Fertility Preservation in the Male

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Introduction

Approximately 50% of all males will be diagnosed with cancer at some point in their lifetimes. A cancer diagnosis is typically fraught with a flurry of clinical activity, which is necessary to clarify the extent of the disease and to delineate the appropriate next steps in treatment. In the midst of all of this clinical activity, patients are often overcome by a wide array of emotions including denial, severe anxiety, and gripping fear. The "good news" in the field of oncology is that the vast majority of men considered to be of "reproductive age" will respond to the oncologic treatments and survive their cancer. The "down side" to this series of events, though, is that males are often left with impaired fertility as a result of their cancer treatments. Male infertility is now recognized as a significant survivorship issue affecting large numbers of males who have been treated for cancer. In this blog, we will provide an overview of the effects of cancer and cancer therapy on male reproduction, and we will discuss some of the methods commonly employed to preserve a male's ability to father children after the completion of cancer treatments.

Effects of Cancer

Before any chemotherapy has been administered and prior to the delivery of any ionizing radiation treatment, cancer itself can lead to impaired male reproductive health. The effects of cancer can include the suppression of key hormones involved in stimulating and supporting sperm production. A decrease in hormone level can arise from the cancer's impairment of the normal hormonal function of the pituitary gland or the testicle. Additionally, the immune system's protective response to cancer can lead to widespread destruction of germ cells (the developing sperm) and other supporting cells in the testicle. Free radicals and other immune system chemical agents can cause widespread destruction throughout the body, including the testicles. The body's aim is to rid itself of cancer, but the fragile, developing sperm are analogous to "innocent bystanders" that can be destroyed by the immune system. These cumulative changes can lead to temporary or lasting male infertility.

Effects of Chemotherapy

In addition to the effects of cancer, cancer treatments can also impact fertility. Chemotherapeutic agents can cause a lasting interruption of sperm production. The dosage of drugs, the duration of therapy, and the age of the patient can all affect the impact of chemotherapy on fertility. Furthermore, the specific drug or combination of drugs is also important in determining the effects on sperm production. For example, alkylating agents are among the most spermatotoxic group of drugs, and the depletion of germ cell stem cells by chemotherapy drugs can cause permanent loss of sperm production. A wide variety of chemotherapeutic agents are commonly available in

clinical practice today, and patients often receive combinations of different drugs. Patients are encouraged to discuss with their physicians the side effects on fertility of the specific chemotherapeutic regimen he will receive *before* the start of treatment. Additionally, "patient friendly" websites, such as *myoncofertility.org* and *livestrong.com,* provide a wealth of information regarding the effects of chemotherapy for patients.

Effects of Radiation Therapy

Radiation therapy, like chemotherapy, can impact male reproductive health. Even very small doses can cause transient or lasting male infertility. The use of gonadal shielding is one common precaution to spare the testicles from damage due to radiation scatter, and this is a particularly critical fertility preservation maneuver when pelvic, groin, retroperitoneal, or proximal upper extremity treatments are administered. The developing sperm are exquisitely sensitive to the effects of radiation treatment, and testicular shielding and sperm banking are important considerations for patients receiving such therapies.

Effects of Surgical Therapy

A number of surgical procedures can impair male reproduction. Any procedure detracting from the normal hormonal secretion pattern of the pituitary gland can lead to absence of hormonal drive for sperm production. Surgeries on the testicles can obviously decrease a male's capability for sperm production, because of the loss of sperm producing tissue. The ejaculation reflex can be hindered by surgery on the spinal cord, the colon, or the retroperitoneal space, and each can lead to neurologic deficits with resultant impaired ejaculation. Removal of the prostate gland alone or the prostate gland and the bladder together can result in loss of an ejaculate and thus interrupted fertility. Finally, procedures can sometimes result in disturbance of the continuity of the excurrent ductal system (epididymis, vas deferens, etc.), the sperm delivery pathway. The key for patients is to ask their surgeon in advance of any planned procedure if fertility impairment can result from the procedure. If the answer is "yes," then sperm cryopreservation should be considered.

Fertility Preservation Methods

Fertility preservation for male patients can be accomplished with cryopreservation of sperm prior to the initiation of cancer therapy. In the vast majority of cases, sperm can be obtained for freezing from an ejaculated semen sample. While patients and clinicians might assume otherwise, sperm banking can be accomplished even for individuals who are patients in the hospital. Effective and seamless delivery of fertility preservation care requires an awareness of the importance of fertility preservation by cancer care providers and the availability of fertility preservation specialists and laboratory staff.

Occasionally, difficulties might arise in the process of fertility preservation. For example, a patient might not be able to ejaculate, which can occasionally be a side effect of anatomical changes due to cancer or medications used to control pain associated with cancer. In this event, certain medications can sometimes be used to help facilitate

ejaculation. If these efforts do not result in success, sperm can alternatively be isolated from the testicle during a surgical procedure called “testicular sperm extraction” (TESE). In a similar fashion, some patients might be able to ejaculate, but they have no sperm present in the ejaculated semen sample. Again, in this event, a surgical TESE procedure can be performed, very often under a combined anesthetic for procedures such as portacath placement or tissue biopsy.

Use of Cryopreserved Sperm

Once sperm is frozen, it remains usable for an apparently indefinite period of time. Sperm frozen for over 20 years has been successfully used to achieve pregnancies. Sperm cryopreserved for fertility preservation must be used in the setting of “assisted reproductive techniques. “ Usually, this consists of employing the sperm in a procedure called *in vitro* fertilization (IVF) with intracytoplasmic sperm injection (ICSI). IVF with ICSI involves the harvesting of oocytes from the female partner and a subsequent laboratory procedure where a single spermatozoon is microscopically injected into each of the oocytes. Typically, two or three fertilized oocytes (embryos) are transferred back into the female partner’s uterus 3-5 days after the initial oocyte retrieval. Any extra embryos can be potentially cryopreserved for future use. Success rates for IVF with ICSI are dependent on both male and female factors, with the age of the female partner being one of the most predictive determinants of success. Overall, typical pregnancy rates for IVF with ICSI are on the order of 40-60% per attempt, with success rates diminishing with increasing female partner age. Couples should initiate a discussion with a reproductive endocrinologist to learn more about the procedure and also about the specific female partner’s prospects for pregnancy with this technique.

How To Initiate the Discussion

Research has shown that many health care providers are unaware of the formal recommendations for fertility preservation discussions with newly diagnosed cancer patients. These recommendations come from the American Society of Clinical Oncology and other physician professional organizations. Numerous investigations have also shown that clinicians sometimes mistakenly assume that a specific patient might not be interested in fertility preservation. As a result, it is imperative that patients become empowered in “breaking the ice” and initiating a conversation about fertility preservation options with their physician. The myoncofertility.org web site highlights five important questions that a patient should ask his doctor prior to starting chemotherapy.
They are:
1. “How is my cancer affecting my health right now?”
2. “How quickly do I need to start treatment?”
3. “Will my cancer or its treatment affect my future fertility?”
4. “What fertility options are out there?”
5. “Can I have a child after my cancer?”

This series of questions will help put the underlying disease process, the planned cancer treatment, and the anticipated change in fertility into the proper context for the patient and their partner to understand and plan accordingly. Moreover, it will serve as a gentle reminder to the clinician that sperm cryopreservation is an aspect of the planned

treatment regimen for that patient that should be considered prior to the initiation of cancer therapy.

Additional Resources

Readers will find a wealth of additional information regarding cancer and fertility preservation at the following web sites:

THE ONCOFERTILITY CONSORTIUM
http://oncofertility.northwestern.edu

FERTILE HOPE GLOSSARY
http://www.fertilehope.org/tool-bar/glossary.cfm

CANCER.NET
http://www.cancer.net

AMERICAN CANCER SOCIETY
http://www.cancer.org

ASSOCIATION FOR CANCER ONLINE RESOURCES (ACOR)
http://www.acor.org

NATIONAL COALITION FOR CANCER SURVIVORSHIP
http://www.canceradvocacy.org

NATIONAL CANCER INSTITUTE
http://www.cancer.gov

THE WELLNESS COMMUNITY
http://www.thewellnesscommunity.org

I'M TOO YOUNG FOR THIS! CANCER FOUNDATION
http://i2y.com