

# Yale CANCER CENTER *answers*

WNPR Connecticut Public Radio



## *Hosts*

### **Anees Chagpar MD**

Associate Professor of  
Surgical Oncology

### **Francine Foss MD**

Professor of Medical  
Oncology

## Options for Fertility Preservation in Patients with Cancer

### **Guest Expert: Emre Seli, MD**

*Professor, Obstetrics Gynecology and  
Reproductive Sciences; Director, Division of  
Reproductive Endocrinology and Infertility;  
Chief, Reproductive Endocrinology and  
Infertility, Yale School of Medicine.*

## **Yale Cancer Center Answers**

is a weekly broadcast on

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*Welcome to Yale Cancer Center Answers with your hosts doctors Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medicine in the Section of Medical Oncology at the Yale Cancer Center and she is an internationally recognized clinician and clinical researcher. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. Yale Cancer Center Answers features weekly conversations about the most recent advances in the research diagnosis and treatment of cancer and if you would like to join the conversation, you can submit questions and comments to [canceranswers@yale.edu](mailto:canceranswers@yale.edu) or you can leave a voicemail message at 888-234-4YCC. This week you will hear a conversation about Fertility preservation and patients with cancer with Dr. Emre Seli. Dr. Seli is Professor of Obstetrics Gynecology and Reproductive Sciences, director of the division of reproductive endocrinology and infertility and chief of reproductive endocrinology and infertility at the Yale School of Medicine. Here is Dr. Anees Chagpar.*

Chagpar Emre is got a lot of titles. Tell us a little bit more about what exactly is your special theme what you do?

Seli So, I am again, I am a faculty at Yale within that context I do take care of patients, but also perform research in animal models. The aim, what I do overall, is to help women get pregnant and everything that I do in the laboratory and in the clinical practice is toward that goal.

Chagpar So, really we are talking about fertility preservation and allowing women to have the experience of getting pregnant and having children. Tell us a little bit more about how that is impacted by cancer?

Seli Cancer treatment generally involves either radiotherapy when radiation is given to patients or chemotherapy and both treatments have a significant negative effect on female fertility. The main reason for that is, women are born with a finite number of eggs that they spend during their reproductive lifetime and any negative impact on their body, at any given time, would affect all their eggs. This is unlike men who continue to make sperm during their lifetime. So, cancer treatment, either with radiotherapy or chemotherapy, would affect a woman's ability to have children in the future.

Chagpar Let's say a woman gets cancer or there are certain kinds of cancers that affect fertility more than other kinds of cancers or certain kinds of chemotherapy that affect a woman's fertility more than other kinds?

Seli That is a good point. Basically, it is not the cancer itself that affects fertility but what we do to treat the cancer. Therefore, the cancer's impact on female fertility is much more determined by when it occurs. Today, the most important cancer as far as female fertility is concerned is breast cancer, not because breast cancer affects fertility in a bad way, although most breast cancers are in older ages, it is the most common cause of cancer at the reproductive lifetime of a woman, therefore, the treatments that we perform to treat breast cancer negatively affect female fertility,

**3:52 into mp3 file [http://yalecancercenter.org/podcasts/2014\\_0330\\_YCC\\_Answers\\_-\\_Dr\\_Seli.mp3](http://yalecancercenter.org/podcasts/2014_0330_YCC_Answers_-_Dr_Seli.mp3)**

and also as far as the chemotherapies, there are certain medications that affect DNA stability in the egg and because in the egg the chromosomes are about to be divided and anything that we give the patient, any medication that bothers that process, it will have a negative impact on fertility.

Chagpar So, particularly for breast cancer this is something that needs to be considered, so let us suppose you are a young woman and you happen to get breast cancer and your world has just been spun upside down because now you have given this diagnosis. Is there any way, after you have dealt with the breast, after it has been treated, that then you can try to restore your fertility or is this something that you really need to think about before the treatment starts?

Seli Another very good question, before, it has to be done before. A few concepts are that because of the available treatments and because again, of the available finite number of eggs that are present in a woman's body, we have to make sure we protect those eggs and interventions to protect those eggs should be done before we give a high dose chemotherapy that may basically kill all of them. Not all chemotherapies are equally bad, and certain chemotherapies, especially the ones that are very strong and are done prior to bone marrow transplantation, those are the worst ones, so if a woman passes the first one or two stages without preserving her fertility, she could still go back and do fertility preservation prior to the most intensive chemotherapy. But the most effective intervention would be before the cancer treatment.

Chagpar For a lot of patients then this is just another thing to think about, they are diagnosed with cancer, they are thinking about life and the universe and everything now that they have been given this diagnosis, but it is important that if they are thinking about having children afterwards that they think about fertility preservation as well. What are the options for them in terms of fertility preservation? As you tell us about those options let us know a little bit more about how long each of those options takes, because I am certain that there are women who say, I really want to have children, but I really want to live more. I really want to get my treatment done in a timely fashion and I do not want to take that risk.

Seli It is actually very simple. There are four main options referred to in preservation today. Two of them are considered established options and the other two are more experimental. The first one, the most established one, is cryo-preserving embryos. This means getting eggs from a woman, making the eggs with the sperm from her partner or her husband and then freezing the embryos. This is a very well established procedure, not only for cancer patients, but for any woman who is undergoing fertility treatment for any reason. It is done maybe 30,000 to 40,000 times in the United States every year. Protocols are very clear. To do this, you need between two to four weeks in order to obtain the eggs and because you need to obtain the eggs there are certain downsides to this approach and the most important one is the need for sperm. Of course a woman could also use donor sperm, but it is a really difficult concept to grasp at that time as you are also diagnosed with cancer. There is also another issue about ownership of the embryo if a negative outcome came from the cancer treatment and that generally causes a negative impact on the decision making process. So the first option is embryo freezing, and the second option is freezing

**8:18 into mp3 file [http://yalecancercenter.org/podcasts/2014\\_0330\\_YCC\\_Answers - Dr Seli.mp3](http://yalecancercenter.org/podcasts/2014_0330_YCC_Answers_-_Dr_Seli.mp3)**

eggs. This was not a successful procedure in the past, but in recent years, in the last five years or so, it has become more and more efficient and in the last year, the American Society of Reproductive Medicine removed the label 'experimental' from this procedure and now this is an established fertility preservation procedure. You still need time to get the eggs, the same time that you needed for embryo freezing. However, it is much easier because you do not need to have a partner or accept donor sperm and there is no confusion about who owns the egg. So those are the two main approaches that we have today for fertility preservation. This third one, which still is considered experimental, is to freeze the ovaries. This approach is extremely useful especially for prepubertal girls from whom you cannot obtain eggs. You can't freeze eggs or embryos from prepubertal girls but you can get a piece of the ovary. Once you obtain the ovary and after the cancer has been treated, you can put the ovaries back into the body. You can either put them back into where we took them from and where the ovaries used to be, or you can also put them back in another part of the body.

Babies have been produced through ovaries that were removed, frozen, thawed, and put back into the same person. Worldwide there have been more than 100 births through this process. However, it is still an experimental procedure. It is quite cumbersome to undergo a surgery and then the freeze and thaw procedure, there are still issues with it, but most importantly the eggs that are in the ovary prior to hormonal stimulation are not mature eggs and the procedure that we called in vitro maturation of eggs obtained from the ovary has not been perfected. So as of today, we are not able to efficiently get an egg from a frozen and thawed ovary in the laboratory and make that egg into an embryo. We do not know how to do that. There has been significant support from the National Institutes of Health. We have done a lot of research in this type of fertility preservation, but it is streamlining it that is the issue. And the fourth approach is not freezing anything, but it involves giving a medication to the woman that would put her into a semi-prepubertal stage. It will push her to an immature ovarian state and there is a belief that if we do that, the ovaries are less affected by the chemotherapy. We do this by affecting the function of a hormone that is secreted by the brain and we can easily do this, it is a single injection, it is not very invasive and it does not take any time, except the jury is still out about whether this is really a useful procedure and also we really do not know the mechanism by which this should work. We prefer quite a bit of a series of experiments in our laboratory and we could not find why it should be helping humans, but there is some data that it could be, so it is offered to women, because it does not have real concerning side effects, it does have some side effects but nothing compared to chemotherapy.

Chagpar Does it affect the treatment that a woman would get with her cancer?

Seli It does not. The first two, embryo cryopreservation and also a cryopreservation would delay cancer treatment up to a month. The most important group of women with cancer who come to us for fertility preservation are women with breast cancer. What happens usually is that these women undergo surgery and there is a period between surgery and chemotherapy, and we try to fit our freezing into that window. Ovary cryopreservation is a surgery. If the woman is undergoing a surgery, then we get a piece of the ovary and there is no time spent other than just freezing the ovaries and the fourth option does not require any lag time.

12:59 into mp3 file [http://valecancercenter.org/podcasts/2014\\_0330\\_YCC\\_Answers\\_-\\_Dr\\_Seli.mp3](http://valecancercenter.org/podcasts/2014_0330_YCC_Answers_-_Dr_Seli.mp3)

Chagpar Let's talk about each of those four options in greater detail. It seems to me that the first two options, the established options, involve freezing of either the embryo or an egg. Can you tell us a little bit more about the details, like where are these stored? Who pays for that? How much does that cost? Does insurance cover it? Because a lot of these questions I would imagine are questions that patients would want to know, but first let me ask you, in the 30 seconds that we have before break, are these questions that you usually get?

Seli Yes, they are.

Chagpar We are unfortunately going to have to break for a medical minute so you will just have to stay tuned to find out the answers to those questions and learn more about fertility preservation with my guest Dr. Emre Seli.

*Medical Minute*

*Breast cancer is the most common cancer in women and in Connecticut alone approximately 3000 women will be diagnosed with breast cancer in 2014, and nearly 200,000 nationwide, but there is new hope. With earlier detection, noninvasive treatments and novel therapies there are more options for patients to fight breast cancer than ever before. Women should schedule a baseline mammogram beginning at age 40 or earlier if they have risk factors associated with the disease. With screening, early detection and a healthy lifestyle breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center and Smilow Cancer Hospital at Yale New Haven to make innovative new treatments available to patients. Digital Breast Tomosynthesis, or 3D mammography, is transforming breast screening by significantly reducing unnecessary procedures, while picking up more cancers and eliminating some of the fear and anxiety many women experience. This has been a medical minute brought to as a public service by the Yale Cancer Center and Smilow Cancer Hospital at Yale New Haven. More information is available at [yalecancercenter.org](http://yalecancercenter.org).*

Chagpar Welcome back to Yale Cancer Center Answers, this is Dr. Anees Chagpar, I am joined today by my guest Dr. Emre Seli. We are talking about fertility preservation for cancer patients and right before the break we were talking about how particularly for breast cancer patients, they get a cancer diagnosis right at the time when they are thinking about having children and how for many patients chemotherapy in particular can prevent them from going on to have children. Dr. Seli was telling us about several of the modalities that are available for patients in order to preserve their fertility. Two of these involve freezing either embryos or eggs and right before the break, I asked Dr. Seli, and I hope that he will answer now, some of the questions that I think our audience would have, like where are these stored? Who pays for that? Does insurance pay for that? How exactly does this work?

Seli I will go one by one, embryo cryopreservation, as I was mentioning, has been around for a long time and it is done for many women who are undergoing fertility treatment without cancer when they produce extra embryos, more than they could use, rather than discarding the embryos many

16:31 into mp3 file [http://yalecancercenter.org/podcasts/2014\\_0330\\_YCC\\_Answers\\_-\\_Dr\\_Seli.mp3](http://yalecancercenter.org/podcasts/2014_0330_YCC_Answers_-_Dr_Seli.mp3)

couples will choose to freeze them. So that is why the embryo freezing procedure has been perfected. In order to generate embryos to freeze, the patient would have to be in an infertility center. They would have to see a reproductive specialist and then they will start treatment, the treatment includes stimulation of their ovaries and when they are ready, they would undergo a procedure called retrieval, and the retrieval will be under anesthesia or sedation and eggs will be removed and fertilized with the sperm, again in the same building as they are undergoing the retrieval, and the embryos would be frozen and stored in the same building. Once the embryos are frozen and stored, the couple would have the opportunity to test for these embryos anywhere they want to go. Let's say if they are in New Haven, they may keep their embryos with us, but then if they move to somewhere else in the country, they could transfer their embryos to another fertility center. It would not be kept in their household, etc. Another common question is how long embryos can be kept frozen and there is no time limit on it, as long as they are safe and the temperature is kept where it is supposed to be. The recovery rate of embryos that have been frozen is around 95%, so it is quite an efficient procedure. As far as the pricing goes, it is pretty similar to an IVF cycle except the patient does not undergo transfer, they undergo stimulation. They undergo monitoring during this procedure, then they undergo egg retrieval to extract the eggs from the patient, but then there is only freezing, but they do not do the transfer, and the cost of this in this country is around \$8000, and whether the insurance covers this or not really depends on the insurance, some do and many do not. At our center and many others, there are financial counselors who try to make it as fast as possible, because you need the approval to be obtained almost overnight to be able to facilitate and do the procedure really fast. There are also certain ways of getting medications for either a low cost or free from certain companies, because there are certain programs for cancer patients who cannot afford medications, because medications are quite costly when you do fertility treatment. So we generally work with the patient and try to get the medications for that specific cycle very quickly and without significant cost to patients if they do not have the financial means or the insurance to cover it.

- Chagpar I guess the next questions is, let's say you are a patient, before your therapy started you went and you had either your eggs harvested or an embryo cryopreserved, and then you go on and you have your chemotherapy and the rest of your treatment for cancer, when can you have that egg or that embryo re-implanted, when can you get pregnant?
- Seli You can get pregnant basically when your oncologist tells you that it is okay to try. They are not completely homogenous in their choices, but in my experience, most of them would ask their patients to be disease free for a long period of time, it could be three years or it could be five years depending on the patient. That has been my experience. They call this remission and they want an extended remission in order to attempt pregnancy.
- Chagpar Okay so you have waited the three years or five years and you say to your oncologist, I made it through my cancer treatment, thank you so much, now what would give me great joy and pleasure is to have a baby, how does that process take place?

21:05 into mp3 file [http://valecancercenter.org/podcasts/2014\\_0330\\_YCC\\_Answers - Dr Seli.mp3](http://valecancercenter.org/podcasts/2014_0330_YCC_Answers_-_Dr_Seli.mp3)

Seli When it is a frozen egg or embryo, what it entails is to put an embryo back into the patient's uterus. We are assuming that our patient did not have a uterine cancer, so she continues to have a uterus, in that case, if she has frozen embryos, what we would do is we would prepare her uterus with hormones and bring the uterus into a state that would accept an embryo and then thaw the embryo and under ultrasound guidance and with a tiny catheter we would transfer the embryo into the uterus. It is quite a simple procedure for us and it is not dangerous at all. It is not a painful procedure and is quite successful. If the patient froze an oocyte then she would have to decide how she wants to make the oocyte into an embryo, basically if she has a husband or a partner then she would use his sperm to fertilize the eggs in-vitro in the laboratory, or if she does not have a partner or husband then she could choose to obtain donor sperm, which is quite easy and then she could fertilize the eggs with donor sperm. Once the fertilization happens, then the embryos can be transferred into the uterus, the same as we would do for a thawed embryo. Once the details are sorted out the procedure is quite simple. It is much more complicated if the patient froze eggs or embryos and also lost her uterus. That would happen mostly with cancers that involve the uterus itself or the cervix and then the uterus would have to be removed. In that case she would have to find a gestational carrier and there is quite a bit of a legal aspect to this but it is well organized, we do it many times every year and what we do is then we make sure they have the right contacts and we make sure that the carrier is a healthy individual who is deciding independently to help this couple and then we prepare her uterus, thaw the embryos and transfer to her.

Chagpar What about the situation where you are implanting these embryos, for many patients who are undergoing fertility treatments for infertility as I understand, there is often an issue of having multiple pregnancies because you implant multiple embryos, is it the same with cancer patients or not?

Seli The same risk persists for the cancer patient. Obviously the fertility potential of each embryo is different and each woman's embryos are different in their ability to result in a baby. So let us say, if a woman is 30 years old either with infertility or with cancer, her embryos are more likely to result in a baby compared to a 35-year-old woman, but if you have eggs or embryos from a 30-year-old woman, one with cancer and one without, are there difference between them? That we do not really know. Some people think that cancer itself may cause a decrease in fertility but this is not really clear yet.

Chagpar When you implant an embryo back, you implant more than just one?

Seli That is what we generally do, but we can implant just one if that is what the patient wants.

Chagpar And what is in terms of a ballpark percentage, what is take rate?

Seli The take rate, if we think about each embryo's ability to result in a baby, it depends on different studies, this could be 10%, it could be 15%, some people give much higher results, but it is

25:23 into mp3 file [http://valecancercenter.org/podcasts/2014\\_0330\\_YCC\\_Answers - Dr Seli.mp3](http://valecancercenter.org/podcasts/2014_0330_YCC_Answers_-_Dr_Seli.mp3)

determined by the age of the woman who produced the egg. So if you are 30 years old and have egg retrieval, your embryos are frozen and kept in the freezer and you come 5 years later you should think of your embryos as the embryos of a 30 year old because they were frozen in time. So there will be a significant difference in the take rate of a 30 year old versus a 40 year old woman.

Chagpar So the amount of time that it has been sitting in the freezer does not play into it?

Seli We do not think so.

Chagpar We have talked a lot about the patients who have had breast cancer because clearly that is the population that is most effected, but you can only imagine that there is a whole cohort of pediatric patients, kids who get lymphomas at a very young age who require chemotherapy. Should their parents be thinking about fertility preservation in them, is this ever something that comes up?

Seli It does come up and it is a very delicate subject. In my experience, and I do not see very young patients very often, I mostly see reproductive aged women, but even the teenaged girls they are not necessarily interested in thinking about having a baby, so if a young girl or an almost teenager gets cancer, then generally their parents are involved and it is a discussion between the whole family and us and we try to explain all the options. It is really stressful for the parents and we always provide psychological support for them, we have a social worker, a psychologist, who talks to them, who helps them ask the right questions to each other and the key concept that we have to communicate to them is, unfortunately for a prepubertal child, so you have an 8 year old girl who is diagnosed with cancer, there is only a single option that I mentioned earlier, the preservation and it is what I described as an experimental option. The only thing we have in our hands is to freeze part of her ovaries because by definition when you are in prepuberty we cannot get eggs or embryos from a girl and the experimental medical treatment that I told you is also not useful because they are already prepubertal so you can't put them more into a prepubertal stage. So it is not an easy conversation to have with them but what I will have to tell them is that there is something we can offer, which is freezing ovaries. However, I cannot reliably guess how helpful it will be in the future because the procedure itself is not extremely well established.

Chagpar Is it ever the case that if we take that 8 year old girl who has a cancer who is treated, that after their chemotherapy, their fertility can come back, or is it that after cancer treatment if you have not done something to preserve your fertility you have kind of burned that bridge?

Seli It can come back. So let me give you details, basically the impact of chemotherapy on fertility is worse for older women, when I say older I mean older reproductive aged woman. So a younger reproductive age woman, let's say a 25 year old woman versus a 45 year old woman. The 45 year old woman who is undergoing chemotherapy is very likely to lose her fertility forever, whereas a 25-year-old may lose it for some time and it will come back but if she loses all her eggs even at age 25 she will not be able to make new eggs.

29:32 into mp3 file [http://valecancercenter.org/podcasts/2014\\_0330\\_YCC\\_Answers\\_-\\_Dr\\_Seli.mp3](http://valecancercenter.org/podcasts/2014_0330_YCC_Answers_-_Dr_Seli.mp3)

*Dr. Emri Seli is Professor of Obstetrics Gynecology and Reproductive Sciences, Director of the Division of Reproductive Endocrinology and Infertility and Chief of Reproductive Endocrinology and Infertility at Yale School of Medicine. We invite you to share your questions and comments with Dr. Foss and Chagpar. You can send them to cancer answers at [canceranswers@yale.edu](mailto:canceranswers@yale.edu) or leave a voice mail message at 1-888-234-4YCC. As an additional resource, archived programs from 2006 through the present are available in both audio and written versions at [yalecancercenter.org](http://yalecancercenter.org) I am Bruce Barber hoping you will join us again next Sunday evening at 6 for another edition of Yale Cancer Center Answers here on WNPR Connecticut's Public Media Source for news and ideas.*