked already about the risk of multiple pregnancies as a risk because of multiple blastocyst transfer. But what I also learned is that the rate of monozygotic twins, that is identical twins, is also significantly higher in IVF pregnancies. And I do have numbers on this.
Erin Welsh	Okay.
Erin Allmann Updyke	The baseline rate in spontaneous conception pregnancies of identical twins is 0.4%. It's super low. It's between 2-3% in IVF.
Erin Welsh	Wow.
Erin Allmann Updyke	And we don't know what the mechanism of this is. The thought is maybe... Because in an identical twin pregnancy, what has to happen is that during the development the blastocyst, usually I always thought of it as the zygote, I don't think I even realized it could happen like post-blastocyst stage, but the blastocyst or the zygote prior to that divides into two separate blastocysts or two separate zygotes rather than implanting two genetically different blastocysts. And that's how you end up with identical twins. So we don't know what the mechanism of this is. The thought is maybe it's related to the culture media that's used, maybe it's related to the timing of the transfer. Again, absolute risk still very low but significantly higher than the population level, which I think is so interesting.
Erin Welsh	That's fascinating.
Erin Allmann Updyke	Yeah.
Erin Welsh	That's fascinating.

Erin Allmann Updyke	And so you asked earlier, Erin, what are some rates here? What are some numbers here? I don't have numbers on like the percent of attrition at every stage in this because that is going to vary so much person to person. There's not like a generalizability on what's the chance that if you have X number of eggs or X number of embryos, that you're going to be able to have a live birth? I don't have those numbers. It's going to vary a lot person to person. But there's obviously a huge question of what's the overall success rate? Like if you go through this whole IVF process, what are the chances that you are going to have a baby at the end of it?
Erin Welsh	Right.
Erin Allmann Updyke	We don't have numbers on that either. And it is in part because it's going to vary so much person to person. But it's also in part because it's going to vary so much location to location. And there's some really interesting papers that I read that are looking at like how do we even define what a success rate actually is? Are we talking about what is the live birth rate per cycle? And usually when we say per cycle, we're meaning one embryo transfer.
Erin Welsh	Right.
Erin Allmann Updyke	Or do we mean per retrieval where you might have to do multiple embryo transfers after that one retrieval? And also are we talking about the success rate of first births or if people then are going through IVF to try and have a second child? Are we looking at total births? Are we combining fresh and frozen cycles or are we separating those two out? There's so much nuance. It's almost impossible. And that being said, people cite rates. Most websites, most papers say up to 40% of cycles of IVF will result in a live birth. And that's a huge generalization. And if you look at global numbers, it's actually also a real overestimation because just... We'll talk more about global numbers next episode but what has been reported to the institution, this like large international institution that tries to monitor IVF globally, in 2021 they reported about 3 million cycles of IVF and about 750,000 babies, a little bit more.
Erin Welsh	Okay.
Erin Allmann Updyke	So that Erin math is about 25% as a success rate per cycle. The CDC has a very interesting calculator where you can input your individual data and it'll estimate your probability of a live birth and you can break it down by one, two, or more retrievals and one, two, or more transfers, which I think is really interesting and paints a more realistic picture though it is still going to vary place to place.
Erin Welsh	That's fascinating because that is exactly what I was thinking. There should be something like that out there. Because it's like there are so many variables that can affect all of this.
Erin Allmann Updyke	Yes.
Erin Welsh	And you could put in all of your own data and still, like will that number be accurate? Higher or lower?
Erin Allmann Updyke	Exactly.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah. It's interesting. We'll put a link to it, people can check it out. It's still just an estimate. But yeah. So that really is IVF in a nutshell and-

Erin Welsh	It's a pretty big nut.
Erin Allmann Updyke	It's a very large nut with a very large shell. And what I do wanna just kind of say as we wrap up this episode before we get into like the changes in technology and the industry that has been born of IVF; what I just want to take a moment to acknowledge is that I tried but I still don't think that this medical description does a really good job of encompassing what it is like to go through this whole process, especially when you want a baby very badly. And so because of that I really just want to say thank you again so much to everyone who took the time to write in and share your story and record yourselves and share it with us and with everyone that is listening because one of the things that I hear over and over again is just how hard this experience is regardless of what the outcome is for so many people. And so I just want to say again thank you so much for sharing your stories. and we'll get to talk a lot more about what IVF looks like on a larger scale and a less personal scale next episode.
Erin Welsh	Yeah. Well said, Erin, I agree. I agree entirely. I think one of the things that has been so incredible, like we keep saying, thank you, thank you, thank you. But just also I think for us to hear the range of experiences-
Erin Allmann Updyke	Yeah.
Erin Welsh	The range of ways that this can feel is really powerful and really important to remember that it's not just one thing.
Erin Allmann Updyke	Yeah.
Erin Welsh	There are commonalities and maybe that is reassuring or helps with a sense of belonging or not feeling so isolated. But then there are things where it's like maybe that's not that way. And so I think that's what I just keep circling back to-
Erin Allmann Updyke	Yeah.
Erin Welsh	Is how important it is to understand that it's not just one thing, it's not just one feeling, it's not just one experience. It's many, many, many, many different things.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	Sources?
Erin Allmann Updyke	Sources?
Erin Welsh	Yeah. I have two main ones, I have several but I have two main ones that I read for this. One is a book called 'The Pursuit of Parenthood' by Margaret Marsh and Wanda Ronner. And the other is a book by Sarah Ferber, Nicola Marks, and Vera Mackie called 'IVF and Assisted Reproduction: A Global History'.

Erin Allmann Updyke	Like I mentioned in the last episode, a lot of my sources ended up overlapping for these episodes but a few that were particularly helpful for this episode was that textbook that I used in last episode which was the 'Johns Hopkins Manual of Gynecology and Obstetrics', there's a few chapters in there. For details on the risks of IVF pregnancies, there was a paper in BMC Pregnancy and Childbirth from 2021 titled 'Assistive Reproductive Technology and Hypertensive Disorders of Pregnancy: Systematic Review and Meta-Analyses'. And a few other papers as well. We will post the sources from this episode and all of our episodes on our website thispodcastwillkillyou.com under the EPISODES tab.
Erin Welsh	Thank you to Bloodmobile for providing the music for this episode and all of our episodes.
Erin Allmann Updyke	Thank you to Lianna Squillace and Tom Breyfogle for the incredible audio mixing.
Erin Welsh	Thank you to Exactly Right.
Erin Allmann Updyke	And thank you to you, listeners. We hope that this is a fun episode. We hope you've got enough in you for one more episode because we've got it coming to you.
Erin Welsh	We've got it coming. Yeah. Next week I believe. So stay tuned.
Erin Allmann Updyke	Yeah.
Erin Welsh	And a big thank you as always to our fantastic patrons. Thank you, thank you, thank you. Your support means everything.
Erin Allmann Updyke	So much. Thank you.
Erin Welsh	Until next time, wash your hands.
Erin Allmann Updyke	You filthy animals.