Preimplantation Genetic Testing: How Might the New Fertility-Related Technology Support You and Your Family?

National Webinar Transcript

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Presented by:

SHARSHERET®
The Jewish Breast & Ovarian Cancer Community

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

Disclaimer

Melissa:
Thanks for being here tonight. Let me thank you for joining us during this difficult time. I want to begin tonight by saying that Sharsheret stands with Israel. We mourn the families and friends of those killed, pray for those injured and kidnapped, and hope for lasting peace. As our hearts are focused on Israel, Sharsheret continues to provide vital cancer support and education to the thousands who depend on us. Tonight's webinar, Pre-implantation Genetic Testing, is part of our 2023 Sharsheret seminar, Pink, Teal, and You, which brings together thousands of people, virtually and in person across the country from October 13th through October 31st. We hope you'll join our national virtual symposia on the latest hot topics in breast cancer and ovarian cancer, attend or host an in-person education and awareness raising program with community partners around the country, and learn about the latest screening guidelines and access the most up-to-date data and materials in our digital resource packet. The upcoming webinars are being added to the chat box below. However you choose to participate, our Sharsheret summit is the source for the latest information on breast and ovarian cancers.
Melissa:
In fact, our summit is an exciting opportunity to raise awareness throughout the United States, North America, and even internationally. I want to take a moment to thank Sharsheret Summit sponsors, Daiichi Sankyo, GlaxoSmithKline, Merck, AstraZeneca, Pfizer, CGEN, Lily, Natera, Eisai, GE Healthcare, and Northwell Health Cancer Institute, and to tonight's webinar sponsor Sherry Helfand Wiener. Additionally, thank you to our summit program partners that you saw in the opening slides, and to the fertility organizations that have partnered with us for tonight's webinar. Today's webinar is being recorded and will be posted on the Sharsheret website along with a transcript. Participants' faces and names will not be in the recording. Still, if you'd like to remain private this evening, you have the option to turn off your video and rename yourself, or you could choose to call into the webinar. Instructions are in the chat box now for both options.
Melissa:
You may have noticed that you were muted upon entering tonight's zoom. Please stay muted during the call. We have a lot of people joining us, and this is the best way so that everyone can hear. If you have questions that arise during tonight's presentations, please add them to the chat, and we will do our best to get them answered during the q and a at the end of tonight's program. If you'd like to send a question privately, you can choose to send it to Melissa Rosen

Sharsheret when you go into the chat box. And that way, everybody will not see it. It will be an anonymous question.

Melissa:

As we move into the webinar itself. I want to remind you that Sharsheret is a national, not not-for-profit cancer support and education organization, and does not provide any medical advice or perform any medical procedures. The information provided by Sharsheret and tonight's speakers is not a substitute for medical advice or treatment for a specific medical condition. You should not use this information, of course, to diagnose or treat a health problem. And if you have any questions specific to your medical care, you'll be advised to speak with your medical provider.

Melissa:

Okay, let's get started. The topic, this topic, family building with a hereditary cancer mutation, is one of great importance. Sharsheret is currently in the process of creating a number of resources to support this community of women, and of men. We have heard from many women and men who carry mutations like BRCA, that when they begin to explore building their families, other cancer infertility organizations felt like maybe they weren't meant for them as there may not have been a cancer diagnosis, and infertility itself may not be an issue. We are working to change that at Sharsheret. By the start of 2024, we will launch a new section of Sharsheret's website dedicated to this issue, that will provide both information and a community with the generous support of Sherry Helfand Wiener. Details will be following shortly. You'll receive more information in this program's follow-up e-blast, including more information about the fertility organizations that have partnered with us on this specific webinar. Now, before we begin the program, I want to introduce to you Naomi, a Sharsheret caller who will share her personal experience with tonight's topic. Naomi, thank you so much for joining us.

Naomi:

Thank you. Thank you for having me. Good evening, everyone. I'm happy to be here to share my journey. And let me just say that I'm just thrilled to hear that this is a direction that Sharsheret is going in, because when I was going through the site, I didn't really have that much support. So it's really wonderful, and I'm excited about the next steps here. I found out I was BRCA-1 positive around 2012, which was shortly after my mother was diagnosed with ovarian cancer. At the time, PGT was not on my radar, in part because I really wasn't in the stage of my life where I was having children, but mostly because of my own ignorance. I didn't really know what was out there and what the options were. I only knew a few other carriers, like three, and one of them was my sister, and none of them I knew had done anything like this.

Naomi:

I wasn't connected to any kind of greater community, any kind of previvor community, and the doctors that I was working with at the time were part of a Catholic hospital system and didn't even inform me that this was an option that was available to me. So I really... Excuse me. It took me a minute. I stumbled into this world of PGT. A few years later. My mom had recently passed from her cancer. She had fought that battle against ovarian cancer and lost. And then right around that time, I became engaged to be married. And it was actually my now husband who suggested that we explore this option before having children. So we connected with an amazing doctor at this prominent IVF center to just learn more. He was totally on board, and I was very hesitant. I was not convinced. Even after this amazing first meeting we had where we really got a lot of our questions answered, I still had a lot of hesitation. The two biggies, I'm sure, come as no surprise. The first of course was cost, right?

Naomi:

The IVF cycle, the medications, the storage fees. There are a lot of zeros that are attached to this process, and there is no guarantee of success, and that's scary. The second big hesitation, which, again, I don't think is a surprise, was what it was going to do to my body. What was it going to do? How that was going to affect my relationship. We wanted to have kids right away, so that meant getting married and no honeymoon period. We would just be diving headfirst into this world of fertility treatments, and that was really overwhelming to consider. It was a really big decision, but ultimately I did take that plunge, and it was a challenge. My body went through the ringer. My emotions were all over the place. My bank account needed a major boost. All in all, I underwent five IVF cycles that were done almost back to back because my process involved what they call batching or storing embryos to use later. And it was a tough almost year, this rollercoaster of physical and emotional stress. I really made it through because I had a wonderfully supported partner.

Naomi:

I had an amazing doctor, and I took my self-care very seriously. I highly recommend that. Get a good heating pad, massages, cookies, whatever you need to treat yourself. Don't hesitate. For the day-to-day, I think it was really helpful for me to keep my eye on the prize. What was I doing this for? And to remember that the side effects are temporary and they're just not going to last forever. You're going to get through. For me, after those five cycles, I came away with five healthy embryos. Not great statistics, but it worked. I took four of those embryos to produce my family of two healthy, amazing children who have way too much energy. That's a problem I'm happy to deal with, and I'm just really grateful. Ultimately, I underwent PGT because, for me, I just wanted that peace of mind.

Naomi:

I didn't want to have my kids have to face the decisions that I have to make about my body. Obviously, of course, I also didn't want them to experience the outcome that my mother faced, and that felt right for me. But I do want to emphasize that PGT is not the only option, and I personally don't believe that there is a right or a wrong decision when it comes to PGT. I'll share that my sister chose a completely different path, and I'm fully supportive of that. We have this conversation a lot. BRCA is not a death sentence. You can live a vibrant, amazing life as a BRCA carrier. Children can as well, right? And I imagine that many of us on this zoom are living proof of that, right? We're doing this right now, so it's an option.

Naomi:

It's not the only one. It was right for me, but it's a personal choice. So I'm going to stop there and let the experts take the lead here, but I just want to thank you guys again for letting me share my story and I'm happy to share more if people have additional questions. And I'm just really grateful to be part of this supportive community.

Melissa:

Thank you so much, Naomi. And dare I say you are an expert yourself as well. Different perspective, but definitely an expert. Thank you very much for sharing your story. I also want to acknowledge that on today's call are two of my Sharsheret colleagues. Peggy Cottrell is a certified genetic counselor and Sharsheret's genetics program manager, and Erin Weinreich is a social worker and Sharsheret support program coordinator. They're going to be monitoring the chat boxes for any questions, and they're also going to be a part of today's q and a session after our main presentation. And of course, you know that they're available to connect after tonight's presentation. Their emails were just put in the chat. And if you would like to talk to one of our social workers for some support while going through this, Erin and our other social workers are there for you. And if you have questions about genetics as you're making these decisions, Peggy is also there for you.

Melissa:

So thank you to both of them for being here and now this evening, we are so honored to be joined by Dr. Sahar Wertheimer. Dr. Wertheimer is an esteemed obstetrician and gynecologist who possesses a multifaceted approach to her medical practice. She's fluent not only in English, but in Hebrew and conversational in Farsi, and she prioritizes providing the highest quality of care to all of her patients while supporting their fertility journey with the utmost respect and compassion. Driven by her passion for educating women on their reproductive health, Dr. Wertheimer goes above and beyond her clinical responsibilities. She currently serves as the chair of the Women's Health Committee for the Jewish Orthodox Women's Medical Association, or JOWMA, a program partner. On tonight's webinar. She's established a monthly webinar broadcast that tackles various women's health issues and attracts a substantial audience of over 2000 live viewers. Through these initiatives, she strives to empower women with knowledge and enable them to make informed decisions about their health, and that is what she's also going to be doing here with us tonight. Dr. Wertheimer, welcome. Thank you. And the screen is all yours.

Dr. Sahar Wertheimer:

Thank you. That was so sweet. I don't know who gave you that intro, but it was very nice. I'm going to upload my slides. One second. Oh, you might have to re-enable it for me. So as she's doing that, I'll just say... Oh, you're muted. Try again. Okay. Okay. Okay. So I am, as Melissa introduced, Sahar Wertheimer. I'm a fertility specialist at HRC fertility in LA. I do take a lot of pride in my passion being education. I also have to apologize. I don't think this is going to be my best talk ever. I have been totally consumed about what's going on in Israel. It's been, I'm sure for all of us, incredibly difficult to continue with life as we know it, but it is inspiring to see organizations such as this reminding us that cancer waits for nobody, neither does infertility, and we need to continue to find our purpose and move on.

Dr. Sahar Wertheimer:

So without further ado, so I wanted to talk a little bit about PGT and IVF and cancer screening panels, and I wanted to touch upon, first of all, cancer susceptibility genes, and then talk about just what is PGT, indications for PGT, and kind of describe that a little bit more in depth, and then a little bit more about the IVF process. Melissa indicated to me that a lot of people's questions have to do a lot with the IVF process. And from what Naomi said, I think it could be enlightening for many. Okay, so basically cancer susceptibility genes are genes that increase your risk for having cancer. We don't know about, and we cannot test all the genes and all the cancers, but there is a group that we have identified to increase somebody's risk because a lot of these genes are markers of checkpoints in your cell cycles that allow cell growth. And when these checkpoints are damaged, they allow continuous cell growth.

Dr. Sahar Wertheimer:

And sometimes just having inherited one gene being a little bit faulty sets you up for the other gene, having a mutation to it and having a higher risk than the normal population, which may have, for example, two healthy copies as in the BRCA1 and BRCA2 gene population. The BRCA1/2 have gotten a lot of press. I'll focus mostly on those because of the increased risk of breast and ovarian cancer, but just be aware that there are other genes that we can test for both in breast and ovarian. As you can see here, colorectal cancer is a big one, endometrial cancer, gastric melanomas, pancreatic, and prostate. And we are identifying more and more genes every day. I think whether or not to be tested for cancer susceptibility genes is a really difficult question for a lot of people. The reason is because it becomes somewhat of an ethical question, and also an anxiety inducing question. So a lot of times, cancer susceptibility genes are good to test for because we can increase your screening for your own incidence of cancer.

Dr. Sahar Wertheimer:

So for example, for the BRCA1/2, we know they increase the risk of both breasts and ovarian, and also they increase the risk, and this is forgotten, but prostate, pancreatic, melanoma. And so men should be tested and asked for their family history as well. But in the event that somebody tests positive for BRCA1 or 2, there's risk reducing measures. And I'll touch on that in a second. And this is a story I'll share from my personal experience with a patient. I had a patient who came in just for egg freezing and we kind of got into a conversation about whether she should be tested for BRCA because her mother had breast cancer and she's... I'm sorry, she was positive for BRCA1, and she was trying to decide if she should test her embryos for it. And she said, "If my mother had..." And this will always stick with me, but she had said, "If my mother had tested her embryos for BRCA and had not implanted any embryos with BRCA1, I wouldn't be here."

Dr. Sahar Wertheimer:

And that was very powerful for me because here is a woman with a great career, great friend network, doing amazing things in the world. And with some risk reduction, she really can reduce her risk to live a normal and hopefully long life. And so I always kind of keep that in mind in the back of my head. It's like this question can be very difficult for people. It's not an easy shoe-in conversation. Okay, so we've identified over 50 genes. Most of them are inherited in an autosomal dominant fashion, which means that their inherited pattern could affect 50% of their offspring. And BRCA1/2, like I mentioned, is not just breast and ovarian, but also endometrial cancer, prostate, pancreatic, and melanomas. So the BRCA1 and BRCA2 confer different risks of breast cancer and ovarian cancer.

Dr. Sahar Wertheimer:

The way we remember it for our boards is 20-40-80, that 20% of BRCA two, really it's 27%, will have a risk of ovarian cancer by the age of 70, 40, and really it's 46%, will have it by age 70 in BRCA one, and then 80% for both of them for the risk of breast cancer. And so those are very significant risks. Their treatment and the different risks have something to do with their status. So breast cancer in BRCA1 is most likely to be triple negative, meaning hormonal receptor negative, and BRCA2 is receptor positive, which sometimes can make it a little bit easier to treat as well. And this is just also an interesting point, but some data has actually shown a little bit of a decreased fertility, not to add to the anxiety of this, but just to really in the means of being more prophylactic and to take action proactively. We do see some data that BRCA1 has a lower ovarian reserve at baseline over the general population. And this study here shows about a 25% lower AMH than non-carriers, and that's very significant.

Dr. Sahar Wertheimer:

There actually has been some other studies that have pointed to other cancer genes as also having lower ovarian reserve than non-carriers. It's not limited to BRCA1, but for our purposes, this is what I'm familiar with. And it is also interesting to me that it's BRCA1 over BRCA2. But I think it also just speaks to the prophylactic measures that give us a reason to test for BRCA. So I wanted to touch on that next. What are the reasons to test for BRCA1, other than increasing our anxiety? BRCA1/2, if you were to test positive, there are things that you can do that can decrease your risk of contracting cancer almost to the general population. So that would be increased screening for BRCA. You can start earlier with breast cancer screening with mammograms, and alternating with MRIs to reduce the risk of radiation.

Dr. Sahar Wertheimer:

For ovarian cancer, unfortunately, this is a little bit controversial because we really don't have a good marker or good screening test for ovarian cancer, but there are some societies that would advocate for increased transvaginal ultrasound screenings, exams, but also really just to take signs and symptoms a little bit more seriously. And then there's also prophylactic measures that you can take. For example, being on birth control pills can decrease your risk of ovarian cancer, and then prophylactic surgeries. So this is the part that Angelina Jolie has made famous and has made a little bit more, I think accepted in society, but you can have a risk reducing surgery both for your breasts and for your ovaries. You can remove both your breasts and decrease your lifetime risk significantly. The same thing for your ovaries. Obviously, your breasts, you need them for maybe nursing. But other than that, your ovaries are a lot more significant in a sense that we need our ovaries for not just fertility, but the hormones that your ovaries give off are important for your bone health and your cardiovascular health.

Dr. Sahar Wertheimer:

And so a risk reducing oophorectomy, or taking out both the ovaries, is a very big decision because it will change the lifestyle in a sense that now, you'll need to be on hormone replacement therapy, you'll have menopausal symptoms potentially if you're not on hormone replacement therapy, or until we titrate your hormone replacement therapy to the right amount, you may have symptoms, and obviously, it ends your ability to have genetic children. And so that's another reason to test, in my opinion, because you can now freeze your eggs earlier and kind of make plans for that depending on your social situation.

Dr. Sahar Wertheimer:

And then obviously, the most important thing, which is what our whole talk is about today, is that you can decrease the risk to your progeny by doing PGT-M. And so I'm going to explain that a little bit more in detail. So what is PGT? So PGT stands for pre-implantation genetic testing, and that's because we can do testing at many different points in somebody's reproductive lifespan. So we can do genetic carrier screening, we can test the embryos once they've been created. And then once you're already pregnant, you can test your pregnancy with diagnostic testing as well. And so PGT allows you to test at the level of the embryos before you've had a pregnancy. And it's not only used for BRCA, we use it for many other purposes and can help obviate the need for a termination for medical reasons.

Dr. Sahar Wertheimer:

So PGT basically is after we have created the embryos, so after we take out the eggs... And I'll go through the whole IVF process in more detail, but once we've created embryos, we do a biopsy of the trophoectoderm, which are the cells that will later become the placenta. Usually, the embryos have reached this stage by day five, six, and seven of their in vitro life. We use different technologies, and this is constantly being a subject of companies coming and trying to sell their new technology to doctors and to see which one will be most accurate, but there's a range of technologies that we can use to then amplify the DNA and to pinpoint who has the mutation that we're looking for. So there's many different types of PGT. The two most common I would say is PGTA, which is almost standard for everyone going through IVF these days, where we can count how many chromosomes people have, sorry, the embryos have, and tell you if it's a normal or abnormal embryo, if it's going to lead to a healthy pregnancy or an unhealthy pregnancy.

Dr. Sahar Wertheimer:

And then we have PGT-M which will look for single gene mutations. This includes BRCA as well as genetic carrier screening that we do and other autosomal dominant mutations. So the way I explain PGT-M to my patients is if we know about a gene ahead of time, then we can test for it. And then there's PGT-SR, and PGT-P, which are not the focus of this talk, but may be very interesting in the future where we can look at polygenetic mutation patterns. Okay, so PGT-A, a little bit more in detail just to explain, PGT-A, A is for aneuploidy, which means an abnormal amount of chromosomes versus a euploid embryo, which is a normal amount of chromosomes. A normal amount of chromosomes would be 46. Most of us have 46 chromosomes where most of us are 46 XX, or females. And you can be 46 XY, which would be male.

Dr. Sahar Wertheimer:

And then there are some variations of 45 or 46 or whatever mosaics where they are compatible with life. For all we know, they look normal. You couldn't tell that they have an abnormal chromosomal pattern. But for the most part, the ones that are compatible with life and will lead to a healthy pregnancy, 46 XX or 46 XY, to keep it simple. PGT-A testing is 98% accurate, and that's the best that we have. It includes chromosomal numbers, so the 46 that we spoke about, and the gender. And my patients always like to know that, so I like to kind of add that on as a little cherry on the cake for doing PGT-A. What it does not tell us is multi-gene genetic disorders. So a lot of times, people want to know if it's going to detect autism or learning disabilities, and we don't have that capability yet.

Dr. Sahar Wertheimer:

There are, like I mentioned, new testing modalities that are looking for de novo mutations, so genes that we may not have known ahead of time, or panels that look at polygenetic inheritance, but I don't think we're there yet to offer it to everybody. It does not include blonde hair, blue eyes. That is a total myth, that you can create designer babies out of IVF. We don't do that. Not ethically, and also not scientifically. Okay. And then PGT-M, so this is, like I said, we know about a single gene mutation ahead of time. So the key word, the emphasis on the single gene mutation, and that's why a lot of times, we need to partner with genetic counselors in order to determine whether somebody is a candidate for the testing that will be helpful for PGT-M. For example, I can have a patient come in and say, "My mother passed away from ALS recently. Is that something you can test for?" And ALS is a complicated one.

Dr. Sahar Wertheimer:

There's many genes that can test for it. If I test for it and we identify a gene, what's the chance that that embryo is going to have that gene that's going to, sorry, that's going to lead to ALS. Is it worth it for you? Are there other genes that we may not be able... It's very complicated. Each disease process is its own kind of knowledge, and sometimes specialized genetic counselors that can speak to it. BRCA1/2, I feel pretty qualified to speak about because I counsel about it very often, especially because of the Jewish population, we have such a high frequency of it. I err on the side of caution and almost always advocate for my patients to be tested, even if they don't meet the standard... Sorry. So to take a step back, American College of Obstetrics and Gynecology, if you read their practice bulletins, they've put out a questionnaire. And from that questionnaire, you can determine who is indicated for testing for BRCA1/2.

Dr. Sahar Wertheimer:

And I just find that in the Jewish population, because our incidence is so high, that maybe we should err on even just... Not meeting the ACOG recommendations necessarily, but I counsel patients that if they want to be tested, as long as they understand what that means, they should be tested. Why not? So the other thing that we can test for, besides getting a family history and saying, "Okay, your mom had ALS or you have a very high incidence of colorectal or GI cancers. Is there something that we can find for that?" Everybody, everybody should be tested for a genetic carrier screening panel. And what that is a test for... These days, we can test for over four or 500 autosomal recessive diseases. And that's just looking for things that we may carry but we're not affected by. It is not necessarily looking for cancer susceptibility genes. It is separate.

Dr. Sahar Wertheimer:

And so everyone at baseline should have that test before they procreate because there's something we can do about it. We can create probes specific... If you and your partner were to overlap, your child has a 25% chance of not just carrying the disease but being affected by it. And some of them are very scary, and also a very high likelihood in the Ashkenazi Jewish population, like cystic fibrosis. And some of them may be an obscure enzymatic disorder that you may decide is not worth creating a PGT-M probe for, but still, in my opinion at least, knowledge is power. You can get onto Facebook groups that speak about it and kind of prepare for a life with a child that may have that. And so just to stress one more time, separate tests. Genetic carrier screening, your doctor should be offering it to you before you're procreating.

Dr. Sahar Wertheimer:
Cancer susceptibility genes, that's a conversation where you get a family history from a patient, they kind of red flag for something and you say, "Okay, let's see if there's a gene we can test you for that if we have a gene, and we can send them to a specialized genetic counselor or Sharsheret." In order to make a PGT-M probe, it usually takes six to eight weeks in order to create the probe. Sometimes it's more complicated and it requires something called linkage analysis where we need DNA from living family members. And that can be difficult sometimes too, because sometimes the family member that had it and prompted this whole exploration may not be alive, and we may not be able to get a live DNA. Different genetic platforms may offer different types of genetic testing. Some may offer de novo mutation testing where you don't necessarily need linkage analysis. So again, a complicated conversation. Reach out to people who know.

Dr. Sahar Wertheimer:
Okay. And now, I just wanted to touch on the IVF process and show you how PGT-A and PGT-M kind of comes into play in this whole thing. So I like to describe IVF as three parts. Part one, we get the eggs out. Part two, we fertilize them, we grow them to embryos, and we genetically test them. This is the in vitro part. And then part three, we transfer them back to the intended parent when they are ready. Could be the next month, could be years down the line. So part one in detail is we usually like to start with menses, and the reason is because... This is an ultrasound picture of the ovary. This is what the follicles look like on an ovary. Each of these follicles are fluid-filled egg sacks. Each one houses one microscopic egg. In a normal menstrual cycle, one of these jumps ahead and becomes the egg that you're going to ovulate that month.

Dr. Sahar Wertheimer:
It becomes the dominant follicle and prevents the rest of them from growing. We like to catch you before that happens and get all your follicles to grow. So this takes about two weeks of injectable medication, at which point you're probably coming in every other day for transvaginal ultrasound and monitoring. And we make decisions and titrate your medications accordingly. When the majority of your follicles look like they're ready, we'll tell you to take a trigger injection, which simulates your ovulation and causes the microscopic eggs to be released from the wall of the follicle. 36 hours later, we'll meet you in the operating room. You're under a light anesthetic so you won't feel it, you won't remember it. There was a podcast that was out recently called The Retrievals. It's scary. Don't listen to it. Most clinics do not use conscious sedation. That being said, we'll then retrieve these eggs using a transvaginal probe attached to a needle, poke through the vaginal wall, aspirate out all the fluid in the follicle, and with it comes your microscopic eggs.

Dr. Sahar Wertheimer:
Our embryologists are going to identify your eggs for us. And then if we're not stopping at the egg freezing stage, but if we're moving on to creating embryos, we will fertilize the eggs with sperm given to us by the partner that morning. And then the female is done. She's going to go home, she's going to recover, she's going to get her menses in another two weeks. In the meantime, now comes the in vitro part in the lab where it's seven days to grow out the embryos, and then we send off the biopsies. So like I said, the biopsy is a few cells of the trophoectoderm, or the cells that will later become the placenta. So they're not touching the actual fetus, or the inner cell mass that will become the fetus. This is good because we're not hopefully damaging anything that's going to become a pregnancy.

Dr. Sahar Wertheimer:
It's also good for your knowledge because sometimes these cells don't reflect the inner cell mass. And we know now that we can have mosaic cell patterns where some of the cells that will become the placenta show one chromosomal pattern and another set of cells will show a

different chromosomal pattern, and that becomes its own complicated discussion. So after we have biopsy the cells, we will freeze the embryos while we wait for the genetic results to come back. And that takes 10 to 14 days. In the meantime, like I said, the female is waiting for her menses, because most women will go on to do their transfer cycle, the cycle after. And then we'll start to prepare the uterus once we have a fresh lining. I think this is probably the most important slide. Naomi had alluded to the fact that you're not guaranteed anything. Unfortunately, that's true, and really, I think it's really important to set expectations at the beginning because it's an emotional roller coaster.

Dr. Sahar Wertheimer:

But I like to tell my patients, "The amount of eggs that I see on your ovary at the beginning of the cycle, the amount that I tell you is your ovarian reserve is not the chances of pregnancy that you're going to have." There's an IVF funnel. Unfortunately, we lose potential eggs along the way. So there's the amount of eggs that we retrieve, and then there's... Sorry. There's the amount of eggs we see on your ovary, and then there's the amount that we retrieve in surgery that had responded to medications. And then from those eggs, there's the ones that will be mature, capable of undergoing fertilization. And then from those, let's say we freeze eggs, eggs have an 80 to 85% thaw rate.

Dr. Sahar Wertheimer:

So it's quite conceivable you could lose some eggs on the thaw. From the mature eggs that thaw, we will fertilize them. We expect about 70% of eggs to fertilize. From those, we expect 50% to make it to the blastocyst stage where we're capable of biopsying them. From the blastocyst, those that come back. A normal chromosomal number depends on the female age at the time that she did the egg freeze. So a 35 year old has a 50% chance of having normal eggs. 50% of those embryos that we send off, we're expecting to come back normal. This doesn't take into account any cancer susceptibility genes or carrier screening genes that we've identified. You have to account for another 50%, if we're talking about an autosomal dominant disease, having that BRCA mutation, for example. If we're talking about an autosomal recessive disease, we have to account for another 25% to be not a carrier but affected. And the genetic report will tell us, this one's a carrier, this one will be affected, and this one is totally unaffected.

Dr. Sahar Wertheimer:

And so once we get that genetically normal embryo, then we can quote really great rates of success with implantation. We can quote, these days, 70%, maybe higher, with a healthy embryo and a healthy female. And that's amazing because a college aged couple in their prime fertility trying to get pregnant is only getting pregnant 25 to 30% of the time each month. So we've taken somebody older, potentially with other infertility causes, and it more than doubled your chance. But it's not truly magic. We did this whole finding a needle in a haystack, increasing efficiency outside of your body. And so just to kind of back up and give a very large overview of the timeline, because this is always inevitably the question I get at the end of every consult, the timeline is that from when we start with your menses till your egg retrieval is probably depending on whether we use a lead-in protocol or not, going to be two and a half to three and a half weeks. Okay?

Dr. Sahar Wertheimer:

Then you're waiting for your menses, which comes two weeks later, to begin to start the preparation of the uterus for a transfer. So I like to tell my patients, from time of retrieval until time of transfer is probably going to be about two months, and that's if we don't get interrupted by a finding on the evaluation of the uterus where we need to do a small surgery to remove it, to make the uterus kind of perfect for implantation. The nice thing I can say is that when we do the transfer and you become pregnant, and we do our first pregnancy test, we also give you back a few weeks because that embryo that we implanted was a day five embryo, and we implanted it in the what's supposed to be like your luteal or implantation phase of your cycle. So you're not like zero weeks pregnant, you're usually four to five weeks pregnant by the time of your first scan. So that is everything that I wanted to say. I'm happy to take questions. Again, I'm sorry it wasn't my usual caliber of presentations, but here we are.

Melissa:

Well, I actually don't think that's true. I think it was a fantastic presentation. And we received so many questions before the webinar even began, as well as some that were posted in the chat this evening. So I'm going to ask everybody, Sahar and Peggy and Erin to join me back on the screen. And let's get right to it because there's a lot of them. Okay. If a patient is... And I think this one's for Dr. Wertheimer. If a patient is otherwise not high risk, but there's a mutation in the family, does she need to be seen by a high risk OB/GYN?

Dr. Sahar Wertheimer:

No. So the high risk OB/GYN comes once you're already pregnant and only needs to be seen if there's a problem or a risk in the pregnancy itself, or with the fetus itself. So if you just have a mutation in your family, I would first recommend being seen by a genetic counselor or a reproductive endocrinologist to see if you can decrease the risk of having a fetus with that gene. If you are already pregnant, then in that case, you may need to be seen by a high risk obstetrician because they're the ones that do the diagnostic testing to see if that fetus is affected.

Melissa:

Okay. All right, thank you. That's helpful. So one thing that we haven't touched on yet is something actually that Naomi did touch on, which is the cost of this. So in your experience, and of course, everybody's insurance is different, but in your experience, first multi-part question, first, will insurance cover the cost for people who are mutation carriers but haven't necessarily had a cancer diagnosis, any part of it, the PGT, the IVF, the storage of eggs or embryos?

Dr. Sahar Wertheimer:

My experience is that some will, but the majority won't. So it really depends on what your insurance is. There are some better insurance coverage plans that are add-ons for employee benefits, like Progyny, that do an excellent job of coverage. Really depends. I think there is some funding. I'm not sure if you don't have a cancer mutation but you're a carrier, if places like Livestrong will help with funding and medications. I don't know. Maybe one of you has experience with that.

Melissa:

Yeah, we're going to actually talk about that in a second, but do you have... And you could tell me. This is not your part of the job and you don't know, but do you have a range of what people should expect to be paying if they had to pay it all out of pocket? And hopefully nobody does, but if that were the case, is there a range you could provide?

Dr. Sahar Wertheimer:

Yeah, my financial counselor might get mad at me, so don't quote me on any of this. We're not supposed to talk financials, but yeah, I think a ballpark is helpful. So for an egg freeze, we're not talking about adding the genetic testing because I cannot test an egg. It's only half of the DNA that we need for a fetus. Testing can only occur once you've created embryos. Genetic testing does add a considerable risk onto embryos. I would say for just standard PGT-A, from retrieval and transfer and all the genetic testing, it's probably about $23,000, $25,000. With the added PGT-M, depending on the mutation, could add another, I want to say $5,000

Melissa:

And that includes everything, including the IVF procedure and as many, many implantations as we're hoping or this patient needs?

Dr. Sahar Wertheimer:

That depends on the center. A lot of centers will have an a la carte option where you can kind of pick what you need, and some centers will have package options. At HRC Fertility, we do do cover all transfers until a successful one, a successful pregnancy.
Melissa:
Wow. Okay, great. So you know what, hopefully nobody does have to pay the entire thing out of pocket, between insurance and grants. I know you mentioned Livestrong. Some of the fertility organizations that have partnered with us this evening may offer some. But we also have a relationship with PAF, and I'm going to actually ask Erin to speak about that for a sec.
Erin Weinreich:
Sure. Hi everybody. Thank you both Naomi and Sahar for your beautiful presentations. I'm one of the social workers, as Melissa mentioned at Sharsheret, and we have a partnership now with an organization called the Patient Advocate Foundation where they are trained professionals to help on the insurance end with fighting denial letters or just getting more clear understanding of what insurances do cover, what they don't cover. And so if anybody has any insurance questions related to any BRCA gene mutation or cancer diagnosis, we help connect them with the Patient Advocate Foundation, that can then help them communicate and advocate for these procedures to be covered in some way, somehow through their insurances. So like Melissa mentioned, my email address is in the chat if you want to reach out and have us connect you.
Melissa:
Okay. We did get a question, Erin, specifically about PAF. Do you know if that organization helps in Canada as well, or is it just the United States?
Erin Weinreich:
Right now, I believe it's just the United States. I had somebody recently who was in Israel who they were looking for some assistance with. And so I think that they are just based in America right now. If anything does change, I will make sure that whoever asked the question will get that answer.
Melissa:
Thank you very much. Okay. Here's an interesting question. What are the risks... And this one is for Dr. Wertheimer. What are the risks of the hormones given to help with the whole process, that are often repeated over and over again in multiple series? So are there risks to either the woman or to a potential embryo with all of that hormones and medicines?
Dr. Sahar Wertheimer:
So there has been extensive data on this. To the woman, there is... And I'm not going to speak to women that have previously had, or that have had breast cancer, but the risk is we have not seen an increased risk of any cancers with doing multiple rounds of IVF, except for some very bad studies have shown an increased risk of a borderline ovarian tumor in women that have done I think upwards of six to eight cycles. And that borderline ovarian tumor is a pre-malignant tumor of the ovary. In and of itself, it's usually not... If you've removed it, it's not necessarily an indication for chemo or radiation. But like I said, not a great study. The overwhelming evidence does not show any increased risk in cancers. And it's really with higher order number of cycles, so I really only counsel on it in my patients that are doing that kind of stimulation number. Sorry. For risk to the fetus, so in terms of cancer risks or anything like that, there was one huge study.
Dr. Sahar Wertheimer:
I think it was a Dutch study where they have these crazy registrars, and they did show, out of millions of patients, a very, very tiny increased risk of cancer. And I don't think it was one specific type. I think it was just an overall increased risk. So it was significant because it statistically was modeled to show significance, but I want to say the risk was almost like 0.00 something. I don't even remember because I don't counsel on it. It's so small. In terms of the pregnancy, we are gathering more and more data that IVF pregnancies are at a slightly higher

risk of placental abnormalities, placentation abnormalities. So that means that the women, during their pregnancy, might be at a slightly higher risk of hypertensive disorders, preeclampsia, placenta previas or accretas and hemorrhaging, and risk of c-section. So I counsel my women, my patients on that, but again, a very slightly higher increased risk than the general population, and one that personally would not stop me from trying to do IVF.
Dr. Sahar Wertheimer:
And we know that if you do a natural transfer where we use your body's own hormonal feedback to thicken the lining of the uterus, as opposed to all medications, you can slightly mitigate that risk as well.
Melissa:
Thank you for that.
Dr. Sahar Wertheimer:
Yeah.
Melissa:
This question, I think, is for Peggy. So once somebody has made the decision to move forward with PGT, and I think Dr. Wertheimer touched on this, but maybe you can clarify for us, does the other partner, in other words, the one that is unaware of any mutation, need to have that genetic testing too?
Peggy Cottrell:
We generally think it's a good idea for the partner to consider testing. And especially if there's Ashkenazi ancestry, it wouldn't be that unusual to find a surprise BRCA1 or BRCA2 mutation. And you would want to have all the information about mutations from both sides of the family before you proceed with this. And we can help get genetic testing at a very affordable price here at Sharsheret.
Melissa:
Thank you. There are so many more questions and we have so little time, but let me ask two or three more. So this one might actually be for Erin as well. The number of appointments when undergoing this process can be dizzying. How important is it to add something else to your schedule by making time to speak to someone for support?
Erin Weinreich:
Sure. I think Naomi actually did touch upon this a little bit just in her own personal experience where her doctors felt differently than she did, and maybe her partner did, or just... There are so many moving pieces to all of this and there's so much information, and so support at every stage of this is of, in my opinion, utmost importance, whether that's with a mental health counselor, a social worker, a therapist, obviously, Sharsheret offers that, so one of the clinicians that we have, and even possibly peer support to just get that support at every stage of making these decisions. So the answer is very important.
Melissa:
Okay, thank you.
Naomi:
I know we're limited on time, but can I just echo that.
Melissa:
Please.
Naomi:
The number one thing when I talk to peers who are asking about this process,, is to make sure you have a strong support system. It is essential as you're going through this. And Sharsheret is a great resource for that.
Melissa:

Thank you, Naomi. Absolutely. So you've heard it from two people. Very important. Two more questions. Okay. If someone knows they carry a mutation and isn't partnered, is it better to freeze eggs now or wait until they have a partner and the embryo is possible? I understand the testing would need to be delayed, but is it important to freeze eggs?

Dr. Sahar Wertheimer:

Yeah, that's a great question. I would say it's better to freeze eggs than to wait, because the most important factor in your success is your age. And that's because with a younger age, we can get more eggs, and also better quality eggs. So quality and quantity, separate but related. And that ultimately starts that funnel wider and allows you to get more normals. So even though you may lose some eggs on the thaw, I would highly recommend not waiting for Prince Charming, but to freeze your eggs, and then when the time comes, do the genetic testing.

Melissa:

So I was going to ask you if there was an age that changed your answer, but your answer is no eggs, take care of the eggs if you-

Dr. Sahar Wertheimer:

Well, yeah. If you were not a genetic mutation carrier, then I would say in your young twenties, that's not really necessary. Maybe wait a little bit longer. But because the genetic mutation care is going to whittle anyways, you're probably going to want to do IVF. So why not do it when you're younger and have better quality eggs? And also because we know that with some of the mutations it can decrease your ovarian reserve and you may want to have risk reducing surgery. For all those reasons, I would say the younger the better.

Melissa:

Okay. This is the last question. And we really are up against the clock, so it's a big question that I'm going to ask you to answer very succinctly. So, I'm sorry in advance.

Dr. Sahar Wertheimer:

Okay.

Melissa:

Great way to end. What does the future hold for pre-implantation testing? Will we ever be able to test eggs instead of embryos? Are there any technological changes coming that would make success more likely, things like that?

Dr. Sahar Wertheimer:

Yeah, absolutely. So no, I don't think we're ever going to be able to test eggs because you need the complement of DNA. But the testing is already changing. It's already improving. Like I had kind of touched upon, we have platforms that are now offering de novo mutation testing, so that means they don't need a template in order to find something in the current embryo. And they're actually making arguments that maybe you don't even need to do genetic carrier screening because we're going to find whatever you have mutated anyway. So that's part of the things on the horizon, the polygenetic panels, very exciting, but also very scary capabilities on the horizon.

Melissa:

All right. Well, you can definitely know that when the next stage or something new comes out, Sharsheret will be there to help educate you about it. I know we need to wrap up now, so I want to start by thanking Dr. Weinreich for her insights, her passion, to my colleagues Peggy Cottrell and Erin Ash for their important contributions, for Naomi, who was so generous in sharing her story. Right now in the chat box, we are putting a link to an evaluation survey. Please take a moment to fill out a brief evaluation that's linked there. Anyone who completes the evaluation is even in the running for an Amazon gift card. I want to thank, once again, our sponsors and program partners for tonight's program, including Sherry Helfand Wiener, as well as all of the amazing fertility organizations we worked with.

Melissa:
And in our follow-up email, you will get a little bit of information about each of those fertility organizations. And thank you to our summit partners that are now in the chat box. I mentioned earlier... And of course, I mentioned earlier the upcoming webinars. So it continues throughout the month. Join us this Thursday, October 26th for our Sharsheret in the Kitchen with cookbook author and Sharsheret board member Kim Kushner, and on Monday the 30th, as we close this year's summit with a webinar on artificial intelligence and breast cancer. I think that's going to be a fascinating topic. There are links in the chat box now so you can learn more.

Melissa:
And please never forget that Sharsheret is here for you and your loved ones. Sharsheret provides emotional support, mental health counseling, and other programs designed to help you navigate through a cancer experience, mutation experience, and now we also know a fertility experience related to that mutation. All are completely free, completely confidential. Our contact information is in the chat right now. And as I mentioned before, our social workers and our genetic counselor are available to each of you. You are our priority. Please don't hesitate to reach out. The chat box holds the survey evaluation link one more time. And again, thank you for joining us, and we look forward to seeing you again. Goodnight.

Dr. Sahar Wertheimer:
Thank you for having me.