

Strategies Help Some Cancer Survivors to Conceive

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NEWPORT BEACH, CALIF. — Gonadal suppression, ovarian pexy, in vitro fertilization plus embryo freezing, oocyte freezing, or banking frozen ovarian tissue are five strategies that offer some hope of future reproduction to young cancer survivors, though none of these strategies have high rates of success, according to a Portland, Ore., pediatric endocrinologist.

The American Society of Clinical Oncology recommends that physicians discuss reproductive issues with every patient before treating cancer and refer to reproductive specialists when appropriate.

Ovarian failure occurs in about 15% of females with acute myelogenous leukemia, 44% with non-Hodgkin's lymphoma, and 32% with Hodgkin's disease, according to one study. Overall, the literature suggests that 34% of females who undergo chemotherapy develop ovarian failure, though alkylating agents such as cyclophosphamide are four times as toxic to the ovaries as other agents, Dr. David M. Lee of Oregon Health and Science University, Portland, said at the annual meeting of the North American Society for Pediatric and Adolescent Gynecology. Radiation therapy can cause ovarian failure or affect the uterus so that subsequent pregnancies carry an increased risk for preterm labor, low birth weight, or miscarriage. Cranial radiation can change hormone output so the patient ends up hypogonadic.

The patient's age and maturity help determine the choice of options for reproductive preservation. For prepubertal patients, the only option is ovarian tissue banking. For postpubertal females who are mature enough socially and physically to undergo hormonal stimulation and oocyte freezing, "that's probably your best course to take" if there's time before or in between cancer treatments, he said. For other postpubertal females of reproductive age, embryo freezing is a possibility.

Dr. Lee summarized the advantages and disadvantages of the different strategies:

► **Gonadal suppression.** The idea is that giving GnRH before chemotherapy could put patients into a hormonally prepubertal state in which they might be less susceptible to ovarian failure. Three small, nonrandomized studies using historical controls suggest some protective effect in patients getting GnRH before alkylating chemotherapy for Hodgkin's disease and non-Hodgkin's lymphoma.

The only prospective, randomized study found no benefit, however—four of eight women given GnRH and six of nine controls had amenorrhea after chemotherapy, he noted. "I think it depends on the clinical situation. I think it's reasonable. There are more studies ongoing" that might provide answers in 3-5 years, he added.

► **Ovarian pexy.** Using surgical techniques to temporarily move ovaries out of the way of radiation therapy might help, yet ovarian failure still occurs in 29%-83% of patients with cervical cancer treated with radiation despite ovarian pexy. The technique cannot avoid chemotherapy toxicity to ovaries.

► **IVF plus embryo freezing.** This proven technique can be helpful if there's a window of time between surgery and chemotherapy for cancer. "It's not experimental. We do it all the time," but it results in a 20%-30% chance of pregnancy per frozen/thawed embryo, he said. The need for hormonal stimulation is a barrier in some patients. The patient needs to have a partner or be mature enough to pick a sperm donor. If the patient doesn't survive the cancer, "orphan embryos" are left behind.

► **Oocyte freezing.** Harvesting and freezing mature eggs, which later can be fertilized, has led to more than 400 pregnancies. Because the eggs aren't fertilized when frozen, the patient doesn't need to choose a partner at that time and won't leave orphan embryos.

The technique still requires in vitro fertilization-like stimulation, yielding 15-20 mature eggs from older adolescents.

Freezing mature eggs is trickier than freezing embryos, resulting in a 1%-4%

chance of pregnancy per oocyte frozen.

► **Ovarian tissue freezing.** Freezing prepubertal ovarian tissue does not require hormonal stimulation or sexual maturity and preserves hundreds of thousands of immature oocytes. Extensive culture or grafting is necessary, however, for a thawed oocyte to reach maturity in this strategy.

Autografting has led to approximately a dozen pregnancies after ovarian tissue freezing, but the technique is still in early development, Dr. Lee said. ■



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CARDIOVASCULAR AND OTHER RISKS Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 6.8 years and 7.1 years, respectively, of treatment with daily oral conjugated estrogens (CE 0.625 mg), relative to placebo.

The estrogen plus progestin WHI substudy reported increased risk of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and DVT in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral CE 0.625 mg combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo.