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*Pathway to Parenthood*

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## **ONCOFERTILITY: STRATEGIES OF FERTILITY PRESERVATION FOR PATIENTS WITH CANCER**

There have been significant advances in the world of oncology. Survival rates among young cancer patients have increased, such that patients can look forward to life after cancer. Cancer treatment generally involves one or all of the following approaches: A) Surgery; B) Chemotherapy; C) Radiation Treatment & D) Immune Modulation Treatment. One of the unfortunate “side effects” of some of these treatments is irreversible impact on future reproduction. Therefore, nowadays it is incumbent upon all oncologists and doctors to discuss options of fertility preservation with their cancer patients prior to the initiation of treatment. If necessary, consultation with reproductive specialists is important to see if it is appropriate or applicable to employ any of the following approaches in an effort to either negate or minimize the impact of cancer treatments on future reproductive potential.

The following approaches have been employed and/or studied by reproductive specialists in collaboration with oncologists:

- 1. GONADAL SUPPRESSION:** Taking gonadotropin releasing hormone (GnRH) before chemotherapy could put patients into a hormonally pre-pubertal state, in which they might be less susceptible to ovarian failure. Data is limited about this approach. Retrospective observational studies suggest some protective effect in patients getting GnRH before chemotherapy. There have been few randomized controlled trials (RCT). The largest one to date, published in JAMA in 2011, evaluated GnRH treatment in women with breast cancer undergoing chemotherapy. They found a decrease in the rate of premature menopause. One of the limitations of this study is that the outcome of premature menopause is different than fertility, and it is unclear if the women had diminished ovarian reserve (DOR). A systematic review and meta-analysis showed that GnRH agonist treatment resulted in a higher likelihood of preserved ovarian function, but when looking at only RCTs, there was no statistically significant difference. Further studies are clearly needed to clarify this point. There is little harm, however, to trying this approach as a measure of last resort.
  
- 2. OVARIAN TRANSPOSITION:** Surgical techniques can be used to temporarily move the ovaries out of the way of radiation therapy. However, studies have determined that ovarian failure still can occur between 30-80% of the time despite this pre-treatment approach. This technique cannot avoid chemotherapy toxicity to the ovaries.

- 3. IVF + EMBRYO FREEZING:** This proven technique can be helpful if there is a window of time prior to initiating chemo or radiation. The ovaries are stimulated with medication to produce many eggs, which are then removed from the body and inseminated with sperm to create embryos. This technique is not experimental and patients can anticipate approximately 30% pregnancy rate from frozen embryo transfer procedures. The need for hormonal stimulation is a barrier in some patients. The patient needs to either have a partner or be mature enough to pick a sperm donor. For both embryo freezing and egg freezing (see next point), it may be important to keep estrogen levels low during the stimulation phase, and this can be accomplished with the addition of aromatase inhibitors. This is especially true for patients with Estrogen Receptor positive malignancies.
- 4. OOCYTE (EGG) FREEZING:** In this approach, the ovaries are stimulated with medication to produce many eggs, and unfertilized eggs are frozen; therefore, there is no need for a sperm donor or partner. Also, the issue of ‘orphan embryos’ is a non-factor. The technique still involves hormonal stimulation, which can be a barrier when dealing with some forms of cancer. In October 2012, this procedure’s “experimental” label was lifted, and it is now a standard procedure offered by many assisted reproductive technology (ART) practices.
- 5. OVARIAN TISSUE FREEZING:** Freezing pre-pubertal ovarian tissue does not require hormonal stimulation or sexual maturity and can potentially preserve hundreds of thousands of immature oocytes. Sophisticated culture techniques will be required to bring such frozen tissue to survival and this approach should be reserved for centers with dedicated tissue freezing programs. The technique is still in the early phases of development and regarded as experimental. The same issues apply to freezing of testicular tissue in males. NYFS currently does not offer this preservation technique.
- 6. SPERM FREEZING.** This can be readily accomplished and can subsequently be used for either intra-uterine inseminations or IVF with intra-cytoplasmic sperm injection (ICSI). The decision as to what approach to use will be dependent on the sperm counts both before freezing and after thaw. There is no limit on the duration for the sperm to remain frozen. Successes have been reported with a long interval (> 10 years) between freezing and subsequent use.

The above mentioned approaches are some of the present day techniques employed by reproductive specialists. Obviously the primary issue is always the cancer and the directives of the oncology team always should take priority. The reproductive team should subordinate decision making to the oncologists; however with close collaboration amongst treating professionals, good decisions can be made with the optimistic potential of preserving future child-bearing potential.

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*This handout is intended as an aid to provide patients with general information. As science is rapidly evolving, some new information may not be presented here. It is not intended to replace or define evaluation and treatment by a physician.*