Interdisciplinary Team To Tackle Fertility Issues in Cancer Survivors

By Karen Ross

Infertility related to cancer treatment is an important quality-of-life issue for the increasing number of young cancer survivors, but research in this area has been limited. Now, with a 5-year, $21.6 million grant from the National Institutes of Health, an interdisciplinary group has begun to explore some of the biological, social, ethical, legal, economic, and educational issues related to fertility after cancer treatment.

Every year, 140,000 people of reproductive age are diagnosed with cancer in the United States, according to the grant’s principal investigator, Teresa Woodruff, Ph.D., professor of obstetrics and gynecology at Northwestern University’s Feinberg School of Medicine in Chicago. Unfortunately, the treatments that can prolong their survival—surgery, radiation therapy, and chemotherapy—can also negatively affect their reproductive organs. For some patients, the fertility risk is low, but many others are left permanently infertile.

The Oncofertility Consortium’s goals are to educate all cancer patients about the possible effects of treatment on their fertility, to develop new technology to help patients preserve their fertility, and to study the social and ethical issues that influence how that fertility preservation technology is used and perceived. To achieve these goals, researchers and doctors in oncology and fertility must work together in unprecedented ways. “We coined the term ‘oncofertility’ to say that we were bringing together oncologists and fertility specialists,” Woodruff said. “These two groups traditionally do not interface.”

Until the grant award last fall, federal funding for oncofertility research was nearly impossible to get, Woodruff said. Because of its inherently interdisciplinary nature, the research did not fit into priorities at either the National Cancer Institute, which funds cancer research, or the National Institute of Child Health and Human Development, which funds fertility research.

In the past, much of the support for oncofertility research has come from patient groups, especially Fertile Hope, founded by cancer survivor Lindsay Beck. Although there were many individual researchers with a deep interest in cancer-related infertility, Beck said, there was “a void” on the funding side. The new consortium’s grant came through a program at NIH that awarded $20 million–$25 million over 5 years to each of nine interdisciplinary research groups, including the Oncofertility Consortium.

The consortium’s core members are drawn from five institutions: Northwestern University; the University of California, San Diego; the University of Pennsylvania in Philadelphia; Oregon Health and Science University in Portland; and the University of Missouri in Columbia.

Also, some 25 other institutions are joining a program called the National Physicians Cooperative, which will link the consortium researchers to doctors and patients. The goal is to have a network of National Physicians Cooperative members so that patients who wish to participate in fertility preservation research can go to a center near their home.

The consortium’s work in basic biology focuses on women because, although cancer treatment can also cause infertility in men, the technology for preserving male fertility—sperm banking—is much more accessible. For women, the only well-developed technology is in vitro fertilization (IVF), whereby mature eggs are collected from a woman’s ovary, fertilized in the lab, and frozen until the woman wants to become pregnant.
Unfortunately, IVF cannot help many women with cancer. The procedure takes several weeks and involves a series of hormone injections, so it is not appropriate for patients who must begin cancer treatment immediately or those who have a potentially hormone-responsive cancer, such as breast cancer.

Reproductive scientists in the consortium are developing methods to use frozen ovarian tissue, instead of mature eggs, as a starting material for IVF. Having an ovary removed and stored before beginning treatment would be feasible for most women with cancer. John Critser, Ph.D., of the University of Missouri is determining the optimal methods for freezing and thawing ovarian tissue. Although there are well-established procedures for freezing single cells, freezing a complex tissue such as the ovary is much more difficult, Critser said. His group is using a mathematical model to evaluate the optimal conditions for freezing such tissue—for example, how fast to cool the tissue and which chemical protective agents to use. The model is later used to inform tests on actual ovarian tissue.

Woodruff and Richard Stouffer, Ph.D., of Oregon Health and Science University are developing technology to coax ovarian follicles to produce mature eggs in the lab. Woodruff’s group has already achieved healthy pregnancies in mice by using mouse ovarian follicles incubated in a cell culture system with a three-dimensional biological scaffold. Stouffer is currently testing the procedure on rhesus monkey ovarian follicles, a more humanlike experimental system.

Other scientists in Woodruff’s group are measuring reproductive hormone levels in cancer patients before, during, and after treatment and comparing the levels with those of healthy control subjects in an effort to develop guidelines to predict the timing and severity of cancer treatment–induced fertility loss. The information will be used to counsel patients about their fertility risk.

Social scientists in the consortium are working to unravel the complex social, ethical, legal, and economic questions related to oncofertility. For example, Woodruff consulted Northwestern bioethicist Laurie Zoloth, Ph.D., when confronted with the ethical issues that arose from the technology she was developing. “We were talking about taking an ovary out of a child,” Woodruff said, which prompted many ethical questions. Who would have custody of the tissue if the child died? What if the child survived and her parents had chosen not to help her preserve fertility? Zoloth, together with Northwestern colleagues Linda Emanuel, M.D., Ph.D., and Dorothy Roberts, J.D., will look into these and other ethical and legal questions raised by fertility preservation efforts in cancer patients, particularly children.

Questions under study by other members of the consortium include the following: How can parents of a young person with cancer make an informed choice about whether to have him or her participate in a fertility preservation program? How do women with breast cancer discuss fertility issues with their health care providers? How much would young women with and without cancer be willing to pay for fertility preservation treatments?

David Dranove, Ph.D., a professor at Northwestern’s Kellogg School of Management, is researching this last question and says that the answer will be a “useful benchmark” for health insurance companies that are deciding whether to cover fertility preservation treatments; generally, insurance does not cover such treatments.

The consortium’s educational efforts are multifaceted, with programs aimed at health professionals, patients and their loved ones, and young people in the general public. For example, the consortium will work with Fertile Hope to reach out to the cancer patient community. “We plan to play a strong role in translating the science into layman’s terms and disseminating it to the patient population,” Fertile Hope’s Beck said.

The grant lasts 5 years, but Beck hopes that NIH’s endorsement of oncofertility research will start a “domino effect,” encouraging more traditional funding sources to get involved. “I hope that great strides will be made to advance the spectrum of treatment options for women.”

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