



Fertility and Pregnancy: Medical Update

November 1, 2008

Elizabeth S. Ginsberg, MD

ELIZABETH S. GINSBERG, MD:

Chime in if you get lost. With a small group, it's really nice that we can just sort of chat instead of having it be really formal.

These are the objectives of the talk: to understand what the risk is of having infertility after breast cancer treatment, and to know what the fertility preservation options are. Both of you, I'm assuming, are after chemo, post-chemo. We'll sort of zip through that, and then understand the data on pregnancy and survivors.

This is a study I just did with Ann Partridge at Dana-Farber [Cancer Institute], who has been very active in doing research in pregnancy and pregnancy concerns in women with breast cancer. We just did a survey study at Dana-Farber, which is the cancer center that we're affiliated with. It has a prospective database, so everybody who is diagnosed with breast cancer is automatically entered. You can really track and see what the outcomes were. One of the questions we were seeing clinically so much, particularly in the past few years, was that women were getting treated with Herceptin or Taxol, and there really wasn't any literature about whether that was worse than AC chemotherapy that pretty much everybody had been getting for a long time.

We looked at that specifically. We did a multivariate analysis, because you have to account for background factors such as smoking – which is worse for ovarian function – age at diagnosis and so on. We looked at women who were on average 34 months out from chemotherapy and looked at multiple different treatments. Dose-dense – I don't know if you guys use dose-dense chemotherapy, but there are different ways you can give Adriamycin/Cytosin treatment. You can do it very frequently or in more spaced-out intervals. Lately a lot of people are getting dose-dense. There were no data at all on whether dose-dense was any different than the way AC/Taxol was given even a few years ago, so we really looked at that.

We also were looking at something that the literature talks about as chemotherapy-related amenorrhea. That just means women who don't have periods after chemotherapy – very, very common not to have periods in the first six months to a year after chemo. That really doesn't mean much. It doesn't mean that you're in menopause if you're very soon out.

We were looking at women who were beyond that brief interval, and showed that somewhere around 60 percent of women weren't having periods that far out. But these were women who were not all very young. These are women at all ages. And the likelihood of not having periods was very strongly related to age.

Basically, we found that what really made a big difference – women younger than 40 were less likely to have chemotherapy than women who were over 40. That's not surprising. The main thing was that tamoxifen use showed up as being something that was very different. If you were over 40 and using tamoxifen, you definitely had a higher risk of having permanent amenorrhea. Tamoxifen at a younger age didn't really add much. Basically, age was an important predictor as well as tamoxifen use in the older patients. Herceptin, Taxol didn't add to the effect of Adriamycin/Cytosin.

This is sort of some old data looking at the impact of chemotherapy with or without tamoxifen on the likelihood of having periods. . . . This is women who had chemotherapy only, tamoxifen only and both, with people having both having higher incidence of amenorrhea. I think the curve was shifted over so far because the majority of those women probably were older, because they didn't really do a multivariate analysis in that study.

One of the important things that we talk about is that when you go through chemotherapy, we really don't know how your ovaries are working most of the time. A lot of different tests can be done. The one that's been evaluated the

most is a blood test called FSH – follicle stimulating hormone – which is a pituitary gland hormone that stimulates the ovaries to ovulate. As a woman goes through her life, and there are fewer and fewer eggs left in the ovaries, the FSH level creeps up. Chemotherapy seems to accelerate that. It definitely results in fewer eggs left in the ovaries, even in women whose periods are very regular. And we know that as FSH levels go up, the likelihood of pregnancy goes down. This was specifically in an IVF population, but you see that in general in women trying to get pregnant on their own.

As you guys all know, if we're doing fertility preservation, we do it in the four to six weeks that people have between surgery and chemo. I'll zip through this, since you both have gotten treated already. We typically do IVF as frontline treatment because we know what pregnancy rates to expect with frozen embryos, whereas egg freezing is much more experimental at this point still.

The thing we worry about theoretically when we're doing IVF is whether there could be an increased risk of a decreased cure rate if the estrogen levels are very high during treatment. We really don't know. I think theoretically it's possible, although really probably not. I'll talk about the effects of pregnancy later. But there really aren't any studies showing that the amount of estrogen in your body makes a difference. It seems to be that if you're exposed to estrogen and you have more duration of estrogen during your life, your risk of breast cancer is higher. It doesn't seem to matter how much you got. So I suspect that the elevated levels for the two weeks that women are on treatment probably don't make a difference.

I do worry about clotting risk when estrogen levels are high. Clotting risk is increased. For breast cancer patients, where it's a very localized disease, there isn't really an increased risk of clotting. But in women with other types of cancers that are more systemic, like leukemia or lymphomas, they



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do have a higher clotting risk. And we worry that the high estrogen levels may make them get a clot somewhere.

Again, the pros and cons of IVF: Obviously, it may be the last chance we have to freeze embryos. On the flip side, there is no guarantee of pregnancy from embryos that result. And we can sometimes overstimulate women, and it can delay the start of their chemotherapy.

There are different ways you can use IVF. There's a group that was adding tamoxifen or letrozole to the standard IVF stimulation, and it basically showed that you can get much lower estrogen levels with letrozole. Theoretically, that would be a benefit to people. If you only use tamoxifen, you get very few eggs, and you also get fewer embryos. You need to add standard stimulation.

These are our data that we presented a couple of years ago at a meeting. We're just writing them up now with some more numbers. About one-third of the patients we see for embryo freezing have breast cancer. That's because women get breast cancer, and men are banking sperm. On average, we get about seven embryos frozen. So getting four is reasonably good.

We expect in our group – and, again, we've had a couple of more pregnancies since we looked at this – it's about a 50 percent delivery rate. That's better than what you get on average with women doing IVF. I think that just means that women who have breast cancer who are doing IVF and freezing embryos just don't have an egg problem. Many women with infertility don't have very good eggs, and that's why they have a problem. We expect pretty good pregnancy rates from that.

Do you want me to just zip through egg freezing, because you guys are kind of beyond this now? Yeah, okay.

This is, I think, more important. This is a slide of a breast cancer study looking at what happens with menstrual periods after chemotherapy is over. Again, it just shows that within the first six months to a year, this is the percentage of women with periods. The younger you are, the more likely you are to still have periods during chemotherapy. But even in the very young women, 85 percent or so have no periods for up to a year after, and then they come back. It's very, very common in the first three to six months after to not have periods. Frankly, if you don't also have menopausal symptoms, it probably doesn't mean much. I do think there's sort of a stress insult to the system,

and unless someone's having horrible hot flashes and a lot of menopausal symptoms, I don't think it usually represents menopause. That's true even for women who are over 40, who can see periods go away and then come back in 12 months.

This slide is just a graphic demonstration of what's happening. Remember, I showed the slide showing that the FSH levels go up as you get older. That also correlates with the number of eggs left in the ovaries. This is a study where they were looking at ovarian tissue pieces, showing that there were fewer numbers of eggs as women got older, which isn't surprising. When women go through menopause, there are virtually no eggs left. That's why menopause happens, because the cells around the eggs are the cells – they're called granulosa cells – that make estrogen, so that when all the eggs are gone, all the estrogen-producing cells are gone, periods stop, ovulation stops.

Now, ovarian reserve testing: These are tests that I'll talk about a bit because both of you are post-treatment, and down the line I don't know if you're going to be planning to try to get pregnant on your own. These are tests that can be done that are helpful. There is no test that tells us if somebody is fertile or not fertile. One thing is: Are you still having periods when chemo is over, yes or no? I'm talking a year out. Then, the other thing is: Until you try to get pregnant, we really would never say that you were infertile, because the majority of my patients in my infertility practice have regular periods. Having periods doesn't mean you're fertile, and having irregular periods doesn't necessarily mean you're going to be infertile.

Until you've tested fertility, I don't think any of these tests mean much. They're very helpful from the standpoint of being able to predict how you're going to respond to fertility treatment. For women who are having difficulty in getting pregnant in any situation, these tests can help us determine what type of treatment is likely to work and what the likelihood of pregnancy is for various treatments.

Age, again, is the most important and most consistent predictor of the ability to get pregnant. As women get older, egg quality diminishes, and a 40-year-old with perfect ovarian reserve testing has a lower pregnancy rate than a 25-year-old with not-so-good ovarian reserve testing. Age is really important because, again, egg quality decreases as women get older.

The next test that we've been using a lot in cancer populations because you don't have to time it in any particular phase in the menstrual cycle is

a hormone called anti-Müllerian hormone. Another name for it is Müllerian inhibiting substance. This is something secreted by those granulosa cells around the eggs. It correlates with the whole follicular pool, because it's secreted by the cells around the eggs. You get an idea of the number of eggs and how responsive the ovaries would be to fertility treatment. There is not as much data on anti-Müllerian hormone as there is on FSH, particularly with respect to IVF pregnancy rates. It's a helpful test from the standpoint of saying, "Gee, the ovaries took a big hit from chemo," or not much of a hit from chemo, from the standpoint of comparing them to normal levels, but not as good at predicting how you would do in response to IVF treatment or other fertility treatments.

Day 3 FSH and estrogen is still kind of the gold standard for women who have infertility and are thinking about IVF, because there are so many studies looking at it. I think any doctor in any program would be able to look at numbers and give you some sort of idea of what treatment pregnancy rate you would expect, and also what kind of dosing of medications you need.

When someone is going through in vitro fertilization, the goal of that treatment is to increase the number of eggs produced in the ovaries so you can get them out of the body and fertilize them in a culture dish and then put embryos back in the uterus. You bypass a lot of what has to happen naturally. The higher the FSH, meaning the fewer the eggs, the more medication you need to get to stimulate the ovarian response. We don't have those kinds of cutoff numbers with AMH levels yet. Most docs can look at an FSH and say, "In my experience, this person is going to need this much drug to get eight eggs," and with AMH, we really don't know what level correlates with what drug dose need.

Antral follicle count is sort of helpful. With AMH, I think we find a bit of discrepancy sometimes. It's actually doing an ultrasound to look at the number of follicles in the ovaries. The only downside is that I think it's easier to do it on day three of a menstrual period. It's not as helpful in women who aren't cycling or women who have irregular cycles, because once you start getting a dominant follicle in one ovary, if you're going through an ovulation process, that ovary – a lot of the follicles get squished by the big one that's growing. So it's better to do it early in the menstrual cycle, but it correlates probably with AMH levels



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pretty well. Just like with any treatment, the best predictor of how the person's going to do with treatment is how they're doing with treatment when they're on it. We know better when women are already undergoing treatment.

If you have a bad test result – and by bad test result I mean if you have an FSH blood test and the level is over 10 to 15, depending on the lab where the FSH test is sent from – for IVF we know that if the FSH level is elevated, the likelihood of pregnancy is decreased by about 50 percent. In women who are over 40, you see very low pregnancy rates in IVF if the FSH level is elevated. For women in their 30s, you see really variable results. There are some studies showing that even in women who are fertile, you can see elevated FSH levels.

So, again, the test itself doesn't tell you whether you're going to be able to get pregnant. It gives us an idea, if you're having infertility, of what kind of treatment you're going to need and what kind of medication dosing you're going to need. If it's elevated, it will tell us your likelihood of pregnancy is going to be lower, but it doesn't say who can and can't get pregnant.

We do expect that there is going to be some elevation in FSH after chemotherapy. We generally don't know where people started from, so if you come back with a level of normal, you probably had a lot of eggs before the chemo started. If you come back with an elevated level, we assume that it was somewhat lower than that before chemo, but we don't really know for sure, because plenty of people in my practice have not had chemo and have elevated FSH levels anyway.

One of the problems with breast cancer treatment – I don't know if you guys are going to be on tamoxifen or something following – is that it really delays everything. What I see in my practice lately is a lot of patients negotiating with their oncologists about how long they're going to take tamoxifen. There's a huge variability from program to program, and also, I think, from patient to patient, based on whether they're lymph node positive, what type of grade the tumor was, whether it was estrogen receptor positive and HER2/neu positive, or only estrogen receptor positive. All of those things play into whether your oncologist will be comfortable letting you get pregnant after two years of tamoxifen rather than five. I think almost all of them, if you have ER-positive tumors, are going to want you to do at least two years of tamoxifen at this point.

Then, again, you're just talking about age. The study that we did didn't show – that tamoxifen itself was really giving a hit if you were under 40, but it did appear to have some increased negative impact on ovarian function for women who were over 40. Age is a problem, and there really is no way to get around that when, from the standpoint of your cure, they want you to stay on it.

The pregnancy rates after breast cancer in the literature are really hard to come by and not very solid. The available data – again, these are older studies looking at huge ranges, and they really didn't do a very good job of looking at other things that factor in to the ability to get pregnant. Some of the studies didn't even talk about how many people were trying to get pregnant. It was just a bunch of breast cancer patients; this many – 5 percent or 15 percent – ended up with kids. You don't know how many were trying. Were 75 percent infertile, or were only 2 percent infertile and most people were getting pregnant without a problem, but most weren't trying?

Ann Partridge, whom I work with at Dana-Farber, had done a retrospective study of the [young women], and she found that about 60 – I think, in that study, about 57 percent of women, and it was only 60 women – 57 percent actually did get pregnant without any difficulty on their own. They're doing a prospective study now at the Farber that's coming out the exact same. This is a prospective study showing that now they have about 58 percent of women trying to conceive who are able to. Most of these women are in their 30s, not in their 40s. The data are pretty good. It's better than a 50 percent chance that even after chemo you'll be able to get pregnant once you try.

Here are slides, so you can read. It's such a small group. From the standpoint of whether it's safe to get pregnant after breast cancer, again, the studies are limited by the fact that you can't randomize women to get pregnant or not get pregnant. The women who get pregnant are the women who really want to, who lobby their physicians and there's a mutual decision that it's okay. The concern is that the studies are all retrospective. You look back over your population to see who did what, and there's always bias in that. Some patients are told not to get pregnant by their doctors, and some patients are told it is okay to get pregnant – it's not a clean study. All you can say is if you're somebody whose oncologist feels is okay to get pregnant, the likelihood of having a recurrence is not worse than the likelihood for women who don't get pregnant.

The general concerns have been about disease recurrence. Estrogen levels are incredibly high during pregnancy. In a natural cycle, the estrogen level mid-cycle is between 200 and 500. If you use letrozole during IVF, that's about the range that your estrogen levels go up to. They don't get much higher than that. In pregnancy, you're going to have estrogen levels up to 3,000 for a long time. And, again, because the studies that have been done looking at populations of women with breast cancer haven't found a difference in women with higher or lower levels of estrogen in their own bodies, we don't really know that that makes much of a difference.

We don't know whether there's an increased risk of pregnancy complications. It doesn't look like it, but we don't know for sure. The concerns have been for women with HR positive disease whether there could be an increased recurrence or decrease in survival. These have been concerns about whether it's okay to let women get pregnant.

This is sort of a survey of a bunch of studies that have been done, and basically none of them showed an increased risk. They were looking at the relative risk of recurrence after breast cancer treatment. They're not huge studies. These are relatively small populations of people, and they were comparing women with breast cancer against control – so, women who didn't have breast cancer. This was the biggest study – 5,000 controls, 173 women with breast cancer, because you have to obviously have people who have been given the okay to get pregnant. None of them showed an increased risk, and, frankly, they had a relative risk that was lower than that of women who weren't getting pregnant with breast cancer.

So, from the data out there, I think you can say that if your doctor tells you it's okay to get pregnant, it probably really is okay to get pregnant, and you'll have a good prognosis.

Again, we think this may be selection bias, and there is some question about whether high-dose estrogen may actually somehow treat it. Could you down-regulate estrogen receptors in the breast cancer? There are some theories that actually bombarding any remaining breast cancer cells with high-dose hormones might actually be good. It's hard to imagine that, but there are a lot of theories out there. I think probably it represents selection bias, in that if you have a pretty good prognosis disease, your doctor is pretty good at predicting whether it's going to be okay for you to get pregnant.



High estrogen and progestin have been used as a treatment modality in older studies. And in culture, you can change the way growth factors stimulate breast cancer cell lines and make them not grow with high-dose hormones. There is some data to support that. We just don't know.

This is just another study. They looked at women who had breast cancer and followed them over time. There were 27 women, and these were pretty big numbers in the study. There were women who recurred and women who died. There were no deaths in women who were pregnant more than five years after diagnosis.

Other options: For women who don't get pregnant – you have embryos frozen but they don't work; you don't get pregnant from them – egg donation is perfectly reasonable. One of the good things, if you want to call it that, about breast cancer is that you're not getting any radiation to the pelvic area. There's nothing about chemotherapy or the breast radiation that you might be getting that changes the way the uterus carries a pregnancy, so there doesn't appear to be any increased risk for the pregnancy itself if you've had breast cancer treatment. There doesn't appear to be any increased risk of premature delivery or any bad pregnancy outcomes.

From that standpoint, the uterus works really well. For women who don't have ovarian function, who are in menopause after chemotherapy, egg donation is a perfectly viable option. In this situation, eggs would not be genetically related to you. They would be from another woman. It can be a friend, a relative, an anonymous donor. There are a lot of programs and agencies around the country. This is a big business now. About 10 percent of IVF cycles in the U.S. – actually, 11 percent in the last reporting year – were egg donation cycles, and mostly not for breast cancer. There are just some people who are not lucky and don't have good eggs, or start trying to get pregnant when they don't have enough eggs to respond to treatment.

You do have to be on estrogen and progesterone to mimic a natural cycle. What happens during an egg donation cycle is that an egg donor is on stimulating medications to get multiple eggs to be produced in her ovaries. We have to synchronize the recipient – we would have to synchronize your uterus so that it was ready to accept the embryos. You can use husbands' sperm; you can use donor sperm for that. You don't have to have a male partner to do IVF with egg

donation or IVF in general. But you do have to be on hormones, and that has to be something that you're going to be ready for, because the estrogen level is going to be a lot higher once you're pregnant in any case.

I've had a couple of women with breast cancer opt to use gestational carriers. One of the patients had positive nodal disease, and she decided that she really wanted to have a baby. Her disease was actually doing pretty well; she was stable for a long time. She had banked embryos after IVF and just decided that she didn't want to get pregnant and carry the pregnancy herself, so she decided to use a carrier. She had twins that way. If you do decide to do egg donation, or IVF in general, you do have to decide with your doctor how many embryos to place in the uterus, because particularly if you're young when you go through that treatment, or if you're using a young egg donor, pregnancy rates are very high, which means twinning rates are very high. You have to decide whether or not you want to have a risk of a twin pregnancy, and you can control that by just putting one fertilized egg, one embryo, into the uterus rather than two.

The advantage, obviously, of using a gestational carrier is that there isn't any pregnancy-related risk to you if there is a risk in terms of high estrogen levels. I should say that if you still have a breast or both breasts in place, breasts are very lumpy and very hard to evaluate during pregnancy. Typically oncologists don't want you to breastfeed afterward, because the breasts get very thick and lumpy. Mammograms are not particularly useful. I don't know about MRI, but ultrasounds aren't particularly useful, either, because the breasts just get so tough, and they feel terrible, you know, when women are pregnant and then afterward if they're breastfeeding. It's hard to monitor breasts in someone who's pregnant or immediately postpartum. That's one of the things that make some women concerned, and the reason why I've had a couple of patients opt to use gestational carriers.

I've also had patients opt to use gestational carriers with egg donors. Their ovaries weren't working, and they couldn't carry the pregnancy themselves, or they were just nervous and felt that if they were going the kind of high-tech route anyway and they financially could afford it, they didn't even want to try to carry a pregnancy because they were concerned about not being able to be monitored as well as possible.

Interestingly, there really isn't any kind of immune reaction to embryos. Embryos are never perceived by your body as foreign. So eggs, sperm – they really can come from any source and they're not rejected.

Another thing, which is a little bit tricky – in Massachusetts, where I practice, we really can't do it – is surrogacy. That would be typically for women who don't have ovarian function, so they're not thought to have eggs left in the ovaries, but they have a partner and their partner's sperm would be inseminated into another woman. It would be the other woman's eggs, and the other woman would carry the pregnancy. In Massachusetts, that baby would legally be the surrogate's baby, whereas with a gestational carrier in Massachusetts, the intended parents are legally the parents even before delivery, and their names are on the birth certificate and everything.

It's really important to look at the legislation and the legal aspects of what you're doing before you go ahead with that. There are a couple of areas in California where you can do a kind of pre-birth adoption even with a surrogate, even if it's that other woman who is carrying the pregnancy and it's her own eggs. But it's legally much, much trickier.

Adoption is an option. The adoption scenario changes constantly, and it's very hard to tell people how long of a wait it is for a baby, what kind of a track record you have to have. Often, if you've had cancer, you need a letter from an oncologist saying that you're free of disease or something like that, and then that should not be held against you. In general, it's very tough to adopt in the U.S. if you're over 40, and that's just for anybody in the U.S. who's over 40.

International adoptions, same thing: There's really a pecking order where the younger a couple is, the more likely they are to get an infant. The older a couple is, the more likely they are to not be allowed to be given an infant and only be able to get a toddler or an older child. Again, which countries are open changes constantly.

Right now, Ethiopia is one of the better countries to adopt from. It doesn't have as many legal hurdles as other places, and the kids tend to be malnourished but healthy. There's not a lot of HIV, and they really take care of them very well. They're not neglected, and they're stimulated and so on. Countries open and close. Right now the wait in China is more than two years; it used to be the fastest place. Things change really, really quickly.



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If you end up looking into adoption, you'd have to get a hold of adoption agencies.

RESOLVE is a national infertility support group. It's very much like LBBC. It's really helpful. These are women who have taken it on to help women with infertility problems. They have really good adoption information that's up to date. They also have conferences all over the U.S. that you can go to. They usually have a bunch of adoption agencies go there, so it's considered one-stop shopping to pick an agency and to find out what's happening.

These are slides that Ann Partridge and I have put together because it comes up all the time in practice. A lot of times, our patients come in trying to negotiate, and I don't play a role. I'm the fertility doctor, so I'm not the one who's saying, "Yes, you can stop your tamoxifen early." We've had patients stop their tamoxifen after a couple of years, have a baby and then wonder about going back on tamoxifen. There's zero data if you've been off it for over a year. It takes a while to get pregnant, often, and then once you do get pregnant, does it make sense to go back on it if you've already been off it for a year and a half? There's just no data. I know at Dana-Farber they have not been putting women back on tamoxifen, just because we don't know.

The other question is: If you do stop tamoxifen, how long should you be off it before you try to get pregnant? Generally they're being told two to three months, because it does have a pretty long half life in your body. That said, you can actually use tamoxifen as a fertility drug. It helps ovulation. I don't know of any studies showing that it does cause birth defects, but in general we want women to be on as little medication as possible when they do get pregnant. I think that's a reasonable suggestion.

When you're on tamoxifen, you may not get your period, and it may not be menopause – it may be the tamoxifen. What your cycles do on tamoxifen can be anywhere. You can have regular periods. You can have no periods and not have ovarian failure. Or you can have intermittent periods and not have ovarian failure. It's a drug that kind of masks, I think, to a certain extent, what's really going on in your body.

Again – I sort of mentioned this already – we really don't know about the two-year window. There's no data, I guess, in that window. From the oncologists' standpoint that I work with, anyway, they feel that's an individual decision, just like some women don't want to take tamoxifen. They just don't want to deal with it at all. That's up to you. Pregnancy is also a personal decision. When your doctors give you a medical recommendation about treatment, it's a medical recommendation that they think is in your best interest. But not everybody goes with what the standard recommendations are, and they do want to sort of work out of the box, and that's a personal decision. Your doctors will give you the advice that they think is best in your specific circumstances.

That was all I had. But there's such a small group of people – ask away. I'll be your consult.

MODERATOR:

Thank you very much, Dr. Ginsberg. It was actually great. . . .

ELIZABETH S. GINSBERG, MD:

You don't have to ask any if you don't have any, or you can whisper them to me after I take the mic off.

WOMAN:

[Off microphone] I have three embryos banked.

ELIZABETH S. GINSBERG, MD:

Great.

WOMAN:

[Off microphone] When I'm ready to kind of start that process, do I still go through the whole process of them sort of – like you mentioned, if I were taking a donor embryo – getting my own body ready with injections and everything and they just try to implant it?

ELIZABETH S. GINSBERG, MD:

Yeah, but it involves different injections than you were on before. Usually we use a medication called Lupron, and that shuts your ovaries down if they're working. Then you'd use estrogen and progesterone to get the lining in shape.

Generally for my patients, too, we see what your periods are doing when you're done with chemo. I always want my patients to try to get pregnant on their own first and then use the embryos as a kind of safety net, because some people get pregnant, and then you may have infertility for another baby, and then you could use the embryos then.

That's it. It's about a five-week process, usually, from when you take your first shot to when you check the pregnancy test. For most programs, survival rate of embryos is around 80 percent, something like that. I don't know what they quoted you, but that's about what we expect – about 80 percent. You might have all three survive. On average you should have two survive, hopefully. . . .

MODERATOR:

. . . I do [want to] remind you to complete your evaluation form. Thank you again, Dr. Ginsberg

ELIZABETH S. GINSBERG, MD:

Oh, you're welcome.

MODERATOR:

– for your flexibility.

[END OF TRANSCRIPT]