

**2004 State of the State  
of Gynecologic Cancers**

*Second Annual Report to the Women of America*



**Gynecologic  
Cancer  
Foundation**

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## About the Society of Gynecologic Oncologists (SGO) and the Gynecologic Cancer Foundation (GCF)

The Society of Gynecologic Oncologists (SGO) is a national medical specialty organization of physicians who are trained in the comprehensive management of women with malignancies in the reproductive tract. Its purpose is to improve the care of women with gynecologic cancer by encouraging research, disseminating knowledge to raise the standards of practice in the treatment and prevention of gynecologic malignancies, and cooperating with other organizations interested in women's health care, oncology and related fields.

The Society's membership is primarily comprised of gynecologic oncologists, as well as other related medical specialists such as medical oncologists, radiation oncologists and pathologists. SGO members provide multidisciplinary care including chemotherapy, radiation therapy, supportive care and surgery.

For more information about the SGO and the field of gynecologic oncology, please visit [www.sgo.org](http://www.sgo.org) or contact the Society at 312.644.6610.

The Gynecologic Cancer Foundation (GCF) was established by SGO in 1991 as a not-for-profit charitable organization to raise funds to support philanthropic programs to benefit women who have, or who are at risk for developing, a gynecologic cancer.

The mission of the Gynecologic Cancer Foundation is to ensure public awareness of gynecologic cancer prevention, early diagnosis and proper treatment, as well as to support research and training related to gynecologic cancers. GCF advances this mission by increasing public and private funds that aid in the development and implementation of programs to meet these goals.

For more information about GCF, its educational materials or research grants, please visit [www.thegcf.org](http://www.thegcf.org) or contact Executive Director Karen Carlson by phone at 312.578.1439 or by e-mail at [kcarlson@thegcf.org](mailto:kcarlson@thegcf.org). For additional information on gynecologic cancers or for a referral to a gynecologic oncologist or a related specialist, please call the toll-free GCF Information Hotline at 800.444.4441.

*GCF is a 501(c)(3) non-profit organization under the U.S. Internal Revenue Code.*

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For more information about women's cancers, visit  
GCF's Women's Cancer Network Web site:

**[www.wcn.org](http://www.wcn.org)**

Log on for a confidential risk assessment to learn about your risk for developing women's cancers. Additional information of interest to women and cancer survivors is also available on the site.

You may also call the toll-free GCF Information Hotline at 800.444.4441 for information on gynecologic cancers or for a referral to a gynecologic oncologist or a related specialist.

# A Letter to the Women of America

In 2003, the Gynecologic Cancer Foundation (GCF) introduced the first State of the State of Gynecologic Cancers report detailing the current scientific and medical knowledge about the most common gynecologic cancers that affect the most women. This report was a tremendous success as proven by the many thousands of women who requested the report, read it and shared their stories with us about diagnosis, treatment and survival.

This year, GCF is pleased to present the second annual report, which takes us one step further in our goal to showcase advances, challenges, promising research and hope.

The goal of the report — to empower the women of America with the latest information about gynecologic cancers in an effort to one day prevent these diseases — remains the same. What is new is our ability to track and report on changes in these cancers from year to year to offer women a sense of progress and a glimpse of the future.

The 2004 report follows the cancers outlined last year: cervical cancer, ovarian cancer (epithelial and stromal cell/germ cell), uterine cancer (endometrial and uterine sarcomas), vaginal cancer and vulvar cancer. Additionally, based upon inquiries from women and current research in the field, we have also included a new section on hormone replacement therapy and gynecologic cancer risk, which we hope will offer women clear information on this critical topic.

While each gynecologic cancer section offers knowledge, we also believe it shows how progress in cancer care can develop in a variety of ways. For example, this report documents advances in the treatment of vaginal cancer, and showcases studies that prove the effectiveness of three chemotherapeutic agents in the treatment of advanced and recurrent endometrial cancer. It also explores the evolution of research by highlighting studies that prove the value of ongoing study and evaluation.

Finally, advances in the legislative arena — a precursor to additional scientific and medical progress — may also give patients greater access to preventive services or optimal care. Following is a summary of some of the legislative efforts that we remain focused on this year:

- *Johanna's Law: The Gynecologic Cancer Education and Awareness Act of 2003* (H.R. 3438), introduced by Representative Sander Levin (D-MI) and Representative Kay Granger (R-TX), would authorize a national gynecologic cancer early detection and awareness campaign directed at women and their physicians.
- *Genetic Nondiscrimination in Health Insurance and Employment Act* (S. 1053/H.R. 1910), introduced by Senator Olympia Snowe (R-ME) and Representative Louise McIntosh Slaughter (D-NY), would prohibit discrimination on the basis of genetic information with respect to health insurance.

- *Providing Annual Pap Tests to Save Women's Lives Act of 2003* (S. 416), introduced by Senator Olympia Snowe (R-ME), would provide for annual screening coverage of Pap tests and pelvic exams under the Medicare program.
- *The Access to Cancer Clinical Trials Act* (H.R. 2021), introduced by Representative Deborah Pryce (R-OH), would require all private health insurance plans to cover routine costs of cancer patients who qualify to participate in a cancer clinical trial.
- *The Cancer Survivorship Research and Quality of Life Act of 2003* (S. 1101/H.R. 2741), introduced by Senator Kay Bailey Hutchinson (R-TX) and Representative Roger Wicker (R-MS), would authorize funds to the Office of Cancer Survivorship within the National Cancer Institute to study the long-term and short-term physical, psychological, social and economic effects of cancer
- *The Cancer Testing, Education, Screening and Treatment Act* (H.R. 1868), introduced by Representative Maxine Waters (D-CA), would establish a program to provide cancer screenings and treatment for minorities and other populations served by public health centers.
- *The Quality Cancer Care Preservation Act* (S. 1303/H.R. 1622), introduced by Senator Sam Brownback (R-KS) and Representative Charlie Norwood (R-GA), would adjust current Medicare reimbursement policies that allow overpayment for cancer chemotherapy drugs and underpayment for essential care needs of cancer patients.
- *The Access to Cancer Therapies Act of 2003* (S. 1037), introduced by Senator Olympia Snowe (R-ME), would provide Medicare coverage for all oral anticancer drugs.

As you read through the report, we hope that this knowledge brings greater awareness and understanding. We also hope that it communicates the most critical point about gynecologic cancer care today — the importance of early and regular gynecologic screening. For regardless of advances and the promises of prevention, each woman holds the ability to help protect her gynecologic health in her own hands. Therefore, the potential of this report is in the information but the power is in the action — learn, understand and get screened.

It can make a difference in your life.

Sincerely,



Karl C. Podratz, M.D., Ph.D.  
Chairman  
The Gynecologic Cancer Foundation

# Commonly Asked Questions

## What are gynecologic cancers?

Gynecologic cancers are the uncontrolled growth and spread of abnormal cells originating in the female reproductive organs, including the cervix, ovaries, uterus, fallopian tubes, vagina and vulva.

## What causes gynecologic cancers?

Biomedical research has discovered that some classes of genes, called oncogenes and tumor suppressor genes, promote the growth of cancer. You can acquire abnormal function of these genes during life (e.g., through smoking, aging, environmental influences) or you can inherit gene mutations from your parents or grandparents. In one instance — cervical cancer — cancer is caused by a sexually transmitted virus.

## Can gynecologic cancers be prevented?

Diet, exercise and lifestyle choices play a significant role in the prevention of cancer. Additionally, knowing your family history can increase your chance of early diagnosis and can help you take action toward prevention. Screening and self-examinations conducted regularly can result in the detection of certain types of gynecologic cancers in their earlier stages, when treatment is more likely to be successful and a complete cure is a possibility.

## Who should treat gynecologic cancers?

Gynecologic cancers should be treated by a cancer specialist, specifically a gynecologic oncologist. A gynecologic oncologist is a board-certified obstetrician/gynecologist who has an additional three to four years of specialized training in treating gynecologic cancers from an American Board of Obstetrics and Gynecology-approved program. This subspecialty program provides training in the biology and pathology of gynecologic cancers, as well as in all forms of treatment for these diseases, including surgery, radiation, chemotherapy and experimental treatments.

## How are gynecologic cancers treated?

Gynecologic cancers are treated by using one or more of the following options: surgery, radiation therapy, chemotherapy and experimental treatments. The choice of therapy depends on the type and stage of the cancer.

## Who is at risk?

Any woman is at risk for developing a gynecologic cancer. This year, approximately 82,550 women in the United States will be diagnosed with a cancer affecting the reproductive organs.<sup>1</sup>

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<sup>1</sup> American Cancer Society. Cancer Facts & Figures, 2004. Available at [http://www.cancer.org/docroot/STT/stt\\_0.asp](http://www.cancer.org/docroot/STT/stt_0.asp). Accessed August 10, 2004.

# Hormone Replacement Therapy and Gynecologic Cancers

The more than 80,000 women diagnosed annually with gynecologic cancers have special needs and concerns relative to the use of hormone medications. Women who undergo menopause as a result of treatment for a gynecologic cancer may have significant symptoms such as hot flashes, irritability, difficulty sleeping and vaginal dryness. These menopausal symptoms can be effectively treated with hormone replacement therapy. However, many women are concerned about using hormone medications and the information regarding the impact of hormones on gynecologic cancers is often confusing.

## Endometrial Cancer

Excess estrogen, whether from pills, patches, or from an imbalance in the body, is associated with an increased risk of endometrial cancer. In contrast, combination medication with estrogen and progestin does not increase the risk of endometrial cancer. Therefore, women who desire estrogen therapy and still have a uterus are advised to use a progesterone medication specifically to prevent endometrial cancer. In a recent important study, the Women's Health Initiative study (WHI) found that the use of combination estrogen and progestin reduced the rate of endometrial cancer by 19 percent compared to women who took a placebo.

In the past, women who were diagnosed with endometrial cancers were often advised to avoid estrogen therapy. Recently however, the effect of estrogen replacement therapy in women with early stage disease was evaluated in a randomized clinical trial conducted by the Gynecologic Oncology Group (GOG), a multi-institutional cooperative group. More than 1,000 patients were randomized to receive either estrogen or placebo after their surgery for endometrial cancer. In this study, estrogen did not appear to cause any increase risk of cancer recurrence. However, the study was not as large as the investigators hoped and, therefore, the authors stated that they could have missed a small increased risk, if present. Women with endometrial cancer should talk with their doctors if they wish to consider starting or staying on estrogen medication.

## Ovarian Cancer

Whether or not estrogen and progestin increases the risk of ovarian cancer is controversial. Some studies have reported that hormone therapy increased the risk of ovarian cancer, while others studies have found no increased risk. Importantly, the Heart and Estrogen/Progestin

Replacement Study (HERS) study did not report an increased risk for ovarian cancer in patients treated with hormonal therapy. However, the WHI results did show that combination estrogen and progestin may increase the rate of ovarian cancer. Overall, 27 ovarian cancers were diagnosed per 100,000 women per year in women who were in the placebo group compared to 42 cancers in 100,000 women per year in women who were in the HRT group. This difference did not reach statistical significance, meaning that the observed difference could have been due to random chance.

The use of estrogen pills or patches for menopause symptoms after surgery for ovarian cancer is also controversial. Some doctors advise against hormone use based on the theory that estrogen might increase tumor growth. There are no randomized clinical trials that prove or disprove this theory. In the absence of data from clinical trials, individual judgment is important. During or after treatment for ovarian cancer, women with menopausal symptoms might benefit from estrogen replacement therapy; however, they must be willing to accept the unknown (but probably small) risk.

## Cervical Cancer

There are two main types of cervical cancers: squamous cell cancers and adenocarcinomas, a gland-producing type of cancer. The risk of cervical cancers is known to increase in women infected with the human papillomavirus (HPV), women who smoke, and women whose immune system is weakened. Hormonal therapy has not been found to increase the risk of squamous cell cancers. In contrast, one study showed that estrogen use might increase the risk for the gland-producing type of cervical cancer. In the recent WHI study, combination estrogen and progestin did not appear to increase the risk of cervical cancer. However, the total number of cervical cancer cases in this study was too small to reliably detect an increased risk. The use of hormone therapy in women with a history of cervical cancer has been studied and researchers have found no increase in the risk of cancer recurrence or decrease survival. In the same study, the women taking hormone therapy reported that they had fewer menopausal symptoms.

## Hormone Replacement Therapy

The National Institutes of Health (NIH) has recently released data on the estrogen-only arm of the WHI and previously released data on the combination estrogen and progestin study in 2002. The results of these two important studies indicate that neither estrogen alone nor estrogen plus progestin should be used to prevent chronic diseases in women. However, hormonal therapy is still the most effective treatment for menopausal symptoms, which can be quite problematic for some women.

Symptoms effectively treated with hormone replacement include hot flashes, difficulty sleeping, irritability, fatigue and vaginal dryness. For women considering taking hormonal therapy for the treatment of menopausal symptoms, the Food and Drug Administration (FDA) and American College of Obstetricians and Gynecologists (ACOG) recommend using the lowest dose for the shortest time required to control the symptoms. We recommend that women with menopausal symptoms talk to their doctors about using hormone medications as well as the other treatment options that are available for menopause symptoms.

# Cervical Cancer

## State of Cervical Cancer

*Cervical cancer is cancer that begins in the cervix, the part of the uterus or womb that opens to the vagina. Cervical cancer is caused by abnormal cellular changes in the cervix and is the only gynecologic cancer that can be prevented by regular screening. It usually affects women between the ages of 30 and 55 but has been found as early as the teen years.*

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*Symptoms:* Symptoms include bleeding after intercourse, excessive discharge and abnormal bleeding between periods, although often there are no symptoms.

*Risk factors:* Failure to receive regular cervical cancer screening (Pap tests) often eliminates the opportunity for early diagnosis and subsequent treatment. Persistent high-risk human papillomavirus (HPV) infection (an infection that lasts over two to three years) has been shown to be the cause of virtually all cervical cancers, although other smaller risk factors include smoking, oral contraceptive use, HIV infection and early age of first intercourse.

*Screening/Prevention:* Over the last 50 years, routine use of the Pap test to screen for cervical cancer has reduced deaths from the disease by 74 percent.<sup>2</sup> A Pap test is the standard way physicians check to see if there are any cell changes that might cause concern. The Pap test involves looking at a sample of cells from the cervix under a microscope to see if there are any cells that are abnormal. It is a good test for finding not only cervical cancer cells, but also cells that might become cancerous in the future.

Usually, health care providers perform the Pap test as part of a routine pelvic exam. It is important for women to know if a Pap test was performed because it's possible to have a pelvic exam without a Pap test. It is also important that women know and understand the meaning of their Pap test results, and follow through with any recommendations made by their health care provider.

In March 2003, the Food and Drug Administration (FDA) approved a new approach to cervical cancer screening for women 30 years of age and older — the use of the Hybrid Capture II HPV test in conjunction with the Pap test. This test combines a Pap test with the test for cancer-causing, or high-risk, HPV. This test is useful because if both the Pap test and HPV tests are negative, then the next Pap test may be delayed for three years. The HPV test can also be performed to help interpret an equivocal Pap test result, ASCUS, which stands for “atypical squamous cells of undetermined significance.” If the HPV test is positive in a woman with an ASCUS Pap result, she should undergo further testing for precancerous cells with a colposcopy examination.

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<sup>2</sup> American Cancer Society. Detailed Guide: Cervical Cancer. What Are the Key Statistics About Cervical Cancer? Available at: [http://www.cancer.org/docroot/cr/cr\\_2x.asp](http://www.cancer.org/docroot/cr/cr_2x.asp). Accessed August 11, 2004.

*Incidence:* In 2004, there will be approximately 10,520 new cases of cervical cancer and about 3,900 women will die from the disease in the U.S.<sup>3</sup> Between 1955-1992, cervical cancer mortality rates declined on average about 2 percent per year in the U.S.<sup>4</sup>

## **Advances in Cervical Cancer**

Using modern technologies, scientists, physicians, engineers and others are working together to create rapid advances in the field of cervical cancer prevention, screening and treatment. Never before has there been such a rapid rate of discovery in this field.

One of the most exciting advances in cancer prevention was reported in 2002 — the first major clinical trial of an HPV-16 specific vaccine. This trial demonstrated 100 percent protection in vaccinated women subsequently exposed to HPV-16. Since that time, newer clinical trials have been initiated, and early results suggest a similarly high level of effectiveness with combination vaccines designed to protect against up to eight HPV types. These exciting studies bring us one step closer to the day when routine vaccination will prevent most cases of cervical cancer.

Issues regarding the duration of protection, the best age to vaccinate and the need for booster vaccines must be answered before widespread vaccinations take place. Researchers and clinicians believe that vaccination holds real promise for future prevention of HPV infection and cervical cancer.

Significant changes also have taken place in the area of cervical cancer screening as new research continues to find ways to make screening more accurate and cost effective. Recent advances include the new liquid-based Pap tests that improve detection of some cervical abnormalities. Automated Pap tests, which are designed to remove the human error involved in reading Pap slides, are still under development. Newer technologies using specialized light sources and spectroscopy are being studied to assist doctors in pinpointing the abnormal areas of the cervix for biopsy. Lastly, a large effort continues to seek a method to eventually replace the regular Pap test (that looks for visible abnormal cells) with a “molecular Pap test” that would identify abnormal genetic changes in the cells, perhaps before the cells look cancerous or precancerous.

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<sup>3</sup> Ibid

<sup>4</sup> Ibid

Progress also is apparent in treatments for invasive cervical cancers. The combination of chemotherapy and radiation therapy, first adopted in 1999, continues to improve survival for women with cervical cancer requiring radiation treatment. Also, a study reported this year evaluated a series of chemotherapy combinations to treat recurrent cervical cancer. The combination of two drugs, cisplatin and topotecan, proved more effective in treating inoperable recurrent cervical cancer than platinum alone in this Gynecologic Oncology Group study. Progress is still needed for these patients. Still, this study is important because it is the first randomized study ever to report a combination treatment that resulted in a measurable improvement in survival time for patients with inoperable cervical cancer.

A significant advance has been made in developing fertility-sparing surgery for select women with early-stage cervical cancer. The new surgery, called radical trachelectomy, removes the cervical and surrounding tissues while preserving the upper uterus. Pregnancy outcomes are still being studied, but the past years have brought small, yet hopeful, reports of safe and successful pregnancies.

# Ovarian Cancer: Epithelial

## State of Epithelial Ovarian Cancer

*Ovarian cancer, the fifth most common cancer among women,<sup>5</sup> usually arises on the surface of the ovary in the epithelial cells. About 85 percent of ovarian cancers are epithelial ovarian cancers.<sup>6</sup>*

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*Symptoms:* Symptoms include unusual changes or discomfort, such as pressure or fullness in the pelvis, abdominal bloating, or changes in bowel and bladder patterns, which are constant and progressive.

*Risk factors:* The risk of epithelial ovarian cancer increases with age, especially around the time of menopause. A family history of epithelial ovarian cancer is one of the most important risk factors. Infertility and not bearing children are also risk factors, while pregnancy and use of birth control pills can decrease the risk of developing epithelial ovarian cancer.

*Screening/Prevention:* Currently, there is no widely accepted and effective screening test for epithelial ovarian cancer. Recently there has been intense interest in utilizing a method called proteomics to screen for ovarian cancer. Specifically, information about a new test called Ovachek<sup>TM</sup> has recently been reported in the media. Proteomics involves the analysis of proteins in the blood. The protein patterns of patients with ovarian cancer are compared to the pattern of women without cancer to learn which changes can be used to diagnose ovarian cancer. Many doctors and scientists agree that at this time, additional studies are needed before doctors or patients will truly understand the meaning of a positive or a negative proteomics test for ovarian cancer.

The Society of Gynecologic Oncologists has issued a position statement on this topic stating that the Society remains committed to the goal of effective screening and early detection, but that recently developed tests require validation prior to endorsement.

*Incidence:* Ovarian cancer ranks fourth in cancer deaths among women and causes more deaths than any other cancer of the female reproductive system.<sup>7</sup> In 2004, it is estimated that about 25,580 new cases will be diagnosed and approximately 16,090 women will die from ovarian cancer in the U.S.<sup>8</sup>

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<sup>5</sup> American Cancer Society. Detailed Guide: Ovarian Cancer. *What Are the Key Statistics About Ovarian Cancer?* Available at: [www.cancer.org/docroot/CRI/CRI\\_2\\_3x.asp?dt=33](http://www.cancer.org/docroot/CRI/CRI_2_3x.asp?dt=33). Accessed August 11, 2004.

<sup>6</sup> American Cancer Society. Detailed Guide: Ovarian Cancer. *What Is Ovarian Cancer?* Available at: [www.cancer.org/docroot/CRI/CRI\\_2\\_3x.asp?dt=33](http://www.cancer.org/docroot/CRI/CRI_2_3x.asp?dt=33). Accessed August 11, 2004.

<sup>7</sup> American Cancer Society. Detailed Guide: Ovarian Cancer. *What Are the Key Statistics About Ovarian Cancer?* Available at: [www.cancer.org/docroot/CRI/CRI\\_2\\_3x.asp?dt=33](http://www.cancer.org/docroot/CRI/CRI_2_3x.asp?dt=33). Accessed August 11, 2004.

<sup>8</sup> Ibid.

## Advances in Epithelial Ovarian Cancer

During recent years, a series of significant advances have taken place in the management of patients with advanced ovarian cancer. Years ago, one study established that the combination of two drugs, platinum agents and a taxane, worked better than chemotherapy combinations previously used to treat ovarian cancer. This combination brought new hope for women with the disease, but much work lies ahead for this deadly cancer.

An important ongoing research trial also is examining the treatment results for women with ovarian cancer if one of three newer drugs (liposomal doxorubicin, topotecan or gemcitabine) is added to the standard platinum and taxane chemotherapy. This study has recently met its enrollment goal with more than 3,800 women participating, and no new patients will be enrolled in the study. The first report of study results will likely become available about two years after the study concludes.

In the meantime, a report this year provided new information from a separate trial that clarified the optimal doses of the medications when one of these new agents, gemcitabine, is used in combination with carboplatin and Paclitaxel for patients newly diagnosed with ovarian cancer.

The long-term results of two other important ovarian cancer trials were also reported this year.

In one study, patients with early stage ovarian cancer were treated either with chemotherapy or with a type of radiation therapy that can be injected directly into the abdominal cavity (intraperitoneal 32P or IP 32P). Ten years later, the disease has relapsed in 35 percent of the patients that received the intraperitoneal radiation and 28 percent of the patients that received chemotherapy, suggesting that chemotherapy is more effective.

A second study was designed to see if women with ovarian cancer who are shown to be tumor free after finishing chemotherapy might benefit from the same intraperitoneal radiation therapy with 32P. These women all underwent a second surgical procedure called a “second look laparotomy” to see if they were really free of tumor. The women who participated in this trial have now been followed for an average of five years and the rate of recurrent tumor in these women is reported to be the same as in women who received no further treatment after surgery. In addition, 8 percent of the women that received the radiation therapy developed serious side effects.

Another important area of interest is the evaluation of treatments that cause fewer side effects. Newer taxanes such as Xyotax (CT2103) and Abraxane (ABI-007) are being evaluated in the treatment of ovarian cancer. Investigators hope that these agents will be at least as effective as the current first-line agent paclitaxel, but will cause less hair loss and nerve damage.

One problem with studies aimed at minimizing side effects has been the difficulty in measuring the severity of some side effects. This has been especially true for agents that cause toxicity to the nerves. This year, the GOG reported disappointing results with one agent that was intended to protect from nerve damage. However, within the same study, the researchers learned that a certain questionnaire provided more sensitive information than a clinical examination about the sensation changes that patients were experiencing. This information will be a significant help when future studies are designed.

Researchers are also hopeful that treatment side effects will be minimized through the use of other promising agents including novel molecular therapeutics that specifically target cancer cell growth, restrict the blood supply to a growing tumor, or block metastasis without the side effects associated with chemotherapies.

Future promising research for ovarian cancer will focus on further development of therapies targeting cell signals and enzyme pathways that are part of ovarian cancer cells, but not part of healthy body cells. Research in this area is in the early stages, but many investigators believe that these cancer specific signals and pathways can be exploited for the development of new therapies, treatments and prevention tools.

# Ovarian Cancer: Stromal Cell and Germ Cell

## State of Stromal Cell and Germ Cell Cancer

*Stromal cell cancer is an uncommon form of ovarian cancer that starts in the cells that produce female hormones and hold the ovarian tissues together. Germ cell cancer starts in the cells that form eggs in the ovary.*

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*Symptoms:* Stromal cell and germ cell cancers can cause pain or discomfort at the beginning stages. Stromal cell tumors can secrete hormones like estrogen or testosterone, and cause symptoms of abnormal uterine bleeding, new onset acne, and facial hair growth. Germ cell tumors can become very large causing pain or abdominal distension. These germ cell tumors may produce HCG, the pregnancy hormone, leading to a false positive pregnancy test.

*Risk factors:* There are no known risk factors for stromal cell and germ cell cancer.

*Screening/Prevention:* There are no known prevention measures for stromal cell and germ cell cancer. Abnormal enlargement of an ovary might be noticed at the time of an annual pelvic examination, increasing the chance for early diagnosis and treatment.

*Incidence:* Only about 5 percent of ovarian cancers are stromal cell cancers and less than 5 percent of ovarian cancers are germ cell cancers.<sup>9</sup> Stromal cell cancers are the most common hormonally active tumors.<sup>10</sup> Germ cell cancer is usually found in adolescent girls and young women between the ages of 16 and 20. Both stromal cell and germ cell cancers usually affect one ovary and most often are found at early stages.

## Advances in Germ Cell Ovarian Cancer

The challenge for the future management of germ cell tumors spans the spectrum of this disease from those with the best prognosis to those with the worst prognosis. To save the lives of the small number of young women who die early from germ cell tumors, we must find ways to identify the extremely aggressive types of this cancer. For patients with relapse of their germ cell cancer, clinical trials of high dose therapy with bone marrow transplant are ongoing at a few cancer centers in the U.S.

In 2004, a series of over 1,400 germ cell tumors were reviewed by German scientists. These scientists concluded that the germ cell tumors affecting young children have important clinical and genetic differences from those that affect adolescents. Understanding these differences may help to define risk for recurrence and help to determine best therapy for the different types.

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<sup>9</sup> American Cancer Society. Detailed Guide: Ovarian Cancer. *What is Ovarian Cancer?* Available at: [www.cancer.org/docroot/CRI/CRI\\_2\\_3x.asp?dt=33](http://www.cancer.org/docroot/CRI/CRI_2_3x.asp?dt=33). Accessed September 3, 2003.

<sup>10</sup> Women's Cancer Network. *Ovarian Cancer Statistics*. Available at: [www.wcn.org/interior.cfm?diseaseid=8&featureid=1](http://www.wcn.org/interior.cfm?diseaseid=8&featureid=1). Accessed August 11, 2004.

A second series from Italy reviewed the clinical course of 95 children and adolescents with germ cell tumors. This clinical series supported the importance of surgically removing all visible tumor whenever possible since all patients who had complete removal of the tumor remained in remission after they completed therapy.

In 2004, the world again enjoyed watching the record-breaking athletic success of Lance Armstrong, who survived a widely metastatic male germ cell cancer. This remarkable return to physical strength after chemotherapy highlights the importance of avoiding the damaging effects of chemotherapy. The most common treatment for germ cell tumors in males and females is a three-drug combination called BEP, which contains bleomycin, etoposide, and cisplatin. Unfortunately, this successful and effective treatment can lead to scarring in the lungs, leukemia years later in 1 percent to 2 percent of patients, a painful decrease in nerve sensation and chronic anemia. Avoiding these lifelong consequences of treatment while saving lives is the challenge for the next decade.

Preserving fertility for the young women with a germ cell cancer is another important consideration that deserves continuing study. These cancers usually only affect one ovary so preserving the other ovary and uterus are often possible. Minimizing the toxic effects of chemotherapy on the remaining ovary is an important consideration that deserves further evaluation. A current Children's Oncology Group study is investigating the possibility of eliminating or decreasing the amount of chemotherapy in select low- or intermediate-risk germ cell tumors.

## **Advances in Stromal Cell Ovarian Cancer**

These malignancies are among the rarest of the ovarian cancers and fortunately, often the least aggressive. The most common stromal malignancy is a granulosa cell tumor.

Although rare, a type of granulosa cell tumor, called juvenile granulosa cell tumor, can occur in young girls. Fortunately, these young patients have an excellent prognosis for cure. A second form of the tumor can occur in a wide range of ages, but most commonly in women in their 60s and 70s. The unique feature of this cancer is its tendency for late recurrence, sometimes 10 or even 15 years after initial surgery. The discovery of the tumor marker, inhibin, has helped with monitoring these patients for recurrence of this cancer.

The slow-growing behavior of granulosa cell tumor is unique in gynecologic malignancy. Solving the molecular biology of its delayed growth may open new avenues for the treatment of this cancer or other cancers.

# Uterine Cancer: Endometrial

## State of Endometrial Cancer

*Most uterine cancers begin in the lining of the uterus (endometrium) after menopause, when a woman's menstrual cycle ends and the endometrium flattens out. This type of uterine cancer, endometrial cancer, occurs when cells in the endometrium become cancerous and begin to invade the myometrium, the muscle of the uterus.*

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*Symptoms:* Warning signs include any bleeding after menopause or irregular vaginal bleeding before menopause.

*Risk factors:* Risk factors include obesity, hypertension, diabetes, inappropriate estrogen use, tamoxifen use and late menopause. Women who have not been pregnant also have a slightly higher risk for endometrial cancer. A high risk for endometrial cancer can be inherited in some families.

*Screening/Prevention:* Currently, other than yearly pelvic exams, there are no screening tests for endometrial cancer that are recommended on a routine basis. A woman may lower her risk for developing endometrial cancer by exercising regularly and eating a healthy diet. Keeping blood sugar and blood pressure under control also helps lower the risk. Women with unexpected postmenopausal bleeding or heavy, prolonged or unexpected bleeding during the menstruating years should have an endometrial biopsy to check for endometrial cancer. A Pap test does not screen for endometrial cancer.

*Incidence:* Endometrial cancer is the most common cancer of the female reproductive organs. In 2004, an estimated 40,320 new cases will be diagnosed and 7,090 women will die from uterine cancer.<sup>11</sup>

## Advances in Endometrial Cancer

2004 has brought many clinical and scientific advances in endometrial cancer including reports from two studies evaluating treatment for early and advanced stage endometrial cancer. Both studies were conducted by the GOG.

The first trial was designed to determine if pelvic radiation therapy could decrease the number of cancer recurrences in women with early stage endometrial cancer. Following surgery, approximately 400 women with certain risk factors were randomized to receive either pelvic irradiation or observation. Cancer recurrences were low overall (11 percent) in this group of women, but the study showed that the number of pelvic and vaginal recurrences was less in the

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<sup>11</sup> American Cancer Society. Detailed Guide: Endometrial Cancer. *What Are the Key Statistics for Endometrial Cancer?* Available at: [http://www.cancer.org/docroot/CRI/CRI\\_2x.asp?sitearea=&dt=11](http://www.cancer.org/docroot/CRI/CRI_2x.asp?sitearea=&dt=11). Accessed August 11, 2004.

group receiving radiation treatment. The study was not designed to determine if radiation improved survival, and some doctors question if the same results could be obtained with fewer side effects by using more localized intravaginal radiation. However, this study was clearly useful in identifying a subset of women with early stage endometrial cancer that may benefit from some form of radiation therapy after surgery.

The results of a second randomized multi-institutional trial answered the important question of whether three chemotherapeutic agents were better than two in the treatment of advanced and recurrent endometrial cancer. A previous GOG study showed that chemotherapy with doxorubicin and cisplatin (AP) was at least partially effective in 40 to 60 percent of patients with advanced and recurrent endometrial cancer. In the new study reported this year, a third chemotherapy agent, Paclitaxel (T), was combined with AP and compared with AP alone, to determine which combination helped the most patients. Women were randomized to receive either TAP or AP following diagnosis of advanced endometrial cancer. The women who received TAP had significantly lower relapse rates and better survival when compared to the women who received AP.

This study will help doctors and patients to select the best chemotherapy option available today. An added bonus is that these results will now be used in the design of new studies to more clearly define the best therapy for patients faced with endometrial cancers.

In addition to traditional chemotherapy for endometrial cancer, novel biologic agents are now being studied for the treatment of this disease. Growth factors have been shown to be important in endometrial cancer. The presence of receptors for growth factors in endometrial tumors, such as the epidermal growth factor receptor (EGFR), can help predict how aggressively an endometrial cancer might behave. Recently, activation of EGFR was shown to be critical in growth, invasion and spread of endometrial cancer cells. In the laboratory, treatment of endometrial cancer cells with an antibody that blocks EGFR can halt cell growth. This laboratory finding has prompted the investigation of two compounds, trastuzumab (Herceptin<sup>TM</sup>) and ZD1839 (Iressa<sup>TM</sup>) for the treatment of endometrial cancer.

The EGFR story is just one example of how the understanding of endometrial cancer biology can lead to new ways of fighting this and other cancers. In this century, clinical trials and basic science research will continue to focus on prevention, recurrence reduction and improved survival for women with endometrial cancer. These efforts will undoubtedly result in improved survival and quality of life for women with this disease.

# Uterine Cancer: Uterine Sarcomas

## State of Uterine Sarcomas

*Uterine sarcomas are a type of uterine cancer in which cancer cells form in the muscle of the uterus (leiomyosarcoma) or its connective tissue (endometrial stromal sarcoma) instead of the lining (endometrium). Additionally, some women develop mixed tumors that contain elements of malignant endometrial and stromal cells (carcinosarcomas). These tumors account for less than 5 percent of all uterine cancers, but behave much more aggressively than their more common counterparts (endometrial cancers).<sup>12</sup>*

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*Symptoms:* Abnormal vaginal bleeding is the most common symptom in women with uterine sarcomas. Leiomyosarcomas can produce pelvic pain or pressure. In addition, fibroids that grow rapidly, especially during the post-menopausal period, should raise the suspicion of a leiomyosarcoma.

*Risk Factors:* Sarcomas have been reported to occur more frequently in women with a history of previous pelvic radiation therapy. A 10-year review of national statistics was published this year confirming that the incidence of these rare malignancies is twice as high in black women as in other races.

*Screening/Prevention:* Due to their rarity, there is no proven effective screening method for these cancers. In addition, there are no known methods of prevention available for this disease.

*Incidence:* There are approximately 40,320 cases of uterine cancer annually, and sarcomas comprise 2 percent to 4 percent of these cases.<sup>13</sup>

## Advances in Uterine Sarcomas

Because of the rarity of these tumors, advances in screening and prevention may be slow. However, several treatment advances have occurred in the areas of surgery and chemotherapy. In general, initial surgery for uterine sarcomas consists of a hysterectomy with removal of the fallopian tubes and ovaries as well as sampling of lymph nodes. Two large clinical studies that were recently published show that the most common type of sarcoma, called leiomyosarcoma, rarely spreads to lymph nodes. This finding is important because it will help some women avoid lymph node removal at the time of surgery.

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<sup>12</sup> American Cancer Society. Detailed Guide: Uterine Sarcoma. *What Are the Key Statistics for Uterine Sarcoma?* Available at: [www.cancer.org/docroot/CRI/CRI\\_2\\_3x.asp?dt=63](http://www.cancer.org/docroot/CRI/CRI_2_3x.asp?dt=63). Accessed August 11, 2004.

<sup>13</sup> Ibid.

Chemotherapy has been used as part of treatment for patients with sarcomas, but its effectiveness has been limited. Most recently, a promising new combination of gemcitabine and docetaxel has been demonstrated to have a response rate twice as high as most previous combinations. This promising therapy currently is being evaluated in patients with early-stage leiomyosarcoma to see if it can prevent recurrence.

There is one final important lesson from the 10-year review of national statistics published this year: Although black women were twice as likely to develop leiomyosarcoma and carcinosarcomas, their survival was equal to women of other races if they received similar treatment. However, the study showed that from 1989 through 1999, black women in the U.S. were less likely to receive radiation therapy following surgery. Based upon this study, it is hoped that women of all races will learn to ask questions and seek appropriate expert care if they, or a family member, are diagnosed with a uterine sarcoma.

Over the past few years, a cautionary note has emerged regarding uterine sarcomas. Reports from both Europe and the U.S. suggest there is an increased risk for uterine sarcomas in women who use the anti-breast cancer drug tamoxifen. It is clear that the number of breast cancer recurrences prevented is many times greater than the number of sarcomas caused by this agent, and no woman should stop taking tamoxifen solely because of this risk. However, women and their doctors should be aware of the risk, and as always, women who use tamoxifen should be sure to report any abnormal vaginal bleeding.

# Vaginal Cancer

## State of Vaginal Cancer

*Vaginal cancer is cancer that starts in the vagina, usually in the epithelium (lining). It is usually diagnosed in elderly women with abnormal bleeding and treated with radiation.*

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*Symptoms:* Vaginal cancer, especially early or precancerous vaginal cancer, may not produce any symptoms.

*Risk factors:* Risk factors for vaginal cancer include advanced age (age 60 and older), HPV infection, smoking and cervical cancer.

*Screening/Prevention:* There are currently no recommended screening methods to detect vaginal cancer; however, many early cases of vaginal cancer or precancerous conditions can be diagnosed through routine pelvic exams and Pap tests. There is no known way to prevent vaginal cancer, but women should be aware of certain risk factors, like HPV infection.

*Incidence:* Vaginal cancer is very rare. An estimated 2,160 women will get vaginal cancer this year.<sup>14</sup> Vaginal cancer accounts for about 3 percent of cancers of the female reproductive system.<sup>15</sup>

## Advances in Vaginal Cancer

Because of its rarity, large studies investigating the prevention and treatment of vaginal cancer have not been done. However, lessons can be derived from the growing body of information about HPV which is associated with many vaginal cancers. For instance, risk-reduction measures such as stopping smoking and treating early precancerous HPV-related lesions are important.

When detected in the pre-invasive stage (Vaginal Intraepithelial Neoplasia or VAIN), treatments such as laser, local excision or even topical chemotherapy have been extremely effective.

Very early-stage invasive carcinoma of the vagina may be treated with surgery but most cases of invasive vaginal cancer are treated with radiation. Radiation therapy is usually given as a combination of external treatments and vaginal implants called brachytherapy.

Although the role of concurrent chemotherapy with radiation has never been formally studied, many clinicians recommend its use with radiation since it has been shown to be effective in improving cure rates in anal, rectal and cervical cancer, and in all tumors that share similar causes and routes of spread like vaginal cancer.

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<sup>14</sup> American Cancer Society. Detailed Guide: Vaginal Cancer. What Are the Key Statistics for Vaginal Cancer? Available at: [www.cancer.org/docroot/CRI/CRI\\_2\\_3x.asp?dt=55](http://www.cancer.org/docroot/CRI/CRI_2_3x.asp?dt=55). Accessed August 10, 2004.

<sup>15</sup> Ibid.

Recent advances in radiation therapy allow the use of needles to deliver the radiation directly into the tumor (interstitial brachytherapy) instead of having implants placed in the vagina (intracavitary brachytherapy). Other advances in technology allow some radiation treatments to be given quickly, over an hour or two, rather than over several hours or even days, making the treatments more convenient and comfortable for patients.

Early diagnosis is important to minimize the need for radical surgery and radiation therapy. Pap tests can detect pre-invasive and invasive vaginal cancer, but in the past, the need for Pap tests following a hysterectomy has been unclear. The most recent guidelines from the American Cancer Society and the American College of Obstetrics and Gynecology state that women who had precancerous changes on the cervix at the time of hysterectomy should continue to get Pap tests to screen for vaginal cancer and pre-cancer.<sup>16</sup> After three consecutive normal tests, these women are advised that they can discontinue screening.<sup>17</sup> Women with no cervical abnormalities can discontinue Pap tests immediately after a hysterectomy.<sup>18</sup>

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<sup>16</sup> American Cancer Society. Detailed Guide: *Cervical Cancer. Can Cervical Cancer Be Prevented?* Available at: [www.cancer.org/docroot/CRI/content/CRI\\_2\\_4\\_2X\\_Can\\_cervical\\_cancer\\_be\\_prevented\\_8.asp?sitearea=](http://www.cancer.org/docroot/CRI/content/CRI_2_4_2X_Can_cervical_cancer_be_prevented_8.asp?sitearea=). Accessed August 12, 2004.; *ACOG Practice Bulletin*, Number 45, August 2003. "Cervical Cytology Screening."

<sup>17</sup> Ibid.

<sup>18</sup> Ibid.

# Vulvar Cancer

## State of Vulvar Cancer

*Vulvar cancer appears as a lesion or lesions on the surface of the vulva or labia. It most often occurs on the inner part of the labia majora or labia minora.*

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**Symptoms:** Vulvar cancer symptoms include itching, burning, bleeding, pain or a new lump in the vulvar area.

**Risk factors:** Risk factors include diabetes, advanced age (age 70 and older) and chronic vulvar irritation. Women with HPV infection are also at risk.

**Screening/Prevention:** There is no known way to prevent vulvar cancer; however, regular Pap tests, pelvic exams and examination of the vulva for changes may lead to early detection. Self-examination with a mirror can help to identify early changes.

**Incidence:** Vulvar cancer is uncommon, representing only about 4 percent of all female reproductive organ cancers.<sup>19</sup> This year, about 3,970 women will be diagnosed with vulvar cancer in the U.S. and about 850 women will die of this cancer.<sup>20</sup> Vulvar cancer is frequently cured, usually by surgically removing the vulvar lesions and the groin lymph nodes.

## Advances in Vulvar Cancer

This disease is undergoing active and broad-based research, ranging from improved education to more effective, organ-preserving therapy. In some respects, however, the greatest challenge is getting women to seek medical attention in time. Too often, early disease-related symptoms are treated “over the phone” by clinicians unaware of the lesion’s seriousness or simply ignored by the patient because of embarrassment. Campaigns to promote self-examination and increased awareness are currently advocated by women’s support groups. Better understanding and treatment of the disease’s pre-invasive state offers promise in earlier case identification and prevention.

Surgery is required as primary treatment for most women with this disease. Gynecologic oncologists are evaluating new surgical strategies to improve outcomes while also reducing toxicity. “Sentinel node biopsy” is an important surgical technique in which one or more particular, “at-risk” lymph nodes are identified with the use of special tracers during surgery. These sentinel lymph nodes can be studied in great detail for evidence of spread. If sentinel node surgery is proven to be as effective as complete removal of all groin lymph nodes, it will reduce the extent of surgery women for many women with vulvar cancer (much like it has for women with breast cancer and patients with melanoma).

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<sup>19</sup> American Cancer Society. Detailed Guide: Vulvar Cancer. *What are the Key Statistics for Vulvar Cancer?* Available at: [www.cancer.org/docroot/CRI/CRI\\_2\\_3x.asp?dt=45](http://www.cancer.org/docroot/CRI/CRI_2_3x.asp?dt=45). Accessed August 11, 2004.

<sup>20</sup> Ibid.

One after-surgery complication which can be a lifelong problem is swelling in the leg in which lymph nodes have been removed. The Gynecologic Oncology Group recently launched a study using a new tissue sealant in an effort to reduce this complication, as well as to reduce infection, inflammation and problems with wound healing following vulvar cancer surgery.

Another area of active research is the optimal treatment of women with advanced disease. Recent experience using radiation and chemotherapy prior to surgery has allowed most women with advanced disease to undergo less invasive and frequently organ-sparing surgery. In fact, in some women, vulvar cancers completely disappeared so that no additional surgery was required. The extent to which chemotherapy adds to tumor regression is currently being studied in randomized trials.

Finally, new treatments are under investigation for premalignant vulvar conditions. Case reports and small clinical series are describing success with immune modifying treatments that help the body to heal vulvar pre-cancer areas and reduce the need for surgery. Premalignant changes of the vulva are a common problem in women with immune problems due to HIV infection. This year a multi-center study demonstrated hopeful news, noting that the frequency of this problem dropped substantially in women receiving effective anti-retroviral therapy for their HIV disease.

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