

The Nuances of Egg Freezing - All You Should Know

The egg freezing procedure has not only given hope to those women who want to preserve their fertility due to medical issues, but also to those who just want to extend their fertility. Just 475 women froze their eggs in 2009, where more than nearly 17K did in 2020. Clearly an increasing number of women are seeing it as an insurance to be able to start or expand a family more flexibly. However, the procedure is not without its nuances and comes with no guarantees. The Ethics Committee of the American Society for Reproductive Medicine (ASRM) highlights that "Providers should ensure that women who request planned OC (oocyte cryopreservation) are informed about its efficacy, safety, benefits, and risks, including the unknown long-term health effects for offspring." We are discussing the hopes and uncertainties around egg freezing and all you should know if you are planning to opt for it, with Dr. Carolyn Alexander of Southern California Reproductive Center. Patient advocate Valerie Landis will provide perspectives from the patient panel.

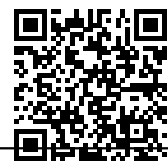
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Shweta Mishra: Hello and welcome to CureTalks. Today we are discussing the Nuances of Egg Freezing- the hopes and uncertainties around it and all you should know if you are planning to opt for the procedure, I'm Shweta, Mishra and I'm honored and excited to have Dr. Carolyn Alexander join us again on CureTalks from Southern California Reproductive Center. Dr. Alexander is an expert in egg freezing and infertility treatments and also work closely with oncologists on fertility preservation of our patients who are about to undergo chemotherapy. Joining Dr. Alexander on the panel is Valerie Landis who has been working in the Women's Healthcare field for more than a decade now and she speaks openly about her personal egg freezing experience. Welcome to CureTalks, Dr. Alexander and Valerie, it's a pleasure to have you both on the panel today.

Dr. Carolyn Alexander: It's an honor to be here. Thank you.

Shweta Mishra: Thank you. Dr. Alexander the Egg Freezing procedure was developed in 1980s and it was originally developed to help people going through serious medical conditions and treatments like chemotherapy, that harms their fertility, and it would help them improve their chances of starting a family post-treatment. But in recent years, statistics tells us that more and more women from a broader group are choosing and exploring egg freezing options and this field has gotten quite a makeover now. So, I wanted to start by asking what is the most common reason in your experience or if a study has been done on that that women are citing to choose to freeze their eggs?

Dr. Carolyn Alexander: That's a great question. I know for myself; I wish I had frozen my eggs but my generation, I'm near 50 it wasn't considered from the American Society of Reproductive Medicine to be a standard of care to offer egg freezing due to advanced maternal age necessarily at that time. In general, the most common reason that clinically in Los Angeles that we talk to patients about Egg Freezing, the biggest reason I see is the OBGYN checks their AMH or their day three FSH and it's borderline or right at a confusingly low level and patients aren't ready to start a family, and they think to themselves, should I think to freeze my eggs. Another common reason is as we get into our 30s, everyone is realizing that by 35 the chromosomes in the egg start to change. And so, there's more of an open discussion, people on social media are talking about thinking about egg freezing. Even at the Midwest Fertility Society Meeting which was I think this past week, I saw notes from my friend who attended where they said, actually, they're going to be discussing, talking about egg freezing by 30 as a discussion point, which is interesting because sometimes when we see patients at 29 or early 30s, we say well let's re-evaluate you could trend your AMH discuss it and then occasionally it'll change to be concerning over a year and we don't understand why nature is doing that other than as time goes by age affects our egg supply and quality, as well as environmental pollutants, plastic, and endocrine disruptors from our makeup and phthalates and things like that, too.



Shweta Mishra: Right, very interesting to know that doctor and that brings me to the question about the success of the procedure. So, could you talk a bit about the factors on which the success rate of Egg Freezing depends?

Dr. Carolyn Alexander: That's a really good question. I always think of cases where the patients didn't have too many eggs frozen, but they got a healthy baby many years later, especially with our cancer patients. Sometimes we have to just we don't have time on our side, to let them try vitamins, acupuncture, weight loss if they're overweight. Think about vitamins and proper nutrition and acai berry there's a lot of prep, we do for our patients, who have the breather of time to think about egg freezing, it's our cancer patients, we're in a time crunch. But what we realized is that the eggs can survive the thaw, 87% or up to into the 90s % since vitrification which is flash freezing eggs, eggs do survive, around nine out of ten of them survive the thaw. I think the challenge is especially since covid hit the sperm parameters have become harder, men are vaping more, using CBD oil, obesity is on the rise with some of the men, sedentary lifestyle, more binge drinking and so we've become more vigilant that before we ever thaw the eggs for eight weeks, the men should be on a strict regimen because we've had it happen, where we thaw 10 eggs, and lo and behold that morning, the sperm looks really concerning, the motility suboptimal, even though a month prior or two, he had a normal semen analysis and potentially the sperm DNA fragmentation goes up with toxins as well as fried food and processed foods as well as a high body mass index and as well as covid. So, even a symptomatic covid may transiently affect the sperm DNA parameters. And I just was reading an article this morning about how environmental air pollution, like if you live near a freeway or particulate matter that can be from the air, that sperm DNA fragmentation, is compromised too. Vitamin D has been shown to improve sperm quality as well. But when people tell me, how are my eggs going to do when I want to get pregnant? Well, I always say half the battle is the sperm and that's why I never took a moment to talk about that. They survive the thaw, but then they have to fertilize and then the genetics of the eggs depends on the woman's age. And so that's where the odds are that around age 35, it takes 15 to 20 eggs to get a pregnancy. And so, as we get older, it takes more eggs for us to get a chance for a pregnancy because it may or may not survive the thaw, they may or may not fertilize and they may or may not be genetically normal.

Shweta Mishra: That's right. So yeah, thank you for pointing that out it's not only the egg parameters, the sperm quality matters a lot right in the success rate. So, thank you for pointing that out, but given all of that, we know there are a lot of factors that are deciding the success of egg freezing. And the procedure is not without nuances, it doesn't guarantee a pregnancy, right? And as the Ethics Committee of the American Society of Reproductive Medicine highlights, providers should ensure that women who request egg freezing should be informed about the efficacy, safety, their benefits and risks involved in this process. So, could you share a bit about how you approach your patients about egg freezing? How do you explain the procedure to them? And the risks involved or the benefits?

Dr. Carolyn Alexander: Yeah, every month, we ovulate one egg, if you're having regular menstrual cycles, and what's fascinating about the ovaries is that you have a pool of follicles in each of your ovaries and that can range each month. Some months, we have five to ten on each ovary. Some months we have three it can vary. On the third day of your period, FSH Follicle Stimulating Hormone level which is from your pituitary gland, if that level is over 10, that's a red flag that there is diminished ovarian reserve. So, it might be harder for us to get a quality and quantity egg supply for that individual. And so occasionally, we'll have a discussion about some eggs and some embryos, even if they don't have a current partner is still really important to take a step back, take a breath and realize that ultimately, for a biological baby for yourself, you would need potentially an embryo which is a much stronger chance of a future pregnancy than the plain egg that again, may or may not survive the thaw fertilized or become an embryo, that's healthy and then it has to implant. The other thing that I talk about is during the two-week process of the injections to grow your eggs, you may feel breast tenderness, headache, mood swings, bloating, and the most common cause constipation, so it's important to avoid constipation in the prep time before you take the injections. We encourage vitamins, acupuncture, get your body exercising, be as healthy and fit as you possibly can. We check your thyroid level, vitamin D level, we check for anemia, we want to make sure everybody's pap smear and breast exam is evaluated. If she's 40, we talk about mammograms. If you have a family history of breast cancer, you may be encouraged to have a mammogram younger than 40 years old. If you also have



any health conditions, such as rheumatoid arthritis, multiple sclerosis, lupus, anything like that, we like to have a chat with your primary care doctor and your doctor, make sure they understand your estrogen is going to go up, which puts us at risk of a blood clot, such as a deep vein thrombosis, or pulmonary embolism.

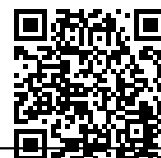
And even though it's extremely rare to ever see that, it's always sort of in the back of our mind as the doctor of 'Do no harm' because we're trying to help you achieve your goal of having some eggs frozen for your future. You may or may never need these eggs. But if you need them, we want them to be the best quality and quantity that we can get. People always say, I want more eggs. Well, I want you to get more eggs too but the blood flow to your ovaries, has a lot to do with your blood pressure, cardiovascular health, whether your cortisol is high and you're extremely amped up and stressed and not sleeping perhaps the bodies like why should I try to ovulate this month, let's forget about it. That's the least of my worries from your mechanics of your body. Your body's in a fight or flight mode from stress. So, in terms of preparing yourself, you really want to have a good support system. Lately I've been really almost writing in my note, who's their support system, some patients say that I don't really want to talk about it with anybody, it's very personal and I understand. But it's really important to have one good friend or a cousin or someone to air it out your fears and your hopes and why you're even doing this. Because if you don't have a person to chat with, I can chat with you but it's still hard and you need another outside person that's guiding you and giving you support. The night the eggs come out, you just have to focus your energy on healing, sometimes patients say I wish this, I wish that, everybody wanted you to get the most eggs possible in the best quality. But you have to just focus that you accomplish the goal to get as many as you could and you did the best you could because some people do the retrospective look. And you asked a really good question Shweta, which is a trigger shot, which is the final moment where the eggs are going to loosen up from the side wall and for the egg retrieval to safely, get those eggs that can play a big role in whether or not we get the quantity we were hoping for and absorption of that shot as well as the timing and as well as staying hydrated and keeping your metabolism healthy with normal bowel movements that will help us get the system to work.

Shweta Mishra: Alright, thank you. Thank you. All these very important facts that you shared doctor and is there also a discussion about success rate and how do you handle that?

Dr. Carolyn Alexander: Yes. So, a lot of people say, how many eggs do I need for the future? Are they going to survive the thaw? I always go over the statistics in detail and their age-related chance of chromosome abnormalities. I always explain that there is no guarantee, I tend to write that too. I wish there was a guarantee but there's no guarantee and then we prepare in the future if they needed that the sperm is optimized as much as possible and our average age of patients is into their later 30s here. So, we're used to telling patients that, you might need a lot of eggs to get a chance for a future pregnancy. And so, it's challenging, I have graphs I can show people at 39 and older. I did see from a European study that egg freezing after 38 is kind of an interesting discussion, but we do see a lot of patients who haven't met the right partner and they realized they want this as an option and it is a five-year retrospective look for us at 37 and took 17 to 20 eggs, to get a pregnancy. So, at 39 we need 25 or more, even higher number to get a chance for pregnancy. And that is a little bit challenging because some of those patients their egg supply, AMH level is low, and their follicle count isn't high. And so, it's a little overwhelming to think how many tries do I need to get enough eggs for the future? So, what I tend to say is, let's focus on one good try, see what we can get and at least have that as option. And we can pivot from there and talk about the future from there.

Shweta Mishra: Right. Thank you. Thank you, for sharing that doctor. And it's really so important for folks to know their best optimal time when they can conceive with minimum efforts. And all this guidance from providers, like, you is so important because nothing is less confusing about this. That's how I know, so thank you for that and I was just talking to Valerie about it. And I know she has some great questions for you doctor so I will pass it over to her now and Valerie welcome to the show again and it'd be great if you can before you go on to ask your questions, please share your egg freezing journey, a bit with us.

Valerie Landis: Well, I felt really fortunate that I worked in the area of fertility or women's health because it



really taught me about my own fertility. It wasn't something that I learned in school or from my friends very much like you were sharing Dr. Alexander, that the window of women before me really taking advantage of egg freezing. I was born in the 80s, 1980s and so I was kind of like the first wave of generation that could access the technology for it to be useful in my age. And so, in 2015, I was 33 years old and decided to take the leap of freezing my eggs for the first time. I was able to successfully freeze 17 eggs. I'm always kind of reluctant when I talk about how many eggs, I froze, because I realize out there, there's a lot of comparison going on and egg envy, so to speak. And I knew I was going to do this multiple times, but I wanted to see what would happen the first time I embarked on it. And it's a learning experience, right? Not only just have how you feel during the procedure, but also what you learn from that egg freezing cycle. And so, I waited two years and I decided to freeze again, to increase my opportunities for how many children, I would want in the future and, and bring the best outcome possible. So, for my 35th birthday, I froze again and got an additional 12 eggs which is great. It was a great outcome. I had a totally different experience on the meds this time where I was severely bloated and had a hard time recovering from my trigger shot, I do believe because it was a different Med order than I have had the first time around because we were trying to shake things up maybe get a little bit more, but I was two years older. The third time, I decided to freeze my eggs was two years after that. But a year, before I froze my eggs, I decided to make myself a guinea pig, and I started using fertility focused vitamins, I made smoothies every day and I really focused on my physical health. And so, in an off-chance or just even how we did our med protocol being older, being almost 37 years old, I was able to collect 32 eggs. No, I can't contribute why that happened? I may be a candidate for PCOS, so they're not all those eggs might be really great viable eggs, but they were a mature level to egg. So, we were able to freeze them. So, I ended up with 61. I put them in long-term storage, for my future of Family Planning. But even today at 40 years old, I haven't used those eggs, yet which is pretty common in the space. And so maybe someday I will I was really hoping to find the right partner and do that as a team. Obviously, the sperm is important, and I didn't feel like at this time period that I wanted to make any of those eggs' embryos, whether with a donor sperm or a partner. And so therefore I'm in this holding pattern until something else shifts. But as we're talking about this topic, I know a lot of patients, think about maybe you could help answer Dr. Alexander what is the perfect age, if we had to pick an age to freeze our eggs and when is too old too old and is there a time limit, we should just give up on that factor?

Dr. Carolyn Alexander: Yeah, that's a good question. It is always going to be younger is better but then what young age is ideal. So that's why a lot of the OB SYNs are checking an AMH level Anti-Mullerian Hormone level as well as a day three FSH oestradiol and LH level. And if an individual is on the birth control pill for many, many years, sometimes the Anti-Mullerian Hormone level can be suppressed, so don't get alarmed if you checked it with your OBGYN and the level is so so. But generally speaking, we are encouraging women to freeze eggs between 30 to 34. Because at 35, the mitotic spindle of the egg starts to get sticky and that's where chromosome problems can pop up. And so, if you had the opportunity or we're thinking about it and you're not ready to start a family in the next year or two, it could be good before 35, to consider egg freezing. Our Ethics Committee here, when we were meeting to talk about eggs, when we get into our 40s, we have a really big heart to heart with all the patients about an embryo versus an egg. But if they're not ready to don't have a partner or don't want to pick a donor sperm, and we'll have a discussion about the risks of egg freezing, and the unknown factor of the genetics. Because then one in four, to one in five of the eggs, has a healthy genetic complement and so it takes a lot of eggs. And so, that's the hard reality when we get into our 40s, it's not that we can't freeze eggs, we do, and we do it. But we talked about it and have a big discussion about how an embryo is better than an egg at that point.

Valerie Landis: Yeah, and that brings me to my next question. I mean since covid, I froze all before covid. So, my last cycle was in 2019, but is there an ideal number of eggs that for each live birth that they should try to shoot for? Or is it a combination of their AMH and their physical health and some of their ovary reserve?

Dr. Carolyn Alexander: That's a good question. Generally, at under 35, we say 15 to 20 because it takes that many to hit the blessing of a one pregnancy by 85 to 90%. So, it is a little confusing. The ASRM- American Society of Reproductive Medicine tells us that each egg has a 4 to 12 percent chance of pregnancy. So, some people use that as a guide so and try to ____ to the higher side of getting good, a



good quantity. I can think of many patients over 17 years of doing this job that had a few eggs and got a pregnancy done when they met the right partner. And then I can think of people who had a lot of eggs and didn't necessarily get a pregnancy. And so it was kind of a little bit of a wake-up call to for all of us. But it isn't always perfect. But we're trying to improve each step especially now again with the male factor part of it.

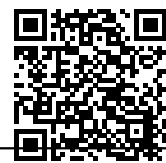
Valerie Landis: Yeah. And that seems to be a more focused area that we are concentrating that maybe have been neglected in the past. Let's talk through a typical protocol for your patients or just the physical stages of going through an egg freezing cycle and each of the timeline that that one would expect, if they're going through an egg freezing cycle.

Dr. Carolyn Alexander: Sure. So, there's typically around five different ways of protocols and three of the protocols need birth control pills. Some patients have never taken birth control pills, or they have chronic hypertension or migraines or contraindication to birth control pills. So, we have many ways and tricks we can do to prevent needing a birth control pill. But Some patients benefit from synchronizing the cohort or group of eggs with birth control pills. During the injections it's around 10 to 12 days of injections called FSH or FSH with LH and sometimes we'll add growth hormone as well as Lupron protocol depending on what your circumstances are. There is an important shot called a GnRH antagonists with protocols, that are called antagonist protocols and that tells your brain not to ovulate. Then, on average, 90% of people need 11 days of shots to get the eggs to mature. Some people, by day nine, the follicles are a perfect size and they're ready to go. And some patients take longer. If you've been on the birth control pill for years and years and years. Sometimes it's important to think about taking a breather month from the pill, but some you have to be careful for contraception because you're used to being on the pill for so long. That being off of it, you could get pregnant. And then the egg retrieval is around, 35 to 36 hours after the trigger shot. That's a 15-to-20-minute procedure that where we carefully get the eggs out and the eggs are flash frozen with vitrification. The week after the eggs come out, I always say, be ready for heating pad Tylenol, we try to avoid aspirin or NSAIDs. So, it's important to just hang in there, takes about seven days to feel better.

Valerie Landis: Well, that very much echoes my experience, and the bloating is very real after egg freezing, and it's surprising how different each egg cycle can be, each freeze can be from each other even when you've experienced it before. Let's talk about some of the advantages and disadvantages. You mentioned embryo freezing or creating embryos from Frozen eggs or fresh, before you go into that whole process for better outcomes, maybe give a little bit of pluses and negatives or advantages and disadvantages of having embryos versus eggs.

Dr. Carolyn Alexander: Yeah, so the embryo is a fertilized egg that's grown over five to seven days to a blastocyst, which has about 100 cells and it has an inner cell mass and a trophectoderm. So that has a much higher probability of surviving the thaw. 99.6% of hatching blast survive the thaw and so that's a little different than 87 to 92 percent to survive the thaw. The other thing about an embryo is it can get graded to good, fair, poor or A, B, C, as well as the opportunity depending on your age and your circumstances and your discussion with your doctor to check genetic testing on the embryo. In a sense if you knew it was tested by the capabilities of what's called next generation sequencing that has a higher probability of becoming a pregnancy, because it's at least overcome some of the genetic checks. The accuracy of genetic testing, and the added confusion with mosaic embryos, where some of the cells are healthy and some are not and that's been opening up a big discussion for us of how to guide our patients who we love so much. We only want everybody to have a healthy baby from their eggs or their embryos and so it's like it's a big and I do put myself in their shoes because I feel it as an older parent, myself. And so, I understand what everybody's going through. And so, it's hard to go over those statistics in patients especially when we're talking to them. It's a little bit of information overload. So, you're talking about eggs, egg quality, then you suddenly throw in, can you try to figure out a sperm source? Like, it just adds so much to the discussion, so I try to take it step by step and see what their personal questions are in that discussion time.

Valerie Landis: Yeah, and that's very critical. Because once you do make an embryo, you can't unmake the embryo, it has the DNA from both parents. So, if you know you're going to use your own eggs but



maybe don't like the parent source of the sperm choice that can't be undone. So, it's a very big decision. It's part of the reason why I didn't make any embryos because I wasn't ready for that, for that choice. Let's talk about is there an expiration date on all the genetic material that we're freezing?

Dr. Carolyn Alexander: No.

Valerie Landis: Is there a timeline that it's no longer good or, is it good forever?

Dr. Carolyn Alexander: Yeah, I was lucky to be on one of those scientific team meets at Cedar Sinai to look at women over forty-five who had eggs or embryos frozen and looked at that. It is a higher risk of preeclampsia or high blood pressure in pregnancy when we get older, as well as placenta issues. We are improving our protocols for embryo transfers to improve pregnancy outcomes for older parents. I think the hard part is in the past, we had encouraged patients to use their eggs within eight years, but we've been blessed, even one of the pictures right here is one of my embryos from eggs from 12 years ago. And so, it was a relatively exciting. I know my friends in Italy have eggs from many years ago that they're making pregnancies with. So, because it's in a glass like state and a vitrified state, we're not seeing them deteriorate or the chromosomes change over time or congenital anomalies increase, but it still typical to talk about within eight years, but we've had pregnancies from 12-year frozen eggs, embryos 20 years, because of cancer patients from the 80s and things. I worked at Johns Hopkins Hospital we had patients, who had embryos from decades prior and they had pregnancies. So, they don't necessarily change over time to our awareness.

Valerie Landis: Right. Because you're freezing at whatever age and it kind of stops the biological clock at that period of time. What is the oldest age that a woman can technically get pregnant? And is there a window that conceiving that frozen DNA, whether it be creation of your own eggs or an embryo that you froze is recommended?

Dr. Carolyn Alexander: Yeah, I mean, it's so now that even colon cancer screening at 45 is changing and we're learning more and more. As long as patients are as physically fit as possible at 45 and their mammogram and Pap smear up-to-date, check Cologuard or colonoscopy and have an annual physical exam with their primary care doctor and don't have a huge red flag. So, a chronic hypertensive patient who has obesity is much harder and riskier to get pregnant at 45 or 50 years old than a patient who's been doing exercising, pilates is at their ideal body weight, doesn't have diabetes. But so chronic health conditions make it much riskier when we're over 45 but our group at Southern California Reproductive Center, help patients into their 50s. But a lot of our patients again are relatively fit and as healthy as possible.

Valerie Landis: So, does it have anything correlating with the menstrual cycle and being in menopause? Can you technically get frozen embryos into pregnancy?

Dr. Carolyn Alexander: We have women in their early 20s who have premature ovarian insufficiency and we're still able to get them pregnant with medications. So, some patients call in their mid-40s and they're like I stopped having my period a year ago, am I still a candidate to consider fertility treatments? You can carry the pregnancy as long as the uterine environment is healthy, even if you're not getting your period but when we don't get our period as women, you risk osteoporosis risk and cardiovascular risk. And so, you always want to talk to your doctor if you're not getting your period regularly.

Valerie Landis: So that's the real advantage of egg freezing is that you can get pregnant at a later age because you froze your DNA, when you were younger.

Shweta Mishra: Absolutely, thank you. Thanks Valerie, thanks Dr. Alexander. Great listening to you both and learning all the facts that you shared in your discussion especially the shelf life of eggs and embryos, wow, 20 years, that's something. Yeah, thank you so much for all this discussion and it's time to wrap up the show now though thank you, Dr. Alexander, thank you Valerie for your very insightful questions and guiding the panel. We will make this talk available very soon on curetalks.com. So, until next time we meet,



thank you everyone and have a great day.

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