[MUSIC PLAYING]

STEPHANIE ROTHENBERG: I'm going to be talking to you tonight about the different fertility preservation options that are available to cancer patients. So there are several indications like Dr. Orwick mentioned for fertility preservation in men and women of all ages. They can be broken down into two main categories: medically indicated and elective.

Today we're obviously going to focus on fertility preservation in the setting of a cancer diagnosis, but you should be aware that there are several other indications. Fertility preservation should be considered for any adult or child where recommended medical or surgical treatment could result in infertility in the future. It should also be considered in an elective setting, particularly for women who desire to delay childbearing, as fertility declines with age.

For boys and men, there are several common scenarios where fertility preservation should be considered, including testicular cancer requiring surgical removal of one or both testicles; any cancer diagnosis requiring chemotherapy; cancer requiring radiation therapy to the pelvis or to the testes; or autoimmune disease that requires treatment with chemotherapy. Sperm banking is the most established method of fertility preservation for adolescent boys and men. For most patients, providing a viable sample prior to cancer treatment should be relatively easy. The most common method for collection is after masturbation. Ideally, multiple samples are collected about 48 hours apart as an outpatient procedure.

The cost is $263 per analysis, which includes freezing in the first year of storage. Storage is then $360 per year after that. There are some programs such as Livestrong who will cover a portion of the cost for fertility preservation, but this varies from patient to patient, and there's more information about that in your folder. The sperm can be frozen indefinitely, as far as we know, and be used in the future when fertility is desired through fertility treatments, such as intrauterine insemination and in vitro fertilization.

There are other methods of sperm collection that are available, including testicular sperm extraction or aspiration, that can provide enough sperm to freeze. The sperm extraction is used in boys and men who have gone through puberty, but do not have sperm in their semen sample or cannot produce a specimen. It is a minor surgical procedure in which a small testicular biopsy is obtained and examined for the presence of sperm. Sperm are obtained with this procedure about 50% of the time and can be used in the future for in vitro fertilization. The procedure itself costs about $500 to $600, and the sperm also has an annual storage fee.

Testicular tissue freezing is the next option. Both sperm freezing and testicular sperm extraction can only be used after puberty. So for prepubertal boys, there is an experimental option available where the testicular tissue itself can be frozen. For these prepubertal boys, one full spermatogenesis is not yet ongoing. It's essential to store the spermatogonia and the neighboring cells as undamaged, integrated tissue. So the preservation of the Sertoli cells and the cell-to-cell contacts in the testicular tissue have proven to be important for subsequent maturation of the spermatogonia.

A portion or one entire testicle is removed with an outpatient procedure and frozen. At this time, protocols to use the tissue are under development, but these have not yet been successfully used in humans to restore fertility. It has been successfully used in research animals, and interestingly in monkeys, reimplantation of the tissue resulted in complete regeneration of spermatogenesis, which is a very promising research project. This is the only option for fertility preservation in prepubertal boys facing gonadotoxic treatment, and the hope is that we can develop the technology to use the tissue in the future. The procedure in first year of storage is covered by the research study, but after the first year, the patient is responsible for the annual storage fees.

Moving on to the female side, there are also several indications for fertility preservation. These include ovarian cancer or benign adnexal disease that require removal of one or both ovaries. An example of a benign condition would be a woman who carries the BRCA mutation and desires to reduce their risk of ovarian cancer in the future by removing their ovaries. Other indications include any cancer treatment requiring chemotherapy or radiation therapy or an autoimmune disease that requires chemotherapy treatment.

While fertility preservation options for women are increasing with continued research, there are several key parameters that must be considered when developing a fertility preservation treatment plan. These include the patient's age, the type of treatment, their diagnosis, whether or not she has a partner, and the time available before treatment must start. These factors need to be considered both by the oncologist and by the fertility specialist.

Impaired future fertility is difficult for children to conceptualize, but potentially traumatic to them as adults and is largely considered to be an important quality-of-life issue by patients. Therefore, there needs to be a collaborative discussion with girls and boys and their parents regarding potential fertility preservation. But potential treatment options should not be withheld from a patient based on their status as a minor.

Embryo freezing is the first option. It is for girls or women who have gone through puberty and have a committed male partner, or who are prepared to use donor sperm. This is an established technology with a predictable likelihood of success. It involves undergoing a cycle of in vitro fertilization, which entails ovarian stimulation with self-administered injections for a period of time to induce ovarian follicular development. It typically takes 8 to 12 days, but a longer duration of treatment is sometimes necessary. They require frequent monitoring with both blood work and transvaginal ultrasounds.

After stimulation, an egg retrieval procedure is done under sedation. The eggs are then fertilized with sperm, either from the patient's partner or a chosen sperm donor. These embryos are then frozen and stored for later use. For patients with a cancer diagnosis, we typically do what is called a quick start, meaning that we start the ovarian stimulation regardless of the point that they're at in their menstrual cycle. That is why they sometimes need longer stimulation in the typical 8 to 12 days and can sometimes delay a cancer treatment if there is a prolonged amount of time needed for ovarian stimulation.

There was a study in 2009 of 81 patients who had breast cancer, where they retrospectively looked at the time from surgery for their breast cancer to starting their adjuvant chemotherapy treatment. Some of the women had undergone fertility preservation during the time between their surgery and the chemotherapy, and some had not. They did not find a significant difference in time to the onset of chemotherapy treatment and felt that the time investment required for fertility preservation appeared to be manageable.

We provided a discounted rate of $5,000 if the patient is cleared by their oncologist to undergo embryo cryopreservation. They will have to pay a yearly storage fee. In the future, if they decide to use the embryos, there are future costs for the procedure to transfer the embryo into the uterus, and these costs all have to be taken into account. The success rate of the procedure is dependent on the patient's age at the time of the retrieval, but it ranges from 30% to 50% per embryo that is transferred.

Egg freezing is also for girls or women who have gone through puberty who either do not have a committed male partner, do not want to use donor sperm, or who simply do not want to use their partner's sperm for fertility preservation. Many women who have a partner and choose this option feel strongly that this allows for flexibility in the future, where they'd have a different partner when they want to have a baby. This process was considered experimental until 2013, but it's now used frequently in clinical practice. It appears to have comparable live birth rates to embryo cryopreservation for these patients.

The process for egg freezing is similar to that of embryo freezing. The difference is that the egg itself is frozen, and no fertilization will take place. When the woman is ready to use the eggs, they are thawed and fertilized by injecting a sperm directly into the egg called intracytoplasmic sperm injection, or ICSI. The cost is the same as for embryo cryopreservation for these patients.

Ovarian tissue freezing is an experimental procedure available to both prepubertal girls, or for women who need to undergo immediate chemotherapy and do not have time to undergo ovarian stimulation prior to starting treatment. This method involves obtaining ovarian cortical tissue by removing an ovary through laparoscopy and freezing small segments of the ovarian tissue. Following treatment, the tissue can then be reimplanted into the patient, either back into the ovary itself, or at other sites, such as the forearm or the abdominal wall. There have been approximately 60 live births reported after the tissue was reimplanted into the ovary or ovarian bed, which continues to increase. There is a risk that the transplanted ovarian tissue could have malignant contamination, which is a particular consideration in women with ovarian or hematologic cancer who desire this procedure.

A significant amount of research is underway to have the ability to do what is called in vitro maturation, meaning that the eggs can be obtained from the tissue without reimplanting it into the body. But this technology is not yet established in humans. Therefore, for patients who are prepubertal or with ovarian or hematologic cancers, there's not a way for them to use the tissue for fertility with the current technology. But with the current research, we're hopeful that in the future they will be able to. The surgical costs for this are covered by the research study, but patients are responsible for storage fees in the future.

Ovarian transposition attempts to minimize the damaging effects of radiation on the ovaries during pelvic radiation therapy. Patients with Hodgkin's disease, for example, typically receive between 2000 and 4,000 gray of radiation, which would lead to ovarian failure and result in infertility. By moving the ovaries away from the main radiation stream, ovarian loss of function may be prevented or decreased.

This procedure can be performed laparoscopically on an outpatient basis. It should be performed relatively close to the time of radiation therapy to prevent remigration of the ovary into the pelvis during radiation treatment. Ovarian transposition has been reported in the literature to have a wide range of success anywhere from 16% to 90%. Risk with this procedure include inadvertent damage to the ovarian blood supply and ovarian cyst formation, and they also may need a procedure in the future to reposition the ovaries, particularly if they're planning to undergo in vitro fertilization.

Finally, there is an experimental medical treatment. Lupron is what's called a GnRH agonist that results in what is essentially a temporary medical menopause. The theory is that by suppressing ovarian function during chemotherapy, there'll be less of a gonadotoxic effect of chemotherapy on the ovaries. Lupron is an injection that's given monthly and ideally should be given two weeks prior to the start of chemotherapy, because after the injection, there is an initial stimulation of the ovaries.

This is a controversial treatment because of the lack of data showing efficacy. The studies to date have been limited by inadequate follow-up in the assessment of surrogate measures of fertility, like return of menses rather than pregnancy rates. There have been several reports, however, that menstrual function and ovulation may be more likely to occur after chemotherapy when Lupron is given during treatment. The use of Lupron for fertility preservation is considered off-label and is not covered for insurance for this indication. It can cost between $400 and $900 per injection and should be continued throughout treatment. There are some instances where insurance will cover its use, such as to decrease the risk of heavy bleeding in the setting of thrombocytopenia related to chemotherapy, or in the setting of a stem cell transplantation.

As you can see there are fertility preservation options available for all cancer patients, regardless of their age or their diagnosis. Some of these treatments are well-established, and some of them are experimental. We're fortunate that here in Pittsburgh, our patients are able to access not only the well-established treatments, but also the experimental treatments, such as testicular and ovarian tissue freezing. While not all patients decide to pursue fertility preservation, it's important that patients who are at risk of infertility because of their treatment are at the very least given information regarding their options. And ideally this information is delivered to them by a multi-disciplinary team.