Fertility and Cancer: Exploring Preservation, Family Planning Options, and the Role of PGT

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Jenna Fields:

Welcome. Thank you, everyone, for being here. We'll get started. And I know more people will join as we go. Thank you so much for being here tonight. This is our webinar, Fertility and Cancer: Exploring Preservation, Family Planning Options, and the Role of PGT with our amazing expert, Dr. Sahar Wertheimer.

I'm Jenna Fields. I'm the Chief Regional Officer of Sharsheret. And I'm based here in Los Angeles. If you're not familiar with Sharsheret, we provide free virtual personalized support, lifesaving education, financial assistance, and genetic counseling to empower those faced with or at increased genetic risk of breast and ovarian cancer.

Today's webinar is being recorded and will be posted on Sharsheret's website along with the transcript, but your faces and names will not be in the recording. And if you'd like to remain private, you have the option to turn off your video and rename yourself. And you can also call into the webinar, and we have those instructions in the chat. We also now have closed captioning available, and so you can display live captions by clicking on the bottom bar, click on Captions, and then click on Show Captions. We will hold a Q&A at the end of today's presentation. If you have any questions during the presentation, please just type them into the chat box and we'll get to as many as we can during the Q&A. And you may have noticed that you have been muted upon entry. Please remain muted during the call. And like I said, just put those questions in the chat.

We want to thank our generous sponsors, the Cooperative Agreement, DP24-0061 from the Centers for Disease Control and Prevention, Daiichi-Sankyo, and Merck. Without their support, we wouldn't be able to bring you this important educational information tonight. And I want to remind you that Sharsheret is a not-for-profit cancer support and education organization and does not provide any medical advice or perform any medical procedures. And we are putting our full medical disclaimer in the chat for you to read if you'd like.

PGT, or pre-implantation genetic testing, is our topic for today's webinar. We know that this is a subject that can feel overwhelming, and we know there are lots of ways to build a family. Sharsheret can help you understand your options and potentially connect you to peer supporters who have had similar experiences. I want to encourage you to check out our new webpage Options for Family Building in PGT, which contains detailed information about the process of PGT. If you are about to undergo PGT or other fertility procedures, we also have a new kit to support your journey, and both the order form for this and the link to our new webpage are in the chat. Sharsheret's PGT resources were developed with the generous support of Sherry Helfand Wiener and Merck. Also, if you're interested in connecting with others, we do have an oncofertility support group that we offer in partnership with Jewish Fertility Foundation. And our next group is this Thursday, August 7th at 8:00 PM Eastern. And that registration link is in the chat as well.

Today's webinar is the first of a two-part series this week on fertility and cancer. This Thursday, August 7th at 12:30 Eastern, we'll be hosting a conversation with our Israel Medical Advisory board member, Dr. Naama Srebnik-Moshe to talk about the role of hormone replacement therapy for pre-vivors and survivors who have undergone surgical menopause. And you can register for that as well in the chat.

As you can see, we know this is a topic that all of you are interested in. We are offering a lot of programming right now to support you along your journey. And we wanted to start tonight's webinar by sharing a personal story from two Sharsheret community members. I want to welcome Sydney and Daniel to this webinar.

Sydney:

Thank you, Jenna. To share a little bit about our story, I always knew that I could test positive for BRCA1. My mom was diagnosed with breast cancer on the age of 40 and tested positive for the gene mutation. And so when Daniel and I got engaged in 2018, we've had conversations, and that was when I decided to go forward with the testing, and I tested positive for the BRCA1 mutation. And at that time, what was best for me and for us was to move forward with the screenings twice a year. Every six months, I would get seen by my doctor and have an MRI screening, and that was how we wanted to proceed for the foreseeable future. We got married in 2019, and then COVID hit. And when COVID hit, doctors decided to postpone screenings and postponed those appointments, and that was when I decided to move forward with a prophylactic mastectomy. Decided to do that in 2021. And Daniel was by my side for the mastectomy and the reconstruction.

And when I decided to move forward with that, obviously Sharsheret was my first call. They had all the resources. I knew Sharsheret from when my mom was diagnosed. She was a peer supporter afterwards as well. And Sharsheret really was there by my side checking in. They even connected me with a woman who had my same doctors to talk to me about their experience who was the peer supporter. They also shared a prop pillow, gave me drain holders, and really prepared me for my surgery; surgeries, I should say. They were just always there and always checking in on me to make sure that I had everything I needed to move forward with this journey in my life. After the surgeries and after I healed in 2022, we really looked into our options and understanding what it looked like from a fertility standpoint and what we wanted to do, and we decided to move forward with IVF.

Daniel:

In 2022, after weighing the pros and the cons, we ultimately decided to proceed with IVF and PGT-A and M, which we expected and were fortunate to have found that it has rooted out the elevated risk from our bloodline, which is an unbelievable thing to be able to do and an unbelievable thing to be able to accomplish for our children and ultimately grandchildren down the line. We went through rounds of IVF, and subsequent to the IVF, we each embryo via PGT-A and M to determine whether each embryo had the BRCA mutation. And ultimately, we were blessed with a number of non-BRCA mutation embryos, one of which we implanted and is now our two-year-old daughter, Maya, which has been truly the greatest blessing of our entire lives.

In recent months, we went through the process yet again, additional rounds of transfers and retrievals, and ultimately are expecting additions coming later this year. God willing all goes well there. And we're very excited and we're very fortunate to live in a time where modern medicine has allowed us to be able to really root this elevated risk out of our bloodline and to be able to pass that onto our children. It feels really, really tremendous to be able to do it.

I should also note it really is a privilege to be able to speak as a prelude to Dr. Sahar Wertheimer who's here on this call, because Sahar was there for us every step of the way and really helped us through our journey in really, really profound ways, so we're incredibly appreciative. Dr. Sahar Wertheimer is someone we admire tremendously in order because she's an unbelievable person and medical professional, because she has the most unbelievable Instagram content in the entire medical field, and because she's my cousin. In that order. We're really tremendously appreciative for Sharsheret, for Dr. Wertheimer, and frankly for modern medicine that's allowed us to be where we are right now and to have a blessing with more on the way. Thank G-d.

Sydney:

And also, being able to share the options with everybody as well. I don't think a lot of people know about PGT-M and what science allows these days, so want to ensure that everyone is just aware of their options.

Jenna Fields:

Thank you so much, Sydney and Daniel. It's truly an inspiration to hear from you. And you can see all the encouraging comments and hearts in the chat. And B'sha'ah Tovah to you both.

Sydney:

Thank you.

Daniel:

Thank you.

Jenna Fields:

And now we're honored to definitely make this a family affair, as you mentioned, and welcome Dr. Sahar Wertheimer as our expert this evening. Dr. Sahar Wertheimer earned her medical degree from Albert Einstein College of Medicine and completed her residency in obstetrics and gynecology in women's health at Montefiore Medical Center. She did her fellowship in reproductive endocrinology and infertility at Cedars-Sinai. She currently works in private practice at HRC Fertility here in Los Angeles and specializes in oncofertility, helping both patients with cancer and those with increased hereditary risk, the family planning or emergent treatments. She also serves on Sharsheret's West Advisory Committee and is being honored this September as our healthcare hero Grand Marshal at Sharsheret's West Coast Dash on Sunday, September 14th. For anyone joining from Los Angeles on this call, please join us. Going to be an amazing morning. And now it is my pleasure to welcome Dr. Wertheimer.

Dr. Sahar Wertheimer:

Thank you for that intro, and Daniel and Sydney for your intro as well. I don't know how many people caught that he said additions with an S, which we're very excited about. And they have been so gracious in sharing their journey. There's actually a video with Sharsheret that brought us all to tears. Highly recommend. And okay, without any further ado, let me share my screen. Okay, sorry, I have to share my screen first, and then... Even when you do the run through. Okay, and now I'm going to go full. One second. Full screen. Okay. Am I good?

Jenna Fields:

Sahar, we can see the... There you go. Perfect. Looks good.

Dr. Sahar Wertheimer:

Can see everything?

Jenna Fields:

Nope, now it's good. You got it.

Dr. Sahar Wertheimer:

Okay. Okay. I am going to be speaking about fertility and cancer, and I really wanted to talk about the before, the during, and the after options and the role of PGT. I wanted to cover what is oncofertility, fertility preservation options, fertility sparing strategies during treatment, as well as post-treatment options and the role of PGT.

Oncofertility is the intersection between oncology and reproductive medicine. And this field of medicine becomes even more pertinent as the survival rates of cancers and our treatments improve, thank God. We've gone from 2010 to about a 50% survival rate in all cancers to 67% five-year survival rate most recently. The breast cancer survival rate is exceptionally good, 90%. And testicular cancer is over 95%. These are reproductive populations. 15% of adult survivors are actually young in reproductive age according to the Journal of Clinical Oncology, and therefore the importance of early intervention is crucial.

ASCO, which is one of the governing bodies of the oncologists, recommends that all patients of reproductive age who are getting fertility impacting cancer treatment be counseled on options prior to treatment. Unfortunately, there is still a very large gap in care mainly because of lack of awareness amongst even providers. And I've seen it improve, I would say, in recent years. And still has a little bit of a ways to go, but organizations like Sharsheret and people sharing their stories are taking us so much further.

There's also, unfortunately, a very great cost barrier. Insurance, it varies state by state. And the amount that they'll cover and the way they want it covered varies. There are organizations out there like Livestrong, like CVS Cares, that help patients and resources. I'm sure Sharsheret and your oncofertility support session, you probably have a lot of these resources for patients to get a hold of, but we really have to come much further on that. And then geographic limitations. Some places, the access to care in general of reproductive medicine, we don't reach everywhere in America. And then there are certain treatment options that are not available everywhere, as we'll discuss.

How much cancer will affect the reproductive potential depends on something that we gonadotoxicity. Gonads is any reproductive organ like your ovaries or testicles, and toxicity is the toxicity of the chemotherapy agent or the radiation that patients would be receiving. And the extent to which they affect is based on the data that we have available. And we do know that there are certain chemo treatments that we call high gonadotoxicity and then certain ones that we call medium and low. Even if you are in the group that gets a low gonadotoxic agent, there's still some uncertainty surrounding it. These are all statistics, so it's still quite anxiety provoking because you don't know, "Am I going to be the case that is going to have more gonadotoxic effects or not?" The fertility impact depends on your age, your gender, the type of cancer, and the type, dose, and duration of treatment.

In terms of fertility preservation, timing is critical. Fertility preservation is going to be the best option in terms of outcome and coming back for those eggs or sperm afterwards. Early counseling gives you this chance to potentially pursue it. It will depend on the type of cancer, how aggressive and how fast the oncologist wants to treat it. For example, a common cancer that we deal with is breast cancer. In most breast cancer cases, the surgeon feels comfortable taking out the tumor and then allowing a couple of weeks for a stimulation before chemotherapy. However, there will be cases that we get where the surgeon wanted to start chemotherapy yesterday and there's no time for fertility preservation. Delays in treatment can cause a compromise in their future reproductive potential, meaning if they've started chemotherapy or if they've needed to... Even if their cancer is affecting or near reproductive organs, and so some surgeries will require removal of adjacent organs. Or lymph node dissections will then dictate you need this out or this out. And all of that depends on the primary cancer. It's also incredibly important to have a multidisciplinary team. The surgeon, the oncologist, the reproductive

endocrinologist, social workers, psychologists or psychiatrists all work together in these cases, and we treat them very urgently. The second we get a call; we will book them or even move consults around.

Okay, in females there are a few reproductive options for preservation. There's oocyte cryopreservation, which is the freezing of eggs, and then there's embryo cryopreservation, which is the freezing of embryos. The main difference is that an egg is just the female's genes, an embryo is the female and male's genes. An egg is one cell, and so when we freeze eggs, even with our most advanced methods of vitrification or flash freezing, we know that eggs have about an 85% thaw rate because they're one cell and majority water content. And so, they don't freeze as well as embryos which are multicellular and therefore hardier. Embryos have about a 98% thaw rate. If a person is in their lifelong relationship, we prefer embryo cryopreservation because we think those will survive the thaw better and also because I can give you a much more reliable predictor of success upon thaw of the embryo. However, if somebody is not yet in that relationship, oocyte cryopreservation allows them that social mobility in the future.

For patients that don't have time to be stimulated, or they are pre-pubertal, the options are quite limited. There is something called ovarian tissue cryopreservation, which is essentially we take the ovary out or we take pieces of the ovary and freeze that tissue with the thought that later we'll come back and place those, as you see in this picture in the bottom right corner, strips ovarian tissue on the surviving ovary that the surviving ovary may not have good eggs anymore because of the chemo and radiation therapy, but it might still have the blood supply. And if we can put these old pieces of tissue, stitch them back onto the ovary, potentially we can stimulate the tissue again and grow the eggs that are there and do IVF. It's largely experimental. The pregnancy rates are obviously not as good as egg or embryo freezing. But the real barrier in oocyte cryo tissue, cryopreservation, is that it's really only done at select centers. It's really not done at every hospital. And so, if somebody needs cancer therapy that badly, that urgently, are they next to one of these centers that we can do oocyte cryopreservation at? And usually, the answer is unfortunately no.

More promising is that there is something called in vitro maturation. In vitro maturation is essentially we go in and take out those eggs even before we stimulated them. We go into the follicles of the ovary that we can see, and we try and get as many eggs as we can. Usually non-mature eggs, we cannot fertilize them and grow them to embryos. However, there is new technology that is actually in phase three trials, and recently there was a baby born from an in-vitro matured egg, so that's very promising. And actually, HRC is one of the places where we are doing these phase three trials. Essentially, we can take out these immature eggs and mature them in vitro, so we don't necessarily need to do the stimulation. This will be life-changing for cancer patients.

In males, the options include sperm cryopreservation, that's the easiest, where we essentially get a sample of sperm and freeze it, or we can get multiple samples of sperm and freeze. There's also testicular sperm extraction. And this will depend on if we think the testicles have been damaged by chemo or radiation, but there's still some sperm in there. A regular semen analysis has over 15 million sperm per ml. If we're now seeing a semen analysis after treatment where it's really hard to find sperm, the count is way low, less than 5 million, with something called a TESE, this is the surgical procedure, the reproductive urologist can literally open the testicle, look in the seminiferous tubules that you see in this picture. They look with microscopes during their surgical extraction. And they will take out pieces of tissue that are then handed off to the embryologist in the lab to find sperm. And this is really remarkable. In patients that a semen analysis comes back with no sperm, we actually can sometimes find microscopic sperm. And all

you need is one per egg. And then testicular tissue cryopreservation, which is the same experimental level as ovarian tissue cryopreservation.

Okay, to speak a little bit to, let's say you couldn't do stimulation or let's say you did your stimulation, but now you're undergoing cancer treatment, what are the measures that we can do to try and limit the gonadotoxicity of the agents that we're using? Again, these are all largely experimental. We don't have great data. Data is actually quite mixed on a lot of these measures, but at least for ovarian suppression with GnRH agonists, the way I like to describe this is like Lupron is a medication that shuts the brain's ovary access down; puts you in a post-menopausal state. And the idea is that maybe with that suppression, we're hiding or making the tissue less active and therefore less susceptible to the chemotherapy or radiation that the patient is getting. And maybe then we can preserve some of the tissues so that when they're done with their treatment, the ovary is more alive. We do it because the downside is very low. I would argue that some people would say the downside is not so low. It actually makes you feel post-menopausal in addition to everything that you're going through with chemo. But maybe they feel so crappy they don't feel the difference anyways. But otherwise, doesn't really have a long-term downside.

Ovarian transposition is a surgical technique where... This is for patients that are going to be getting radiation to the pelvis or lower. The ovaries are in a surgery right before radiation affixed to the pelvic wall, anterior pelvic wall or sidewall to bring them out of the field of radiation so that if radiation is going pelvis and lower, the ovaries are not on the field of radiation and hopefully less damage by the radiation.

And then there's gonadal shielding. Gonadal shielding is more for patients that we're not necessarily targeting the ovaries or the testicles during their radiation therapy. And so those can be covered the same way that when you get an X-ray, they might cover other parts of your body or cover your pelvis when you're getting an X-ray for your upper body to just try and shield the gonads from getting the radiation rays.

And then surgical planning for fertility sparing options is referring to cancer surgeries where there is a plus or minus on removing some of the reproductive organs. For example, uterine cancer or some type of ovarian cancers. By and large, the treatment will be, for some of these cancers, to remove the entire uterus, ovaries, fallopian tubes, cervix. But when we keep in mind fertility sparing, we know a patient wants to still procreate after this surgery, we will adapt and potentially compromise in a sense of not taking out organs that they need for reproduction. For example, cervical cancer, sometimes they will do something called a trachelectomy where they won't take out the uterus, fallopian tubes, and ovaries. It depends on the cancer type and chemo and everything. And they'll try and keep those in place until after the patient has completed reproduction and then go back perhaps and take them out. That really depends on the primary cancer type and what the literature or the guidelines say about these in-between options where the gold standard is to remove everything, but we're trying to spare them.

For pediatric and adolescent considerations, there's just limited options. And this has to do with the fact that they're pre-pubertal and there's not much that we can try and save at that point. Their bodies may not respond to something like Lupron because their brain to ovary access is not activated yet. There's also ethical and legal challenges in consent, and therefore early sensitive counseling with family involvement is very integral.

And then there's post-treatment options. After treatment, the options range. From natural conception, there will be people whose periods resume who can get pregnant on their own. They always have a question of, "Do I have to wait for a certain amount of time until the chemo is out of my system?" The answer is usually yes, but the answer of how many months becomes a little bit more speculative than concrete. There's IVF with cryopreserved gametes. The whole

point of freezing the eggs or the embryos or sperm ahead of time, now we can come back and use them.

Use of donor sperm or eggs if their ovarian reserve has been so affected by chemo and radiation or if their sperm has been... And they can't produce; there's third-party reproductive options where we can get donor eggs and donor sperm. This is obviously very hard for couples when they're first contemplating it because it's not their genetic material, and it takes a lot of support and destigmatization. I think a lot of patients come around to it, and once they've gone through it, they express that, "This feels like my baby. It is my baby; I went through everything with it." But I think it's a big mental load to get used to. And I find that for these patients; support groups go such a long way. To speak to somebody else that's gone through it and can tell you from the other side what they feel and that they don't regret it, and that essentially day to day this feels like their baby, it doesn't feel like some foreign baby just because the genetic material isn't there is just paramount.

And then there's gestational carriers. Gestational carriers are for patients who have maybe hormone-sensitive cancers in the past or, like a lot of our breast cancer patients, there is a lot of guidance on can they stop their... Some of these breast cancer patients will be on tamoxifen for long-term, and can they stop that tamoxifen, which is a hormonal agent, in order to get pregnant and then go back on it? And there is a lot of very positive reassuring literature that we have on that. However, some people may not want to take that risk. And it is way less risky to have a third-party gestational carrier carrying the pregnancy. It's just a conversation. And then obviously there's always adoption, which is not as easy as everybody would make you think. Oh, just adopt. Adoption is a very expensive and emotionally taxing process as well.

And then this is the passion of this talk, which is PGT. PGT is life-changing, as Daniel and Sydney had mentioned, and so many other couples. PGT allows you to... Well, first of all, genetic screening where we've come with cancer screening. We now have a panel of I think 40 plus genetic mutations that we can check for different cancer genes. And they're not all as straightforward as the BRCA gene and really need a very experienced and knowledgeable genetic counselor to help you understand what exactly you're getting into. What is the inheritance pattern of this gene? If I pick an embryo that doesn't have it or I look for it, do I still have this risk? It's really complicated, and each gene is so different.

My overall feeling, I have such a low threshold to get genetic cancer panels on my patients. I encourage almost anybody that even has a trace of a family history to get it unless they think it's going to really, really increase their anxiety. Because most of these genes, there's something we can do about it. It's not just to live with your anxiety for the rest of your life, but really... For example, the BRCA gene, if you know have that gene, you can almost reduce your risk of the general population with a prophylactic mastectomy, removal of the breast, and then after childbearing, prophylactic oophorectomy, which is removing the ovaries.

And it's not to say that those are small things. I would argue that they're quite emotional, and a lot of emotional baggage can come along with that. Women have said they feel less like a woman; you're taking away their integral parts. However, the argument is to be made that to have the risk of the general population to be around for your children is just there's no measure on that. And the fact that we've come so far in science to be able to do that I think is amazing, and I want to be able to offer that to all my patients. I think that if you were to go by the guidelines that insurance carriers set out for you, you need to have X, Y, Z amount of red flags in your family history for this to be covered is a disservice. And especially in the Jewish population where... We've had this conversation before with Jenna, but we know in the Ashkenazi Jewish population for sure, but also in the Sephardic Jewish population, which is quite overlooked, we have certain cancers that make us higher risk, and therefore I think a lower

threshold should be for getting these cancer panels tested. It's both for your own health, and also PGT allows it to be for the health of your offspring.

And so what we do with PGT is essentially if you test positive for one of these mutations, we can create a probe that matches your mutation and checks the embryos to see if the embryos, A, carry it, have two copies of it or none at all, and therefore decide if you want to put back that embryo or not. And it is a very personal decision.

I will never forget this one patient that I had in my fellowship who sat in front of me with her mother. She was a BRCA2 carrier and really was having a hard time deciding if she would want to test embryos or not because her argument was, "I'm a BRCA2 carrier, and if my mother had done this, I wouldn't be here today. Look at all this potential of life that I have, and I'm living just fine, and I have BRCA2." I heard that. I felt it in my bones. And I would just say the option is there and knowledge is power, and you get to make that decision based on whatever feels right for you. It does require IVF to be able to do PGT testing on your embryos before implantation. The other option would be to get pregnant and then test the pregnancy. And I think that that would be really traumatic to have to... Or the debate terminating a pregnancy that was a carrier of a certain mutation, in my opinion, way better to know and to decide before. PGT-A is the standard testing that we do on all embryos for everybody with infertility or even just gender balancing, whatever it may be. PGT-M is what we're speaking about specifically when we're looking for certain cancer genes or heredity conditions.

And I spoke about the psychosocial considerations. Ethically, in America it's considered very ethical. I think where ethical alludes to is there are genes and there are certain cancers and where the risk is not 100% that you will have this cancer or it's not even a majority percent. And so, are we making people go through unnecessary procedures? Are we potentially preventing... I don't even want to say preventing life because I feel like that's going into Catholic language of IVF. But for the gray areas, ethical considerations become really complex. And we are starting to enter into that territory, though I would argue that with cancer genes, usually it's quite straightforward.

And so, I think I already touched on this, but BRCA is one that everybody is very familiar with, and in no small measure due to... Sharsheret has done a wonderful job educating the public and really popularizing it. There's lesser-known cancer genes like Lynch syndrome, which is colon cancer. There are other breast cancer genes like the CHEK2 mutation that are also quite common. And the population and also the decisions surrounding it are so complex because the inheritance pattern is not very straightforward.

By the way, just a fun fact about the BRCA gene, the males with BRCA have a much lower chance of manifesting than the females with the breast and ovarian cancer. There are still cancers that are BRCA that affect males like breast, but also prostate and pancreas, melanomas, but much smaller percentage. And therefore I've had patients who really interestingly decided to transfer a male that may or may not have had BRCA, they didn't test their embryos at that point, and then they went back and tested it, but until they were retesting it decided to transfer a male because of the lower risk to the male. And these are just all the variety of decisions that can be made with all this information.

Okay, and I think that that's mostly what I wanted to say there. Future directions. We still have such a long way to go. Like I mentioned, I'm very excited about the in-vitro maturation. I think it'll be great for IVF in general, but specifically for the cancer patients that don't have a lot of time, I think it will be life changing. We need way more data and centers doing tissue cryopreservation. We need to improve it so that when we do it, we're actually getting better results than what we're currently getting. What we're currently getting, the pregnancy rates are not incredibly high.

And just imagine even the hormonal benefit of ovarian tissue, cryopreservation, not even to speak about the reproductive potential, which is the hormones that your ovaries give you.

One of the concerns with tissue cryopreservation in cancer patients is that depending on how that primary cancer spreads, so some cancers spread more lymphatically, some spread more via the blood, and so the thought is that maybe some of this tissue is seeded with cancer or potentially has it in the DNA to eventually metamorphosize into cancer. And so, these are anxieties that we as a field still have. And again, this will depend on the type of cancer, how it spreads, where we think its metastases go to primarily and things like that. Okay. I think I went backwards. Any questions?

Jenna Fields:

Sahar, I'm going to ask people to put questions into the chat.

Dr. Sahar Wertheimer:

Okay.

Jenna Fields:

This was wonderful. Thank you so much.

Dr. Sahar Wertheimer:

My pleasure.

Jenna Fields:

I just learned so much from this talk. And I'm really excited about the research updates that you shared, that a lot of it was news to me and I'm sure many people on this call, so thank you.

Dr. Sahar Wertheimer:

Yeah.

Jenna Fields:

As we're waiting for questions in the chat, a few that came in in advance that I'd love to ask you. Firstly, for people looking for a fertility preservation specialist, are there any national databases or places that people can go or tips you would recommend when someone is choosing a provider?

Dr. Sahar Wertheimer:

All reproductive endocrinologists and infertility specialists are trained in fertility preservation. Some of us may be slightly stronger with fertility preservation in patients with cancer. The difference is that in somebody who has a limited amount of time to get their stimulation done, we do things a little bit differently. We will do something called a random start protocol where we don't necessarily wait for the right point in their cycle to start, we just start. And the idea is anything is better than nothing. And there are also other add-ons that we do. We add a medication called Letrozole if they have a hormone sensitive cancer to try and lower the estrogen that their body sees. Also, experimental. But adding estrogen to a protocol requires a little bit of knowledge of how Letrozole will affect the estrogen values that we're seeing as well as the growth of the follicles, when to trigger, et cetera.

But I would say you're probably okay with most major centers. Speaking to those experimental things like ovarian tissue cryopreservation, I don't if there is a database. I think at that point, it would be calling places in your state and asking. I personally do a lot of data or crowd-surfing through my REI class, my graduation class. And so those are access groups that your REI may have that they may be able to help you with the best place to go to see where could they do ovarian tissue cryopreservation, if that's something you're very set on, which I would argue isn't always worth it, it would be an REI at a major center in your area.

Jenna Fields:

Amazing. Thank you so much. Another question that came in, there's a focus everywhere in society around having children earlier, and certainly just the concern around getting your ovaries out by a certain age if you're high risk is something that is on the mind of people who have hereditary cancer risk. For folks who are BRCA positive and looking to do egg freezing, what is the recommended age that people should consider doing that? And is it younger than the general population who is considering egg freezing?

Dr. Sahar Wertheimer:

The guidelines are it depends BRCA1 versus BRCA2. BRCA1 is a little bit younger. However, I would argue that that shouldn't even matter. I would love to see those patients in their mid to late 20s, to be very honest. I don't know if that'll be very popular, but I think the reason is, first of all, there is some data, and I didn't mention this. There is some data that certain patients with cancer mutations like BRCA actually have a lower reserve than the general population. Maybe there's something in that same how the BRCA affects the ovaries, maybe there's some sort of commonality. But we do see lower AMHs in those patients, and so I would argue they should be doing fertility preservation for more than one reason. And you will get the best bang for your buck the younger you are. You have your ovarian quantity and your ovarian quality decrease with age regardless of if you have a cancer mutation or not.

If you know you're going to be doing IVF anyways for purposes of PGT, why not get the best bang for your buck and do it young? I would love to see all egg-freezing patients in their mid to late 20s for the same reason; those eggs will survive the thaw better. A higher percentage of them will be normal, lead to normal embryos in pregnancies. But certainly, in somebody who's a BRCA1 or 2 carrier, I would love to see them in their 20s. It's not too late in your young 30s, but I think you're better off if you come younger.

Jenna Fields:

I actually, I heard you do another talk maybe a year or two ago, and you did speak, and I'd love to hear you share with this group the current research around success in freezing an embryo versus an egg and what the differences now. What is the research showing?

Dr. Sahar Wertheimer:

Embryos are heartier. They're multicellular. They're hundreds of cells by the time we freeze them, and so they have a 98% fall rate. It's certainly possible an embryo could not survive a thaw, but it's quite devastating and quite rare. Eggs have about an 80% to 85% national thaw rate. At our center last year, we had a 90%. You certainly could get a little bit better at certain centers. However, it's very conceivable that you will lose a small percentage on the thaw. That's because eggs are majority water content and they form icicles when they're frozen, even with the flash freezing that now most major centers have transitioned to. It's just something you have

to account for if you're freezing eggs. I still don't want to see my single patients making embryos to improve their chances. And it does happen, by the way. I still want to see them have that social flexibility, but I just take it into account when I'm counseling them on how many I'd like to see them freeze.

Jenna Fields:

Is there any research on sperm freezing and this difference between embryo and sperm freezing?

Dr. Sahar Wertheimer:

There's no difference. Sperm freezing works quite well. And it's just one of the unfair gender discrepancies in the field of IVF. Sperm freezing is quite easy, it's quite quick. You don't have to be stimulated for two weeks, and you can do it multiple times, so it's easier.

Jenna Fields:

Okay, and question-

Dr. Sahar Wertheimer:

Oh, you mean with respect to age? Should younger men be freezing their-

Jenna Fields:

I was talking about freezing, but actually what is the answer in regard to age? Does it change?

Dr. Sahar Wertheimer:

Not much of a difference. Not much of a difference. But yes, there are certain markers that we're seeing elevated in older men, so men above 40, depending on what study you read, 45. We see higher rates of autism, schizophrenia, certain things we think are linked to advanced paternal age. That would maybe be a reason. It's so easy and cheap to freeze sperm that why not? Though in orthodox Judaism a little bit more complicated. But yeah, still very different than eggs.

Jenna Fields:

You spoke a little bit of ethical considerations, and obviously for many people, consulting with their rabbinic authority is very important in this process, and I just wanted to acknowledge that as well.

Dr. Sahar Wertheimer:

Yes. And we work closely with PUAH, Bonei Olam. And they are usually very pro-preserving people's fertility. It's very interesting that when you get into the minutiae of the law, there's a difference in premarital and marital, at least for men in terms of freezing. But find a rabbi that lets you do it because they exist.

Jenna Fields:

Okay, question in the chat, the average cost of IVF and PGT, if that's something that you know. And how difficult is it to get insurance coverage if you are BRCA1 or 2 positive? I'm assuming doing preventative PGT.

Dr. Sahar Wertheimer:

That is a very hard question to answer because it varies state by state and it varies by insurance carrier, so I can't speak to it on a wide level. It's very, very different. There are certain mandated states. Even mandated states have different qualifications. Some cover egg freezing, some don't. Some cover fertility preservation, some don't. You have to go to your local practice and find out. Oh, and the cost, I just don't like to speak to cost, but let's say somewhere between $20,000 to $30,000 is probably most likely.

Jenna Fields:

Okay, I appreciate that. And I see Vita, who I know as a genetic counselor, mentioned that employers are now offering coverage, so looking at your employer health insurance.

Dr. Sahar Wertheimer:

Yeah, employers. Well, you're talking about California? California has a mandate that's supposed to be happening in January where large employers are supposed to be adding insurance coverage. But I don't know if she's [inaudible 00:46:09].

Jenna Fields:

Yes, in California. Yeah, yeah. Okay, another question in the chat. How would you handle PGT in a case of BRCA1 with a BRCA2 positive partner? Each partner carrying one of the two mutations.

Dr. Sahar Wertheimer:

Dang. I would handle it the same way. We'd have to do PGT-M probes, both the 1 and the 2, and really hope that there's a good amount of unaffected embryos. The way I would handle it is really just setting expectations with a couple ahead of time of you might need more cycles than somebody with just one mutation. And that's because unfortunately we don't have a way of making sure that the ones that are affected with BRCA1 are also affected with BRCA2. And it's completely random. And it's not necessarily linked to the chromosomal number being normal or abnormal, so that's another hurdle.

In somebody who's 35 years old, you expect 50% of their embryos to be normal and 50% to not be normal. And then the BRCA autosomal dominance, so you're going to expect 50% of the embryos to be affected with the BRCA gene. And I don't know if it's going to be the 50% of normal embryos or how it's going to overlap. That part is totally up to chance. And it's different every cycle. You may have one cycle that you've got nothing and it's really discouraging, and then the next cycle you might do really well. Unfortunately, there's no way. You just have to keep banking embryos.

Jenna Fields:

Someone has submitted a question in advance about testing for rare genetic issues like P10, Cowdens. If people wanted to investigate what the panel was for PGT and what they're able to test for, where can they find that information?

Dr. Sahar Wertheimer:

I usually start with a genetic counselor. They're very knowledgeable. A genetic counselor who does fertility and knows, they're very knowledgeable. They've had more rare cases than I have

in specific gene mutations, but they've worked with the majority of centers. And so, I start there. I ask the genetic counselors, "Is this something that we can test for?" And then we actually have to submit the case to the platform that is going to be doing the PGT testing, so it gets vetted by the platform as well. Even if it's a known gene, like we know is going to be approved like BRCA, I still need to submit the case to let's say Cooper Genomics or whoever's doing the PGT testing to accept it.

Jenna Fields:

Do you have a standard panel that they offer, but then they can add more? Is that what you're saying when you submit the case? Or-?

Dr. Sahar Wertheimer:

Generally, all the genetic diseases that we test for on the genetic screening panel we can do PGTM for. If it's something that somebody told me like, "In my family, this person had this kidney disease, and it was due to this mutation," that is something that I would run by the genetic counselor and then the platform. If it's not necessarily on the panel, then yes. It doesn't mean that we can't necessarily test for it, I just have to do some more research.

Jenna Fields:

Okay, that makes a lot of sense. That's our questions for this evening, Dr. Wertheimer. Thank you so much for your expertise. I just thought this was phenomenal, and I learned so much.

Dr. Sahar Wertheimer:

Thank you for having me.

Jenna Fields:

Thank you for sharing with everyone here.

Dr. Sahar Wertheimer:

Thank you for having me. And thank you to Daniel and Sydney for coming and paying attention. We'll see you next week in New York.

Jenna Fields:

Yes. Yes. Well, we started with a family affair, we'll end with a family affair.

Dr. Sahar Wertheimer:

We'll end it with a family affair.

Jenna Fields:

Yeah, thank you, Sydney and Daniel. And thank you again to our generous sponsors, the Cooperative Agreement DP24-0061 six one from the Centers for Disease Control and Prevention, Daiichi-Sankyo, and Merck. Please take a moment to fill out our brief evaluation as you're logging off. This allows us to improve and learn and get feedback for all of our programming.

Reminder that this is the first and a two-part series on fertility. The next one will be this Thursday on Life After Surgical Menopause for Hereditary Cancer Risk and the Cancer community. That's happening this Thursday at 12:30 Eastern. And our next oncofertility support group is also happening this Thursday at 8:00 PM Eastern in partnership with Jewish Fertility Foundation. Please check out all of our Sharsheret programming on our website. We offer all of our recordings there. And please know that Sharsheret is here for you, should you need us. We have a lot of programming around fertility and the cancer experience, and we're here to support you as you face this in your own life. Never hesitate to contact us if you have any questions, including contacting Sharsheret's genetic counselors who can talk more specifically about this issue as you as well. Thank you again. Thank you, Dr. Wertheimer, Daniel, and Sydney.

Dr. Sahar Wertheimer:

Thank you, Jenna. Thank you for having me.

Jenna Fields:

It's such a pleasure to do this. And we'll see you all again soon. Have a good night.

About Sharsheret

Sharsheret, Hebrew for “chain”, is an international non-profit organization, that improves the lives of Jewish women and families living with, or at increased genetic risk for, breast or ovarian cancer through personalized support and saves lives through educational outreach.

With regional offices in the Midwest, Northeast, Southeast, West, and Israel, Sharsheret serves 275,000 women, families, health care professionals, community leaders, and students. Sharsheret creates a safe community for women facing breast cancer and ovarian cancer and their families at every stage of life and at every stage of cancer - from before diagnosis, during treatment and into the survivorship years. While our expertise is focused on young women and Jewish families, approximately 25% of those we serve are not Jewish. All Sharsheret programs serve all women and men.

As a premier organization for psychosocial support, Sharsheret works closely with the Centers for Disease Control and Prevention (CDC) and participates in psychosocial research studies and evaluations with major cancer centers, including Georgetown University Lombardi Comprehensive Cancer Center. Sharsheret is accredited by the Better Business Bureau and has earned a 4-star rating from Charity Navigator for four consecutive years.

Sharsheret offers the following national programs:

The Link Program

Peer Support Network, connecting women newly diagnosed or at high risk of developing breast cancer one-on-one with others who share similar diagnoses and experiences

- Embrace™, supporting women living with advanced breast cancer
- Genetics for Life®, addressing hereditary breast and ovarian cancer
- Thriving Again®, providing individualized support, education, and survivorship plans for young breast cancer survivors
- Busy Box®, for young parents facing breast cancer

- Best Face Forward®, addressing the cosmetic side effects of treatment
- Family Focus®, providing resources and support for caregivers and family members
- Ovarian Cancer Program, tailored resources and support for young Jewish women and families facing ovarian cancer
- Sharsheret Supports™, developing local support groups and programs

Education and Outreach Programs

- Health Care Symposia, on issues unique to younger women facing breast cancer
- Sharsheret on Campus, outreach and education to students on campus
- Sharsheret Educational Resource Booklet Series, culturally-relevant publications for Jewish women and their families and healthcare Professionals

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