

JANI JENSEN: My name is Jani Jensen, and I'm an assistant professor in the Department of Reproductive Endocrinology and Infertility at Mayo Clinic in Rochester, Minnesota. And I'm the author of "Fertility Preservation" which is appearing in the January 2011 issue of *Mayo Clinic Proceedings*.

Fertility preservation is a new discipline, and it refers to strategies used to promote or retain fertility for patients that are undergoing treatment for life-threatening illnesses. Now, we usually think of this in context of cancer therapy, but it can apply to other serious illnesses, including things like lupus, or treatment of other myeloproliferative disorders.

In this year alone, nearly 1.5 million Americans are going to be diagnosed with cancer. Now, of this group, approximately 10% of them are in the reproductive age. When you speak to reproductive age patients who have a new diagnosis of cancer, you'll find that a high number of them are very concerned about their ability to have children in the future.

If you ask adolescent females, for example, about their desire for fertility, over 80% of them will say that they want to try any strategy to preserve fertility, and 93% of them said they would do it even if they're told that it's experimental.

Recognizing this, in 2006, the American Society for Clinical Oncology issued guidelines recommending that all oncologists tell reproductive age cancer patients of risks to their future fertility of cancer treatment and refer patients who are interested in fertility preservation to a reproductive endocrinologist for fertility preservation counseling.

Now, despite the fact that these guidelines have been in place for over four years, nearly half of all oncologists at one large academic medical center reported that they had never referred a patient to a reproductive endocrinologist for a fertility preservation consult. Risks to future fertility vary depending on cancer treatment.

One of the particular concerns we have is the use of alkylating agents-- for example, Cyclophosphamide-- for cancer treatment. Now, alkylating agents aren't cell-cycle specific, so they can affect the very primitive sperm and egg cells. And in the case of primordial stem cells-- for sperm-- once they're gone, they can't be regenerated.

Women are born with a finite number of eggs. And once all the eggs are depleted, we never have an opportunity to make any more. So protecting the ovarian reserve and oocytes we already have is of critical importance.

For post-pubertal men, the most successful strategy is sperm banking. Now, sperm banking has a long history in both human use, as well as in agriculture. And the samples are relatively simple to collect and store. Frozen sperm can subsequently be thawed and used either for insemination into a female partner's uterus or with a high-tech procedure, such as in vitro fertilization, where sperm are thawed and then directly injected in an egg to make an embryo that's placed in a woman's uterus.

So for post-pubertal women, there are also a few options. The most mature technology is embryo cryopreservation. Now, embryo cryopreservation relies heavily on strategies from in vitro fertilization, which has been around, now, for over 30 years.

One of the concerns that women have is the length of time that's required to either undergo embryo or egg freezing. Typically, we recommend that women undergo treatments between the time they maybe have surgery and then begin chemotherapy. For women who do not have two to three weeks needed to undergo these procedures, we have other options.

One of them is ovarian tissue cryopreservation. Ovarian tissue cryopreservation, though, is still considered more experimental than the mature technologies of embryo or egg cryopreservation, and so patients need to be cautioned about this. But for women who don't have sufficient time to undergo the other two procedures, this can be a very valuable option.

The last option that we have for reproductive age women is to try to suppress the ovaries. Now, the data on ovarian suppression and return to fertility are mixed, but the theory is that shutting down communication between the hypothalamus, pituitary, and ovaries-- even temporarily-- can put the eggs in a state of quiescence, and thereby protect them from chemotherapeutic agents, which are designed to attack dividing cells.

Patients can have some side effects that are menopausal from them from getting these agents. But in general, they're tolerated very well. Since this is a new discipline, there are many unanswered questions and a lot of areas of controversy.

One of them, for example, is that-- are there some patients who are just too ill to even offer fertility preservation? In my experience, sometimes I find that patients who have the worst prognosis are often those who desire fertility preservation the most.

Another area of controversy is in care of adolescents. So parents need to authorize or give consent to fertility preservation treatments to patients who are less than 18 years old.

Another area of controversy is who should pay? So not all insurance companies will cover fertility preservation procedures. Recognizing this, many large academic medical centers have developed programs to give discounted prices to cancer patients who are undergoing this type of treatment, and there are also several good programs that offer discounted or even free medications for the patients, which can be a significant cost.

Another area of concern is whether or not the treatments may worsen outcomes for patients. And this is particularly true for cancers like breast cancer, which can be hormonally responsive. Data that have been published to this point are relatively short-time, with outcomes ranging between two and five years.

But what some of the larger studies of women with breast cancer who have undergone fertility preservation have shown is that women who have done this seem to be at no increased risk of cancer recurrence or mortality. Women often ask when the best time to attempt pregnancy would be after cancer treatment.

Now, there's not a consensus opinion, but most experts recommend that women delay trying to conceive for at least one, and ideally two or more years after cancer treatment is completed, because the risk of recurrence is highest in that window. One question that patients always ask is if there is a risk to the offspring that are born from cancer survivors.

We now have reassuring data from large studies that have looked at several thousand children born to cancer survivors that have shown that there's no increased risk of having birth defects or any type of childhood malignancies. Patients are often very reassured to hear this.

SPEAKER:

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