PATH2 PARENTHOOD fact sheet

UNDERSTANDING YOUR FERTILITY PRESERVATION OPTIONS

BACKGROUND

In 2010 it was estimated that 1.5 million men and women would be diagnosed with cancer, with approximately 10% being younger than 45 years of age, and 1% younger than 20. Excellent scientific and clinical advancements in oncology and treatments of cancers have improved the overall 5-year survival rate to nearly 80% for young adults[1]. Rightfully so, survival remains the primary focus of cancer treatment. Yet, it has long been recognized that cancer therapies can result in infertility due to premature gonadal failure. With the life-saving success of cancer treatments, and the unintended side effect of infertility, this has created a significant quality-of-life issue for young cancer survivors. Thus, fertility preservation has become an important and growing field of medicine focused on diagnostic, preventative, and application of assisted reproductive technologies as preemptive and therapeutic strategies to predict or protect future reproductive potential in both men and women.

Cancer therapies, both radiation and chemotherapies, cause subfertility or infertility due to damage of male or female germ cells, thus necessitating medical intervention in order to maximize retention of fertility. However, treatment modalities used for other medical conditions such as glomerulonephritis, lupus, and myelodysplasia can also be associated with reduced fertility and thus necessitate fertility preservation. Lastly, adolescent and young adult females with genetic conditions such as Turner's syndrome, (known to be associated with premature ovarian failure), can benefit from proactive screening and fertility preservation[2].

The impact of cancer therapy on female or male fertility is difficult to predict but is understood to be dependent on the following factors: patient age at the time of treatment; dose of radiation exposure or adjuvant therapy; site of radiation exposure; duration of treatment; and type of treatment used. The most severe damage to female and male gametes and future reproduction comes from radiation of the ovaries or testicles and cancer drugs in the "alkylating agent" category, including cyclophosphamide, mechlorethamine, chlorambucil, and melphalan.

Interestingly, concerns for future fertility are significant in individuals newly diagnosed with cancer and/or their family members. A survey in the late 1990s found that approximately 75% of men and women under 35 years of age who are childless at the time of malignancy diagnosis desired children in the future[3]. Furthermore, 81% of adolescent females diagnosed with cancer, and 93% of their parents, have expressed interest in fertility preservation, even if options were described as experimental[4]. Finally, it is imperative to appreciate that the first goal is to cure the cancer, even if the treatment regimen causes infertility. However, there are several options, ranging from standard medical practice to experimental techniques that may help to preserve fertility if applied before cancer treatments.

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PRESERVING FERTILITY BEFORE CANCER THERAPY

• **Men**—Semen samples can be collected and frozen before starting chemotherapy or radiation therapy. Freezing of semen (seminal plasma and the sperm) is a well-establish medical laboratory procedure and can be performed by a commercial sperm bank or laboratory specializing in fertility practices. A single sample, or multiple semen samples, can be cryopreserved prior to initiating cancer therapy. The male must be post-pubertal to facilitate sample collection by masturbation. These samples can be stored for years and can be used post-cancer therapy for insemination in an attempt to initiate a pregnancy. If the samples have poor initial count and motility, freezing/thawing survival, and/or limited supply, the sperm can be used in in vitro fertilization (IVF) and/or intracytoplasmic sperm injection (ICSI).

• **Boys**—The lack of complete sperm production, and the difficulty of obtaining a semen sample, in prepubertal boys presents a dilemma. A fine needle testicular aspiration or testicular biopsy can be performed and testicular tissue can be cryopreserved[5]. These cryopreserved testicular samples can survive. However, currently this approach is experimental and speculative in humans, primarily due to the uncertainty of how to proceed with thawed tissue and/or functionality of these cryopreserved germ cells.

• **Women**—If radiation will be administered to the pelvic region, the ovaries may be surgically repositioned out of the direction of radiation exposure to reduce the risk of egg damage. If time and circumstances allow, postpubertal women may be treated with IVF. Embryos created from IVF can be frozen, stored for many years, and used later in life after cancer therapy in an attempt to establish pregnancy. These are standard fertility medical procedures. Limitations of this approach are age, time, expense, availability of sperm from a partner, and possible delay of cancer treatment.

In the past decade significant advances have been made in preserving female fertility. While many of the below approaches do not have the years of experience that IVF affords, they are rapidly growing in application and can be successful. With this said, they are still considered investigational and/or experimental.

- Ovarian suppression before cancer therapy. It has been speculated that suppression of ovarian function may reduce egg damage in response to cancer treatments. Sparse and conflicting data exist that ovarian suppression before cancer treatment with birth control pills or other means of hormonal suppression, is protective of future fertility[6,7]. Currently clinical trials are being conducted to address this treatment option.
- Egg Freezing. This option is very similar to IVF in its limitations, except that a sperm sample is not needed and embryos are not generated. Once cryopreserved, the eggs can be stored for many years. Recent experience has demonstrated that egg cryopreservation by two methods: slow-rate freezing or vitrification can give rise to egg survival, fertilization, embryo production, pregnancy initiation, and healthy offspring[8,9,10]. In a 2009 survey it was reported that over 900 children had been born worldwide with the use of egg cryopreservation[11].
- Ovarian Tissue Freezing. This experimental approach requires surgery to remove a small section of ovarian tissue. This tissue can then be frozen and stored for many years. Studies have demonstrated that frozen tissue can survive thawing, can be reimplanted, and can function for a limited period of time. Recent reports in the medical literature support the premise that these tissues can preserve fertility, yet world-wide experience is quite limited[12].

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FERTILITY AFTER CANCER THERAPY

• **Men**—It is difficult to predict how sperm production will be influenced by chemo- radiation therapies. If sperm production is impacted initially it can rebound after months to years. Semen analyses at six month intervals after therapy may be advisable. If sperm are consistently low or absent, intrauterine insemination, IVF, and/or ICSI may be necessary to achieve pregnancy. This could be performed with ejaculated sperm, if present, or cryopreserved sperm. Testicular sperm isolation may be used in individuals without sperm in ejaculate or cryopreserved sperm. If sperm are not obtainable, and no samples were previously cryopreserved, pregnancy may be possible using

• **Women**—Again, prediction of impact of cancer therapy on female fertility is difficult and follow-up after cancer treatment is necessary. Once the physician has advised that attempting pregnancy is safe, women should consult a fertility specialist to check for ovarian damage and discuss reproductive options. Many women will be able to conceive naturally or with assistance from a fertility specialist. If significant damage has occurred to the reproductive organs, couples may wish to use previously cryopreserved embryos, eggs, or tissues. If these are not available, couples may want to consider egg or embryo donation, a gestational carrier, or adoption for establishment of pregnancy and family building.

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