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Cancer and Childbirth: Mutually Exclusive No Longer

By JANE E. BRODY

MaryBeth Zea of Little Falls, Minn., was only 28, married but childless, when breast cancer struck in 1988. The surgeon who performed her mastectomy told her that because her cancer was not hormone-sensitive, pregnancy would probably not make much difference to her chances of a recurrence. He told her that pregnancy was a personal choice.

But MaryBeth was afraid that the stress of pregnancy and its outpouring of hormones could stimulate a regrowth of cancer. She also feared what would become of a baby if she should get sick again. And so she chose to remain childless and devote herself instead to her marriage and career, now as a still-lively portrait photographer.

When Randi Gaier, a 34-year-old mother of two preschoolers in Wynnewood, Pa., was treated for Hodgkin's disease 15 years ago, surgeons first moved her ovaries out of the radiation field before administering the radiation therapy that cured her. Still, she worried enough about the possibility of a recurrence and whether her body could sustain a pregnancy to wait six years into marriage before trying to start a family.

Today, as millions of men and women of childbearing age and younger are surviving cancer, the question of reproduction is arising as a paramount consideration in planning treatment. Among the issues are the ability to preserve fertility while curing the disease and the safety of pregnancy for both mothers with cancer and their future children.

In a continuing study of more than 20,000 survivors of childhood cancers, the two greatest concerns mentioned by former patients two and three decades later are "Can I have children?" and "If I have children, will they be healthy?" said Dr. Leslie Robison, an epidemiologist at the University of Minnesota Medical School, who directs the project involving 25 cancer centers. "Today more than 75 percent of children with cancer are being cured, yet we know little about the side effects of treatment (beyond the first 10 years)."

While some cancer treatments — drugs as well as radiation — can cause sterility or reduced fertility in men and women, preliminary evidence suggests that cancer therapy, in general, affects the ability to reproduce and to produce healthy children less than previously thought. At the same time, new ways are being devised to reduce the effects of cancer treatments on fertility and on pregnancies already in progress when a cancer is discovered.

In the first report on reproductive issues from the 25-center study, soon to be published in *The American Journal of Obstetrics and Gynecology*, the researchers found that while higher rates of miscarriage and lower birth weights were observed among the offspring of former patients, "there are a large number of live births, births of healthy children, a lack of congenital abnormalities and very low cancer rates," Dr. Robison said.

"The data are extremely reassuring," she added. "It's a very good news type of report." The researchers would not provide details of the findings before publication.

Dr. Giuseppe Del Priore, director of gynecology



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Randi Gaier, above, was treated for Hodgkin's disease 15 years ago. Surgeons moved her ovaries out of the radiation field before administering the therapy. Dr. Dan Shapiro, right, stored sperm before receiving treatment for Hodgkin's.



Joshua Epstein for The New York Times

oncology at Bellevue Hospital in New York, and his colleagues at the New York University School of Medicine noted in the January issue of *Contemporary Obstetrics/Gynecology*: "Less than a generation ago, reproductive-aged women with cancer generally had little to hope for and even less to look forward to. But things have changed. Many cancers are no longer a death sentence. More and more women with cancer are now becoming pregnant and raising legitimate fertility concerns."

Today, a doctor could tell Ms. Zea of Minnesota and other women like her that pregnancy is no longer ill-advised. Even women whose breast cancers are discovered during pregnancy should no longer be advised to terminate the pregnancy, because there are no data indicating a therapeutic benefit from such an abortion, the New York experts said.

The estrogen produced in pregnancy is weaker than estrogen produced in other women and is less likely to stimulate breast cancer growth, even if the woman's tumor is estrogen-sensitive.

Today, too, even cancers directly involving the reproductive organs — ovaries, uterus and cervix — can sometimes be treated in ways that permit future pregnancies and

the births of healthy babies. Many of the modern chemotherapeutic agents are less damaging to ovarian function than the older drugs and do not induce permanent early menopause. Thus, a woman's fertility may return months or even years after treatment ends.

Fears that potent anticancer drugs will damage the DNA of a woman's eggs or a

Some treatments keep the reproductive parts out of harm's way.

man's sperm and result in birth defects have not been borne out by experience.

As Dr. Elyse H. Cardonick, a perinatologist at Thomas Jefferson University Hospital in Philadelphia, wrote in the March/April issue of *Coping* magazine, "The medical literature contains reports of children born of parents previously treated for cancer, including Hodgkin's disease, leukemia, melanoma and breast cancer, and an excess

of birth defects or medical diseases is reported compared to the general population."

She continued, "There is also no report of damage to the children's chromosomes, despite their parents' preconceptual cancer therapy."

Dr. John J. Mulvihill, a pediatric geneticist formerly with the National Cancer Institute and now at the University of Oklahoma Health Sciences Center, has studied this question in thousands of patients who were treated for cancer early in life and were followed for decades. He said in an interview, "We can be quite reassuring that if fertility is maintained, there will be no increased risk of birth defects or genetic disease."

There are, however, cancers that run in families, and susceptibility to these cancers could be transmitted to patients' children, but the treatment itself is not now considered a factor influencing genetic risk.

Dr. Mulvihill said he would like to do more detailed studies to determine whether subtle injuries to the human genome might occur from the chemicals and radiation used in cancer treatments.

"Our knowledge of the genetic effects of environmental insults come largely from studies in mice," Dr. Mulvihill noted. "Maybe people are protected against environmentally induced genetic insults. Perhaps the testes and ovaries are different, less vulnerable than other tissues. We know that mutations must occur, but maybe it's a rare event. We have to study this at the DNA level."

While there is still much to learn about reproductive issues following cancer, even information available now fails to reach a very large percentage of cancer patients. Only about half of cancer patients of childbearing age receive adequate information about the possibility of having children after treatment, according to the findings of a pilot survey conducted in 1999 by the Cleveland Clinic Foundation.

While men and adolescent boys with cancer who wish to preserve their fertility can easily bank sperm for future insemination before starting treatment, only about a quarter of childless men do so, the survey indicated.

Dr. Dan Shapiro, a clinical psychologist at the University of Arizona Medical Center in Tucson, fathered two children with sperm stored more than a decade earlier, before he underwent extensive fertility-destroying treatments for Hodgkin's disease. "The possibility of banking sperm before treatment," he said, "is still not being mentioned to many young cancer patients."

The reproductive issues for women with cancer are far more complex and less certain to succeed. It takes weeks to stimulate the development and release of mature eggs, and during that time, cancer treatments must be delayed. Then, the eggs must be fertilized and grown into early embryos before they can be frozen for future impregnation. For some cancers, like breast cancer, the potent hormonal stimulation needed to harvest eggs could further endanger a woman's health.

Although at some research centers, ovarian tissue is being frozen for future egg

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Trying Childbirth, While Fighting Cancer

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development, no human pregnancies have been achieved with this approach, Dr. Cardonick said. And in girls and women whose cancers must be treated with extensive abdominal radiation, including young girls with Wilms's tumor, the walls of the uterus can become unable to support a pregnancy.

Even if cancer treatment leaves a woman's reproductive organs intact, some lifesaving cancer drugs, for

example, adriamycin and bleomycin, can damage the heart or lungs, making it difficult to go through pregnancy. But it is possible to assess in advance, with various tests, a woman's ability to withstand the biological and physical demands of pregnancy.

Also, refinements in radiation therapy often make it possible to protect reproductive organs from radiation damage without compromising the success of treatment. Modern diagnostic tools, like magnetic resonance imaging, may permit an accu-

rate assessment of the extent of a tumor without exposing the patient to radiation, and high-dose radiation used in treatment can now be delivered to a more circumscribed area.

In some cases, as with Ms. Gaier of Pennsylvania, a woman's ovaries can be moved surgically as far as possible from the radiation field to reduce the risk of permanent damage in cancer treatment.

Even for the thousands of young women who develop cervical cancer each year, there are now treatments that can preserve their fertility. For

example, Dr. Priore's team noted, surgical removal of only the cervix and not the neck of the uterus, is now routine. Surgeons can then place purse-string sutures at the end of the uterus to improve the chances of holding on to a pregnancy.

For women whose ovarian function is permanently suppressed by cancer treatment that results in premature menopause, pregnancy is possible through in-vitro fertilization of a donated egg, Dr. Cardonick said. "Even if there is no ovarian function as a result of chemotherapy, a wom-

an can carry a pregnancy," she said.

Cancer specialists agree that it is unwise for a woman to become pregnant during cancer treatment because it can be difficult to predict whether she will survive her current disease. Also, if a pregnant woman must be treated with radiation, the chances of harm to a developing fetus are considerable.

Chemotherapy, however, is different. Even as long ago as 1987, scientists at the National Cancer Institute reported that "if a pregnancy is begun, there is room, with present limited knowledge, for reassurance that the human fetus may survive unharmed even after exposure to modern multiple-agent chemotherapy

during the first trimester."

Dr. Mulvihill, who took part in this report, suggested the possibility that "there are protective mechanisms in transporting substances across the placenta or other factors that somehow protect the fetus."

Dr. Cardonick recommends that decisions about future pregnancies be dictated in part by the time period during which a cancer is most likely to recur, if ever. Since most recurrences of breast cancer and melanoma occur within two years of diagnosis, a woman may delay pregnancy until that high-risk period ends to increase the likelihood that the child will have a healthy parent, she and other experts said.