Fertility Following Cancer-New Hopes & New Horizons

There are Winners!
The battle against cancer now has many winners. About one in three Americans will contract cancer in their lifetime with a growing proportion of patients surviving. Once these survivors reach the reproductive years, questions and concerns about conceiving a family often arise.

Why Can Cancer Treatment Cause Sterility?
While the cancer itself may cause infertility, it is more often the treatments including surgery and radiation combined with chemotherapy that often cause the greatest damage to the reproductive organs.

Cancer chemotherapy works by killing the rapidly dividing cancer cells. Radiation therapy works through local targeted tissue destruction. It is currently not feasible to completely separate the invading cancer cells from nearby normal tissue. Structures such as the testes and ovaries are inadvertently involved in the “cell kill” process of cancer treatments.

In the Male…
In the male, the testes are quite sensitive to the numerous cancer therapies available and it is common for the man to become temporarily sterile following therapy. Depending upon the extent/duration of the cancer treatment, the sterility can be permanent. While the progenitor sperm cells that create sperm are often damaged, the cells that produce testosterone (Leydig cells) are infrequently affected by the cancer therapy.

New techniques are now available including micromanipulation in which only a few live sperm are needed to fertilize a human egg. With these micromanipulation techniques, even sperm of very poor quality, as is frequently found in the newly diagnosed cancer patient, may be cryopreserved and eventually used to produce a child.

When possible, men should have their testes carefully shielded from radiation treatments. In addition, different types of radiation minimize the scatter of radiation and the potential damage to the testes. There are times, however, that the radiation must be administered quite close to the testes.

The testes may be able to recover from the cancer treatments. Most men who are without sperm for four years following completion of the therapy will remain sterile. Even with the best of therapeutic intentions, the testes may be rendered sterile following cancer therapy.

In the Female…
In the menstruating female, the ovaries are also quite sensitive to the cancer therapies. It is common for the female to temporarily stop menstruating during therapy. The younger the patient, the more likely the
menses will return following therapy. Depending on the age of the patient, the type of cancer therapy and the duration of therapy, some women will enter menopause following the cancer treatment.

When possible, women should have their ovaries shielded from radiation treatment. In some instances, the ovaries can be surgically shifted and repositioned away from the radiation treatments.

For those who do not enter menopause immediately following treatment, early menopause (often termed “premature ovarian failure”) is quite common although somewhat difficult to predict.

**Thinking Ahead:**
If possible, prior to the initiation of any cancer surgery or the actual cancer therapy, gonadal cells (sperm/eggs) or gonadal tissue (testicular/ovarian) can be collected and frozen in liquid nitrogen and stored for later use.

In the past, sperm has been routinely cryopreserved prior to surgery, chemotherapy and radiation therapy in the cancer patient. Technologies continue to evolve in the cryopreservation of eggs, ovarian and testicular tissue.

<table>
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<th>Patient</th>
<th>Tissue or Cells</th>
<th>Common Use?</th>
<th>Theoretical Use</th>
<th>Considered?</th>
<th>Comments</th>
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| Pre-pubertal Male Child      | Testicular Tissue | Not at present.    | 1. Transplantation back into the body following therapy.  
2. Maturation of sperm cells in the laboratory.  | Experimental     | If near puberty, In Vitro Fertilization may be used if mature sperm cells are found. |
| Pre-pubertal Female Child    | Ovarian Tissue  | Not at present.    | 1. Transplantation back into the body following therapy.  
2. Maturation of sperm cells in the laboratory.  | Experimental     | It is hoped that In Vitro Maturation (IVM) will be perfected in the future for the ovarian tissue cryopreserved today. IVF techniques will then be needed to create embryos. |
| Adult Female                 | Ovarian Tissue  | Not at present.    | 1. Transplantation back into the body following therapy.  
2. Maturation of eggs in the laboratory combined with IVF | Experimental     |                                                                                       |
| Adult Female                 | Eggs            | Becoming more common. | 1. Thawing with fertilization through direct sperm injection combined with embryo transfer procedures | Investigational  | This technique is available although it requires stimulation of the ovaries with removal of the mature eggs. |

Experimental: While there may be some experiments that show the technique works, the process is still being examined in detail.
Investigational: Some studies show usefulness but it is not yet standard-of-care.
Standard-of-Care: The technique is practiced frequently and has enough supporting data that it is accepted within clinical practice.
Will the Children Be Normal?
Children conceived from cancer survivors are not at any higher risk for birth defects. Genetic mutations are theoretical and have not been conclusively shown in humans.

Summary Comments:
Cancer, a life-threatening illness, is being adequately treated and even cured in a number of patients. The cancer survivors are free to enjoy the precious life given to them and fulfill a wish to start a family. Current technology makes starting a family possible through the prevention reproductive cellular destruction through the use of cryopreservation techniques. New hopes and horizons are truly there for the cancer survivor.

It is hoped that techniques to use thawed sperm, oocytes and gonadal tissue will be perfected in the future for the patients who survive cancer today.