

A photograph of two surgeons in an operating room. They are wearing white surgical masks, blue scrubs, and hairnets. They are holding a newborn baby who is wearing a colorful striped hospital gown. The background shows medical equipment and a sterile environment.

**Gynecologic oncology  
surgeons  
spare patients' fertility,  
enhance quality of life**

*by Jeannie Glickson*

**A**t a recent celebration at the Memorial Sloan-Kettering Cancer Center in New York, NY, an onlooker would view many sights not commonly seen in a cancer center. A boisterous group enjoyed food and drinks in a brightly lit room filled with colorful crepe paper and balloons. The guests, many of them young children, laughed and clapped at a clown hired for the occasion.

This joyous gathering marked the 10-year anniversary of Sloan-Kettering's use of fertility-sparing surgical procedures. In attendance were most of the 20 children born to mothers who received treatment for first-stage cervical cancer with a radical trachelectomy (removal of the cervix). Annually, 10 to 15 patients receive the radical trachelectomy at Sloan-Kettering.

Today, fertility-sparing procedures are also commonly performed in young women with ovarian cancer. If only one ovary is cancerous, and the cancer is in Stage 1A, fertility-sparing surgery becomes a hopeful option for patients still wanting to conceive. The surgery might include removal of the cancerous ovary, but would leave the unaffected ovary and the uterus.

### *Diagnosis no longer ends pregnancy hopes*

In 1943, George Papanicolaou, MD, and Herbert F. Taut, MD, published "Diagnosis of uterine cancer by the vaginal smear" in the *Yale Journal of Biology and Medicine*. The study set in motion the worldwide use of the Pap smear to test for cervical cancer.<sup>1</sup> Since World War II, the Pap test has become the most widely used cancer screening method in the world, detecting cervical cancer during its most

treatable early stages.<sup>2</sup> Thanks to a vaccine that fights the human papillomavirus, which causes most cervical cancer, along with enhanced screening, cervical cancer—once among the most common cancers affecting U.S. women—now ranks 14th in frequency.<sup>2</sup>

Nonetheless, each year in the U.S., approximately 12,200 new cases of invasive cervical cancer are diag-



MEMORIAL SLOAN-KETTERING CANCER CENTER

Opposite, background photo: Dr. Abu-Rustum and John P. Diaz, MD, in the operating room. Foreground: A child held in the arms of her mother—a fertility-sparing patient—at the 10-year anniversary party. (Photo courtesy of Memorial Sloan-Kettering Cancer Center.)

This page: Surgical partners Yukio Sonoda, MD (seated left) and Dr. Abu-Rustum enjoy the 10-year anniversary celebration with Sloan-Kettering fertility-sparing patients and their children.

nosed, and about 4,210 women die from the disease.<sup>3</sup> Cervical cancer often strikes women in the prime of their childbearing years: 42 percent of cervical cancer cases are diagnosed in women under the age of 45.<sup>3</sup>

The psychosocial impact of a cervical cancer diagnosis can be shattering, especially women still in their childbearing years. Forced to face immediate questions about their fertility, many young cancer patients experience depression, grief, stress, and sexual dysfunction.<sup>4</sup>

The radical trachelectomy, a delicate and complex procedure performed only by gynecologic oncologist surgeons, gives hope to young cervical cancer patients who want to bear children. The late Daniel Dargent, MD, of Lyon, France, pioneered the procedure, reporting on it in the medical literature in 1995.<sup>5</sup> During the procedure—which can be performed

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through the abdomen or vaginally—the surgeon removes the fatty tissue around the cervix, the surrounding lymph nodes, and upper two centimeters of the vagina. The surgeon then attaches the uterus to what remains of the vagina, and replaces the cervix with a cerclage that allows the patient to carry an embryo.<sup>5</sup> In most cases, the cerclage is permanent and will require that any offspring be delivered via cesarean section.<sup>6</sup>

Before performing the trachelectomy, the surgeon conducts a lymphadenectomy—removing lymph nodes in the patient’s pelvis and examining them under a microscope to determine if the cancer has spread.<sup>6</sup> If the cancer has spread to the lymph nodes, the surgeon halts the trachelectomy, opting instead for a more radical treatment of the cancer, according to Sloan-Kettering’s Nadeem R. Abu-Rustum, MD, FACS, FACOG, director of minimally invasive surgery and director of resident and medical student education, gynecology service. “Only women with 1B disease or less, generally meaning that the cancer is limited to the cervix, and has not spread to the lymph nodes, are eligible for this fertility-sparing surgery,” Dr. Abu-Rustum said.

“The trachelectomy completely changes the way surgeons look at young women with cervical cancer,” explained Dr. Abu-Rustum. A generation ago, he said, surgeons treated most women with invasive cervical cancer with a radical hysterectomy, including the removal of the uterus, cervix, ovaries, fallopian tubes, and a portion of the upper vagina, as well as tissue around the cervix and the pelvic lymph glands. Depending on the stage of the cancer, Dr. Abu-Rustum added, female patients still receive chemotherapy or radiation therapy.

Through a cone biopsy, a more extensive form of cervical biopsy, Dr. Abu-Rustum said, the surgeon often can remove abnormal tissues that are in the cervix, leaving behind a margin free of abnormal cells. A large cone biopsy or a simple trachelectomy in select patients is sufficient for treating select early-stage cancers, he said.

### *Candidates for the procedure*

“First and foremost, the patient has to have the desire to preserve fertility,” said Julian C. Schink, MD, professor of obstetrics and gynecology at Northwestern University Feinberg School of Medicine and chief of the division of gynecologic oncology at the Robert H. Lurie Comprehensive

Cancer Center of Northwestern Memorial Hospital in Chicago, IL. “It’s a complicated decision, but as surgeons, we can help patients understand what’s possible today. We’ve broken down major barriers to fertility preservation.”

Oncologists must address a number of myths on the subject of cancer treatment, according to Dr. Schink. “One of the biggest myths,” he said, “is that any treatment beyond the treatment for cancer will compromise the patient’s health. This is just not true.”

Dr. Schink also emphasized the importance of recognizing patients as a diverse group with unique needs and goals. “Patients have a wide range of desires, and what works for one patient may not work for another. Many patients don’t want their fertility preserved, and their immediate response is, ‘I never wanted to have children anyway,’” Dr. Schink said.

“Just because someone can do this procedure does not mean that they should. There is a lot that goes into determining who is a candidate and in what cases it will be successful,” agreed Stephanie V. Blank, MD, assistant professor in the division of gynecologic oncology at New York University School of Medicine, NY. “Obviously, I would not recommend fertility treatment if it compromised the patient’s health. We evaluate the patient’s fertility before we take any extra steps because we want the steps to be useful.”

“Not everyone offers these procedures, but certainly consideration of fertility has become a standard part of treatment decision making in women of childbearing age,” Dr. Blank said.

Appropriate and extremely thorough patient counseling should come at the very beginning of the decision-making process. “It’s very important that the expertise of a gynecologic oncologist be available to the patient,” Dr. Blank added. Attaining this input often requires referral of patients who live in low-population areas to large medical centers.

At the Mayo Clinic, as with all accredited cancer centers, the decision of whether a patient is appropriate for fertility-sparing procedures rests on the circumstances of each case.

“It’s a three-way decision,” said Dean E. Morback, PhD, assistant professor within the Mayo Clinic’s division of reproductive endocrinology and director of the in vitro fertilization and fertility testing laboratories. “It’s a decision that fertility specialists, the oncology team, and the patient must make. Our job is to make sure that patients know all their options.”

“You have to be very strict with the criteria you use for deciding which patients are suitable for these procedures,” added Dr. Blank. “Fertility-sparing procedures cannot compromise our patients’ health.”

Although some patients with cervical cancer address the fertility issue immediately, David M. Kushner, MD, division chief and medical director, gynecologic oncology, University of Wisconsin School of Medicine and Public Health, Madison, generally finds that at the beginning of the experience, patients want mostly to hear about a cure for their disease. As patients begin to believe in their survival prospects, he said, those who are in the childbearing years start thinking about their fertility.

“Talking about their fertility is difficult for some patients,” Dr. Kushner said, “because the discussion is about the effect that treatment is going to have on them for the rest of their lives. But it’s an important conversation, and many will say five years later, ‘I am so glad that we talked it through rationally.’”

### *Radical trachelectomy changes outlook*

“Many surgeons once considered fertility-sparing procedures taboo because the focus was always on cancer survival,” according to Dr. Kushner. “Even today if the uterus is not going to be used for reproductive functions, we remove the uterus and cervix.”

Dr. Kushner noted that when the fertility-sparing trachelectomy first came into practice, the stitch around the cervix often failed, resulting in a high rate of miscarriages and pre-term deliveries. This unraveling of the stitch is less common today, he said, because surgeons have learned that leaving a small (one centimeter) piece of residual cervix improves term delivery rates without affecting cancer treatment.

When a patient receives radiation to treat cervical cancer, other organs tend to shut down, Dr. Kushner said. Using a procedure that has become standard, Dr. Kushner and his team will transpose the ovaries in a woman still of childbearing age—maintaining the blood supply but moving the eggs away from the uterus, often into the upper abdomen near the liver.

“As surgeons, we are always thinking of ways that we can improve the quality of life, and as gynecologic surgeons, providing ways to maintain patients’ sexuality and ability to reproduce,” Dr. Kushner added.

\*To maintain confidentiality, patients are identified by first name only.



HUGE GALDONES/GALDONES PHOTOGRAPHY

Dr. Schink goes over a surgical procedure on a lap simulator with Angelique Boyd, a high school student participating in the February 2011 Senior Oncofertility Saturday Academy “Oncofertility and Surgery Day.”

### *Directly impacting patients’ lives*

“It’s rewarding to have this kind of impact on a patient’s life,” Dr. Kushner said. “I get fabulous holiday cards from many of the patients, and it is especially gratifying when we see patients with their babies at follow-up appointments.”

For example, being diagnosed with Stage 1 cervical cancer was devastating news to 37-year-old patient Kathleen,\* an Illinois resident who received treatment from Dr. Kushner. Kathleen had no symptoms of the cancer, which was discovered only when she sought help from her primary physician after unsuccessful efforts to become pregnant.

“After I was diagnosed, I thought immediately about my ability to have children,” Kathleen said. “When I found out about the procedure that would give me the chance to conceive and carry a child, it was a ‘no-brainer.’” Although she is still trying to get pregnant, undergoing the procedure has given her hope.

### *Ovarian cancer*

Several different types of cancer can occur in the ovaries, the seventh most common type of cancer among American women, and of approximately 26,000 cases diagnosed each year about 15 percent occur in girls or younger women.<sup>7</sup>

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If diagnosed early, the survival rate for ovarian cancer is approximately 90 percent, among the highest for all cancers. However, because there are few external symptoms of ovarian cancer, and there is little or no screening for it, the disease often goes unnoticed and begins to metastasize to both ovaries and to the abdomen.<sup>7</sup>

During a routine physical examination, a gynecologist discovered a cyst in 33-year-old patient Tracey, of Queens Astoria, NY, and ordered an ultrasound. When the ultrasound indicated cancer confined to the left ovary, Tracey, who has a family history of cancer, sought the help of Dr. Blank.

“My initial thought after being diagnosed was just that I wanted to live,” Tracey said. “But I had a huge bundle of emotions to deal with. All of my thoughts about my future were tied up with wanting to start a family.”

Dr. Blank removed the left ovary and fallopian tube from the patient and followed up with three rounds of chemotherapy. In February 2010, approximately 12 months after Tracey’s chemotherapy ended, she gave birth to a baby girl.

“I trust everything Dr. Blank tells me,” Tracey said. “I didn’t realize that after I had my daughter I would still be living with the fear of recurrence, but that fear is even stronger now that I have my daughter. Dr. Blank always tells me that my feelings are normal and that the majority of fertility-sparing surgical patients do not have recurrences. Sometimes I joke with her that I ask her the same questions because I need to hear her reassurance.”

### *Preserving the patient’s oocytes*

Embryo cryopreservation, a long-used technique based on infertility therapies such as in vitro fertilization, refers to the freezing, storage, and thawing of oocytes. But two requirements for this procedure prohibit some women from pursuing this option: (1) radical surgery, chemotherapy, or radiotherapy must be delayed for two to three weeks, and (2) a partner’s or donor’s sperm must be available. To use embryo cryopreservation, a woman must use hormone medications that stimulate multiple eggs to grow at once and undergo a surgical procedure to harvest her oocytes, which are then combined with a partner’s or donor’s sperm to create an embryo. The embryo is then frozen for use at a later time.<sup>9</sup>

Chicago resident Noelle, a 38-year-old ovarian cancer patient of Dr. Schink at Northwestern Memorial

Hospital, was a suitable candidate for this procedure. When Dr. Schink told her he could harvest and preserve her eggs, Noelle recalls that the prospect of cryopreservation eased the pain of a cancer diagnosis.

“I felt like this was a way of saving part of myself,” Noelle said. “When you have cancer, so much seems to be taken away from you. This was one thing that I felt I had control over.” Dr. Schink and the nursing staff at Northwestern provided ongoing support and information. “They were sincere and kind in the way they treated me, and they always made me feel like I was their only patient,” Noelle said. “They didn’t feel sorry for me. They were there to support me.”

Today, Noelle offers her support to other cancer patients by volunteering for the Imerman Angels, a not-for-profit organization that matches individuals diagnosed with the same type of cancer for one-on-one supportive relationships.

### *New technology*

Researchers at the Mayo Clinic have discovered promising fertility technology that should give cancer patients new reasons for hope, said Jani R. Jensen, MD, assistant professor of obstetrics-gynecology, at the Mayo Clinic in Rochester, MN. “One of our procedures is to remove the whole ovary and then cut strips off the surface, and often we find immature eggs during the dissection process. One possibility is that we can freeze the tissue pieces and potentially implant them in the patient at a later time. Another possibility is to harvest the immature eggs and try to treat them with medications in the lab to mature them and subsequently freeze them for later use.”

The essential factor is how much time the patient has to undergo the procedures, according to Dr. Jensen. “In some cancer cases, chemo has to be started the same day as the diagnosis,” she said. “To grow enough eggs to be able to harvest, we usually need two to three weeks.”

Also, through a process called in vitro maturation, the Mayo Clinic is experimenting with a technology, now being tested on animals. Immature eggs that are harvested from the ovarian tissue strips are cultured outside the mother’s womb and treated with hormones until they become mature. Then the immature eggs are fertilized with sperm and used to create an embryo.

“We currently don’t know much about the developmental potential of these embryos, and we worry that they may be particularly fragile compared to embryos

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created with our standard techniques,” according to Dr. Jensen. “However, particularly for patients in whom it would be dangerous to transplant ovarian tissue back—such as those women with ovarian cancer—this may be one of their only options. We see in vitro maturation of immature eggs to create embryos as a significant possibility for the future, and it’s an area of active interest for us.

“We recently purchased a special incubator with a microscope—known as an embryoscope—that allows us to watch these embryos develop over time in a highly controlled environment,” Dr. Jensen added, “We believe this will give extra support to these embryos and also teach us a lot about how these embryos grow.”

### *Effects of chemo, radiation on fertility*

New approaches to sparing fertility make it possible for many gynecologic cancer patients to bear children. But many forms of cancer treatment have unavoidable effects on reproductive health. Chemotherapy induces cell damage, and its impact on fertility depends on the type, dose, and length of treatment. Certain alkylating agents, according to Dr. Jensen, attack cancer cells but can also damage healthy reproductive cells.

“Certain drugs are more toxic to the reproductive organs than others,” according to Dr. Schink. Chemotherapy and radiation can be gonadotoxic, compromising the functioning of the ovaries and affecting the physical function of the uterus, he said. The degree of severity of fertility decline depends on many factors: age and ovarian reserve status at the initiation of therapy and type of therapy and dose.

Cyclophosphamide, a drug widely used in combination chemotherapy regimens, can cause direct destruction of egg cells and is linked to follicular depletion.<sup>10</sup> Other agents such as vincristine, Adriamycin, and platinum agents are mutagens and can cause chromosome rearrangements and deletions in cells. Ovarian failure or premature menopause might not occur directly after chemotherapy or radiation, but often the ovarian reserve is affected, and long-term fertility may be compromised.<sup>11</sup>

### *Team support for fertility-sparing surgical patients*

A patient with a cancer diagnosis who is a potential candidate for a fertility-sparing procedure needs support—first, to help her make a decision about her fertility, and then, to guide her through the cancer experience. A multidisciplinary team approach to

caring for cancer patients is part of the standards that the Commission on Cancer requires of all accredited cancer centers.<sup>12</sup>

At Northwestern Memorial Hospital, the division of fertility preservation offers an interdisciplinary approach to care with a fast, direct path to fertility preservation. The oncology team involves 17 full-time employees, including a licensed clinical social worker, psychologists, a psychiatrist, a psychiatric nurse practitioner, dietitians, and a fertility patient navigator.

“Our patients are the beneficiaries of our collaborative approach to care,” Dr. Schink said. “You need an oncologist who believes that the patient’s survival is the first priority, and you need a fertility team that respects some cancer patients’ desires to have children. You need strong players on both sides.”

“Every female patient who undergoes fertility preservation surgery meets with a clinical psychologist who remains available to the patient and her family should she want to use these services,” said Kristin N. Smith, fertility patient navigator for Northwestern Memorial Hospital’s oncology program. “We also have reproductive endocrinologists and urologists who make themselves available to newly diagnosed patients and survivors who want to address fertility after cancer.”

Team support enhances the patient’s experience—but sometimes the strongest support can come from other patients. Dr. Blank’s patient, Tracey, said she often yearns for a support group with other women who have experienced similar conditions. “When this happens, it raises a host of feelings and questions that you might not otherwise have,” she said. “I think it would be valuable to connect with people who have gone through the same thing.”

### *Cancer’s impact on the whole being*


Each year, approximately 80,000 women in the U.S. receive a diagnosis of gynecologic cancer, which has an immediate, all-encompassing impact on their lives. But gynecologic surgeons continue to employ fertilization-sparing techniques that change the rules about what happens to women who are diagnosed during their childbearing years.

For today’s gynecologic oncologists, the technological advances have produced a more optimistic future for many women and families and have enhanced the concept of what’s possible.

Fertility-sparing procedures are the wave of the present and the future, and Dr. Schink is convinced

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that the numbers will continue to rise. He points out that Northwestern was one of the early movers of the procedure, and patients would travel to Chicago to benefit from the expertise of the hospital's surgeons and staff.

"Some of our demand has declined, because patients can receive the same procedures at many other locations around the country," Dr. Schink said. "That's a good thing." 

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