



## **Season 2, Episode 8: Beyond the Basics of Infertility Treatments with Dr. Anat Hershko Klement**

Benyamin Cohen:

This is Hadassah On Call: New Frontiers in Medicine. I'm your host, Benyamin Cohen. In each episode of this podcast, we'll get an inside look at what goes on behind the scenes at one of Israel's premier medical centers. We'll travel to Jerusalem to meet up with the doctors and nurses at the Hadassah Medical Organization. From striving for peace through medicine to performing surgeries with robots, they're working on medical breakthroughs that are impacting people around the world. That's what Hadassah is all about: the power to heal our world together. From cornea transplants to developments in pediatric oncology, we'll learn about the latest cutting-edge research coming out of Hadassah Hospital. All that, plus the inspiring stories of patients who have recovered from near-death experiences. Our appointment starts now. This is Hadassah On Call.

Benyamin Cohen:

The last week in April is National Infertility Awareness Week, which is why we decided to have as our guest today, Dr. Anat Hershko Klement. She's the director of the IVF Unit at Hadassah Hospital's Mount Scopus campus in Jerusalem. We had a fascinating discussion about fertility preservation, pregnant women and the COVID vaccine, and the doctor reveals what medical breakthroughs are giving her hope for the future. So without further ado, here's our conversation.

Benyamin Cohen:

Doctor, welcome to the show.

Dr. Anat Hershko Klement:

Thank you. I'm very happy to be with you.

Benyamin Cohen:

Well, we're over Zoom, so it's good to see you. Now that we have the vaccine, hopefully I'm looking forward to coming back to Israel soon and meeting you in person. That would be great. I know there's been a lot of lockdowns in Israel. How have you stayed productive and motivated when you're stuck at home?

Dr. Anat Hershko Klement:

Well, first of all, the IVF units and all of the reproductive actually treatments were locked down only at the very first one. Later on, we kept on our routine as usual. So the very first one was quite difficult, both for us and for the patients. We were all unsure about what's going to be, how their future will look like. It's an atmosphere of uncertainty, which I believe that not only Israelis have been experiencing, but it's a worldwide uncertainty, I think, we've all been experiencing this last year. So we were actually holding their fertility treatments at the very first lockdown a year ago. And later on, we just came back to routine.

Benyamin Cohen:

When you were growing up, did you know you wanted to be a doctor?

Dr. Anat Hershko Klement:

Actually, yes, but I had what we call differential diagnosis. I had a few other options in line, so I was considering to be a vet and eventually I married a vet.

Benyamin Cohen:

Oh, wow.

Dr. Anat Hershko Klement:

Yes. Then I started med school actually even before my military service. There's an option to do that in Israel. Then, I was having second thoughts, "Is it really what I want to do?" So I stopped everything up to one year, did my military service and then decided that's the right thing for me and went back to med school.

Benyamin Cohen:

I'm always curious about why people choose their specialization in medicine. I'm curious, why did you choose to work in fertility issues? Did fertility touch your own personal story in some way?

Dr. Anat Hershko Klement:

No, not really. The very first choice here in Israel is that you're doing your residency in gynecology and obstetrics. It's a six-year program that you're doing after you graduate med school. As part of this residency program, you are also exposed to the infertility field. So basically my first choice was the OB/GYN field, which encompasses everything. Both surgical aspects, internal medicine, you can deal with ultrasound imaging, you can do endocrinology, like we do, the infertility specialists. There are so many aspects combined into one profession that it's really amazing. You can find your way along the residency program. I didn't always know that I'm going to end up as a fertility specialist, but during the last two years of my residency program, I found it the most fascinating field. I see it as a privilege to face these women, couples, and to be able to assist them in their journey to become parents. After doing it for many years, I still feel very, very privileged.

Benyamin Cohen:

Have you always been at Hadassah? How did you make the decision to work there?

Dr. Anat Hershko Klement:

I actually live in the center of Israel, though, I know that for Americans, Israel is a tiny drop. I still live in Tel Aviv region and I was working there as a senior physician in one of the public hospitals. Then, I was offered to join Hadassah as a unit director. Of course, I was very honored to become one of the Hadassah physicians. And for the last year, that's what I've been doing.

Benyamin Cohen:

You know the last week in April in America, we call it National Infertility Awareness Week. It's always interesting, on the one hand, we read about so many people, like celebrities, who are struggling with infertility and they make it common, make it popular, make it something that people discuss, which is great. But on the other hand, I think, and I've even had people in my own family who have had issues with fertility, it's almost a taboo conversation. It's hard that people don't want to talk about it in public. And so, it's hard to know just how prevalent infertility really is. So how common is it, I guess, is the first question I have?

Dr. Anat Hershko Klement:

Well, generally speaking, we assume that around 10% of couples trying to conceive will face an infertility issue. Obviously, it's a changing concept since the age of conception has gone through a tremendous change in the Western world. Women, with all their rights, they are pursuing their careers so they are postponing conception age until their late thirties sometimes. So obviously, in this kind of reality, you can assume that fertility will be an issue because of the age, not because any other changing reasons, but that's a very important thing. In parallel to this trend in the Western society, we're also becoming more and more aware to fertility preservation decisions, which are taken. Women are becoming more aware of the option to what we call to perform a social egg freezing, meaning they don't have an indicated medical reason but they choose to do it in order to make sure that they have some kind of insurance in case they will have reached a decision to have a family in their late thirties or even in their forties.

Benyamin Cohen:

How do you define infertility? How do you know if a couple is trying to have kids, at what point do you put that definition into place?

Dr. Anat Hershko Klement:

Yeah. So there's a clear definition. The definition is one year of unprotected intercourse without achieving a conception. That's the medical strict definition. It doesn't mean that you have to find out why, if a woman or a couple addresses you earlier, especially after the age of 35. Because of the tremendous effect of the age over fertility, women addressing us after six months of trying to conceive and failing to reach a conception, we will start investigation as soon as six months if the woman is older than 35 years old. Basically, we don't necessarily wait one year. In addition, we don't wait for one year if there are additional causes. For example, if a woman addresses the infertility clinic and she's 40, then you'll obviously advise her in a different way than you will advise a 25-year-old woman who addresses the fertility clinic, right? In any case, that she went through a surgical procedure involving the ovaries. In this case, you also be very cautious in telling her to wait more. You will do at least part of the investigation to make sure that you can tell her to safely wait and not do something as soon as possible.

Benyamin Cohen:

What's the percentage of – we've talked about women – what's the percentage of male infertility?

Dr. Anat Hershko Klement:

Yeah. That's an interesting question. It's quite different, I think, in one place in the world than the other. We know that male infertility is responsible for at least 20 to 40% of couple infertility. But from my experience, in some places in Israel, it's might be even as high as 50%. I think in Israel, we get to see a lot of male infertility. It's interesting. I don't think it was investigated in terms of research, but that's at least the reality that we face here.

Benyamin Cohen:

Do we know why?

Dr. Anat Hershko Klement:

No, that's what I said. No. I don't know any research that gives us explanations for why is it so common, but we get to see it a lot.

Benyamin Cohen:

I'm fascinated about how the views of infertility have changed from 20 years ago, let's say. Are you seeing more single women or religious women, Jewish or Arab, then you have in the past?

Dr. Anat Hershko Klement:

Yes, definitely. I completely agree. Yes. I think our society here, at least in Israel, is more flexible regarding the terminology of the family. A family can be a mother and a father, two mothers, two fathers, it can be a single parent. As long as you are accepting all these definitions and society is more flexible about it, then yes. For sure. We see much more different kinds of families addressing us for assistance and single mothers using donor sperm. I don't have numbers or figures. Regarding the more Orthodox population: I can even tell you that for this last year, generally speaking, we've been facing a tremendous increase in fertility preservation cycles. So egg freezing, socialized egg freezing I was talking about earlier. A great percentage of these patients are defining themselves as religious. I think this is a very impressive change in the Orthodox population, realizing that if you wish to preserve fertility, then that's the efficient way to do it.

Benyamin Cohen:

It's interesting because in both religious Jewish and religious Arab populations the role of families is so important.

Dr. Anat Hershko Klement:

Yeah. I think if you're acknowledging the importance of family and you see yourself in the future as a parent, then you realize that's a very efficient way of ensuring it.

Benyamin Cohen:

When we return, Dr. Hershko Klement talks about the root causes of infertility and the medical breakthroughs happening around fertility preservation.

Dr. Anat Hershko Klement:

That's a true revolution. We can talk about, you can discuss a few revolutions in our field and one of them is definitely the method of freezing.

Benyamin Cohen:

All that and much more after a quick break.

Benyamin Cohen:

With the COVID-19 vaccine now being delivered across the globe, Hadassah Hospital is at the forefront of caring for patients in a post-pandemic era. Hadassah recently opened a multi-disciplinary clinic to help treat people suffering from COVID after-effects – everything from lung damage to mental health issues. Keep up to date with everything that Hadassah Hospital is doing to help combat this deadly disease by visiting our website at [hadassah.org/covidupdates](https://hadassah.org/covidupdates). That's [hadassah.org/covidupdates](https://hadassah.org/covidupdates). We're posting frequently about how our doctors, nurses and researchers are working to roll out the vaccine and prevent the further spread of COVID-19. You can also follow Hadassah's latest coronavirus updates on our social media accounts on Facebook, Instagram and Twitter.

Benyamin Cohen:

And now back to our conversation with Dr. Anat Hershko Klement, the director of the IVF unit at Hadassah Hospital's Mount Scopus campus.

Benyamin Cohen:

We've talked about age and I'm wondering besides age, is there another common reason why women would have trouble conceiving?

Dr. Anat Hershko Klement:

Oh, there are what I call the traditional reasons. So there are mechanical problems involving the fallopian tubes, which are transferring the embryo to implantation into uterus. These tubal factors are quite common. We were discussing male factor, but that's in cases of couples. There are problems related to ovulation, all kinds of ovulatory disorder that we know. And there is the most frustrating thing: there is the unexplained infertility. This is very frustrating for both patients and physicians, where you did the entire investigation and you couldn't track a reason. You cannot tell the couple or the woman why she or they are facing a difficulty. These are around again, we come back to the 10% rule, 10% of our patients are facing unexplained infertility.

Benyamin Cohen:

Is there anything that a couple can do to help boost their fertility?

Dr. Anat Hershko Klement:

Like what? What do you mean?

Benyamin Cohen:

I mean, I don't know if it's food or exercise or some kind of pill, maybe some kind of vitamins. I don't know.

Dr. Anat Hershko Klement:

I think there is something that they can avoid. Smoking. That's the most deleterious exposure we know of, which has a very tremendous effect over fertility. We know we can measure it infertile patients. For the same age of the female patient, exposure to smoking will reduce the number of retrieved eggs by

half. That's a lot. Yes. So definitely smoking is the thing that you should avoid if you want to keep your fertility, because it's not only the nicotine, it's all the other toxins that are in there. Other than this, of course, keeping a healthy diet, doing exercise, keeping your BMI in the normal range. All of these, of course, can contribute to fertility and to the successful implantation. But I wouldn't call it a boost, it wouldn't boost your fertility.

Benyamin Cohen:

I would assume there's some genetic issues as well, that there's nothing they can do about. Is that correct?

Dr. Anat Hershko Klement:

These are not that commonly acknowledged, both for the male and a female. So we find more and more genetic causes that can explain severe sperm issues and severe egg depletion in an early age. But these are only a few. We still cannot offer a screening panel that can diagnose genetic issues for infertility. We're not there yet.

Benyamin Cohen:

You've talked a lot about fertility preservation. So there's lots of different reasons, lots of different ways people can do this. If you have a woman who's getting older and wants to, like you said, have an insurance policy, she can preserve her eggs. But then there's also a situation where you have, let's say a kid with pediatric cancer or a teenager with pediatric cancer, and before they do the chemo treatments, there's a way to extract and freeze that so that when they are older, they have those options available. Is that something that Hadassah works in, in all these different types of areas with fertility preservation?

Dr. Anat Hershko Klement:

Yeah, of course. We deal with medical fertility preservation as well as the social cases. There are, as you said, there is always the option of performing a tissue preservation, but that's a complicated thing to do because you have to perform a procedure in order to remove the entire ovary in the very young pediatric population or a piece of the ovary. If the patient is older and then you have to preserve the cortical tissue of the ovary, being hopeful that your patient will recover. We know that the oncologist did the tremendous improvement and we have more and more cancer survivors. Of course, if the chemotherapy was turning the young patient infertile, because we know that the chemotherapy can completely destroy the ovarian reserve, then we can offer implanting those cortical tissue back. That's another operation. Okay. So obviously you need to know that the tissue that you're transplanting back is not harboring any malignant cells. But yes, that's a very important aspect in the fertility preservation of the pediatric population.

Benyamin Cohen:

Again, with fertility preservation, I want to know about the advancements that we've had in the last generation or so. It used to be something called slow freezing, and now there's flash freezing. Can you explain the difference?

Dr. Anat Hershko Klement:

Yeah. That's a true revolution. We can discuss a few revolutions in our field and one of them is definitely the method of freezing. So we were discussing social egg freezing, how come we can assure our patients that when you're back, the eggs will survive the thawing, will be fertilized, and will develop into an

embryo. We can do that because of this flash freezing technique, which is called vitrification. That's a very efficient procedure performed by a well-trained embryologist that can freeze the eggs and the embryos in a way that will avoid their destruction during the procedure and has very successful thawing rates. It's revolutionized our entire attitude because in fertility medicine, we're all trying to avoid a complication called ovarian hyperstimulation syndrome. This syndrome is highly related to pregnancy. In the past, pregnant patients were, on one hand, very happy to become pregnant, but on the other hand, had a very high chance to suffer from ovarian hyperstimulation syndrome.

Dr. Anat Hershko Klement:

This complication can get quite serious because it can cause breathing difficulties and hypercoagulation, very prolonged hospitalization. If you know that you can freeze the embryo and wait until the entire hormonal storm has settled down, and then you can safely implant the embryo into the uterus without any complication but with the same success rate, maybe even more, then everyone is happy because you're still keeping your pregnancy rates. And I said, maybe even increase your pregnancy rates and I can explain why. But, you can avoid the most serious complication of the OHSS, the ovarian hyperstimulation syndrome. We can do it safely now thanks to the vitrification, to the flash freezing you were mentioning.

Benjamin Cohen:

Are there differences in fertility preservation in Israel versus the U.S.? I was reading a statistic that said in Israel, 70% of female cancer patients opt for fertility preservation compared with 50% elsewhere in the industrialized world. Why do you think that is?

Dr. Anat Hershko Klement:

It's a matter of awareness and of what we call multidisciplinary attitude. So as long as in your hospital, in your center, you have a very good communication with the oncologist and your oncology coordinator and you have a trained staff that you can very quickly be recruited to perform fertility preservation, then it works. But I think all over the world, the Western world, we should say, people are becoming more and more aware. If you read the statistics about what percentage of oncology patients are being offered fertility preservation, we're rising. The trend is rising everywhere. Here we also have, for example, we have the breast oncology center. We discuss the patients together. If they refer a patient to us, we see them immediately. We're also holding together a BRCA clinic.

Benjamin Cohen:

A BRCA gene.

Dr. Anat Hershko Klement:

Exactly. So we have a BRCA clinic together with the oncologist. We make sure that we're together, give the patients the entire consultation that they need.

Benjamin Cohen:

A few months ago, I was interviewing one of your colleagues who opened up what they call I think a post-COVID clinic for people who have had COVID, but they have strange after effects. He was telling me the reason they're so successful at this clinic is because it's multidisciplinary. And so you have patients whose after-effects can run the gamut, whether it's a lung issue, a digestive issue, a neurological issue, a psychological issue, and all of these doctors are able to help out.

Dr. Anat Hershko Klement:

Yeah. I agree. When you have a multidisciplinary team, things work better. Here in Mount Scopus, we have, for example, the recurrent pregnancy loss clinic. So there is an infertility specialist and endoscopists, specializing in uterine procedures, and we have a psychologist and we have a nurse and we have a geneticist. This is exactly, I think, the right attitude to treat your patients, because it's not only a matter of surgery, it's not only a matter of genetics, right? You need to have good psychotherapy in order to deal with such a devastating situation. So, I think that's the best, the teamwork. That's the key.

Benyamin Cohen:

When we return, the doctor talks about her research at Hadassah Hospital and the importance of getting all of her fertility patients vaccinated against COVID.

Dr. Anat Hershko Klement:

Obviously we're looking into the COVID vaccines as everyone, trying to realize if this... Israelis are very bothered by a possible effect of the vaccine over fertility, though there is absolutely no evidence that a vaccine can harm your fertility. So we're trying to look into this as well.

Benyamin Cohen:

All that, and much more, after a quick break.

Dina Kraft:

I'm Dina Kraft, the host of a podcast called "The Branch," which tells the stories of relationships between everyday Israelis and Palestinians, Jews, and Arabs. Amid conflict, entangled histories, stories of human connections and friendships can get lost. The mission of this podcast is to find them and bring them to you. In this season, I talk to artists, midwives, soccer teammates and environmentalists. All of them and many others, too, who work together in spite of the barriers between them. "The Branch" brings you stories of real people forging strong connections and having important conversations, even when it's complicated. Brought to you by Hadassah. Find us anywhere you listen to your podcasts or [Hadassah.org/thebranch](https://www.hadassah.org/thebranch).

Benyamin Cohen:

And now, back to our conversation with Dr. Anat Hershko Klement.

Benyamin Cohen:

I want to talk about your research specifically. I know we've talked a lot about infertility in general, but I want to talk about your research specifically. You've looked at how the impact of miscarriages and how they may or may not impact future fertility issues. Can you explain that and anything else you've learned about how miscarriages impact fertility?

Dr. Anat Hershko Klement:

Yeah. So it's very interesting. We've done the research, which was now during the last week it was submitted for publication. It has not yet been published. We try to look into the possible correlation between recurrent pregnancy loss and future cancer morbidity. Okay. You've asked why? Why is it even related, right? How can recurrent pregnancy loss effect future cancerous events? So our thoughts were that a certain type of cell called natural killer cell, which may be more active in cases of recurrent



pregnancy loss, which were not explained. We could not find out the reason for the recurrent pregnancy loss. Maybe this hyperactivity of the natural killer cells is actually beneficial against cancer cells developing during life. This is just a theory. We didn't prove it. Okay. But we did follow for long term patients with recurrent pregnancy loss. We were assisted by the National Registry of Cancer in Israel.

Dr. Anat Hershko Klement:

There is a registry, every cancerous morbidity in Israel must be reported to the center. It's something that you can completely trust when you do research, that you know you can identify your cases. Together with the Sheba Medical Center and the Israeli Center for Disease Control, which is the cancer registry, we followed these patients with recurrent pregnancy loss and compared them to patients that gave live birth in the same year. We could compare the exposed population and the non-exposed, which gave birth to a live child. We were very surprised to find out that there is a significant decrease in the gynecology-related morbidity in their recurrent pregnancy loss population. This is a very initial cohort. We think that other groups should follow and we will have to look into it if it's indeed consistent and other cohorts show the same biological behavior.

Benyamin Cohen:

Is doing medical research like this easier in Israel because of the socialized medicine and you have so much data available?

Dr. Anat Hershko Klement:

Yeah. I think because it's a small place, you know everyone. The atmosphere is definitely collaborative. I think I had a very good experience lately with such collaborations. And obviously, once collaborating, you can have a larger cohort and your conclusions are based on more data.

Benyamin Cohen:

Right. Is there any other research you're working on now that is giving you hope to help your patients conceive in the future?

Dr. Anat Hershko Klement:

There are a few things I'm looking into. I don't know if they can change the reality, but at least give some reassurance. For example, a big research project we've been doing with Clalit look at Clalit's health services, looking into infertility among rheumatology patients. We're trying to test whether a certain exposure to specific categories of treatments used by rheumatologists in different disease conditions may or may not reduce their fertility potential. I think, no. I think the answer is no, but I think it's a very reassuring finding that we will report soon. I hope. That's one example. There are a few things going on. Obviously, we're looking into the COVID vaccines, as everyone, trying to realize ... if Israelis are very bothered by possible effects of the vaccine over fertility. Though there is absolutely no evidence that the vaccine can harm your fertility. So we're trying to look into this as well.

Benyamin Cohen:

Is there a public health campaign to ease people's fears about getting the vaccine if they're pregnant?

Dr. Anat Hershko Klement:

Well, there are the guidelines of the Israeli societies that completely support the vaccination. Obviously, the easiest thing will be to get a vaccination before pregnancy. Here in the fertility clinics, that's the best spot to do because you offer your patients, they're addressing you for infertility and you advise them: Get a vaccine and then we'll start the treatment. That's so much easier than having doubts once you're pregnant, if to complete a vaccine or no.

Benyamin Cohen:

Let's say a woman is already pregnant. Is there an appropriate time for her to get the vaccine or as soon as possible is the correct answer?

Dr. Anat Hershko Klement:

The problem is that we don't have validated data yet that we can present and say, "Listen, these are the number of pregnant patients that were vaccinated. This is the complication rate. There is absolutely no risk to the fetus or the mother if you're doing it in the very first trimester." We're still not there yet, but we're gaining more and more information and data regarding the safety of the vaccine. As I said, Israel now offers the vaccine to pregnant patients at any point, but with a certain, how would I call it, giving you some room to think in the first trimester. So in the first trimester you can consider if to complete the trimester and then perform the first vaccine. That's something to consider because it's mainly because we think that any bleeding or any complication, the vaccine will be blamed for it. Okay. Not because necessarily it has any causal relationship. Okay.

Benyamin Cohen:

It seems like it's almost a perception issue that you have to battle.

Dr. Anat Hershko Klement:

Exactly.

Benyamin Cohen:

What medical changes in the area of infertility would you like to see happen in the next decade or so?

Dr. Anat Hershko Klement:

First of all, the most challenging thing is how come that even if you transfer an embryo that you've tested genetically and is normal, how come that the chance for pregnancy is only 50%, right? That's a riddle. There's something in the implantation that we have to understand better. I think we have to dig in this implantation and understand more the uterine part of it. The uterus is something we have to understand more. I'd be very happy to get a more clear notion about the endometrium, the cascade of implantation and how can we work it out better. That's one thing. Obviously, our ability to assist patients who lost their ability to conceive because the ovary behaves sometimes in your early twenties or thirties as if they were menopausal. Okay. At this point, there's nothing we can... Well, sometimes there's something we can do, but most usually there's nothing we can actually do to cure them unless they happen to freeze their eggs in a very early point in life. I think we'll get there when we will be able to take a cell from a different tissue and educated it to become an egg, an ova, and perform a fertilization. I think that's enough to start with.

Benyamin Cohen:

Do you foresee a time in the future when, I don't want to use the word cure, but when infertility is not as big an issue because of medical advancements?

Dr. Anat Hershko Klement:

Yeah. Most definitely. I think our ability to educate cells, as I told you, and turn them into something else, that's a game changer. It will happen. Yeah.

Benyamin Cohen:

You think it will happen in your lifetime?

Dr. Anat Hershko Klement:

Yes, definitely. I plan to live more than 10 years. Yeah. I think we'll get there.

Benyamin Cohen:

Dr. Hershko Klement, thank you so much for joining us today. I know we caught you in between procedures today to have this conversation. So I know you're busy and I really appreciate you taking the time to chat with us.

Dr. Anat Hershko Klement:

Thank you. It was my pleasure and I really wish to meet you in person here in Jerusalem.

Benyamin Cohen:

I look forward to returning. Thank you so much.

Dr. Anat Hershko Klement:

Bye, bye.

Benyamin Cohen:

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