The Center for Women's Healthcare
Weill Medical College of Cornell University

Women's Health Advisor®

Helping Women Over 40 Make Informed Health Decisions™

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Ovarian Cancer Update

Women rely on Pap smears for the early detection of cervical cancer; mammograms and breast self-exams for breast cancer; and fecal occult-blood tests and colonoscopies for colorectal cancer. But for ovarian cancer, which accounts for more deaths in the U.S. than any other gynecologic cancer, there are no reliable early-detection tests. As a result, the vast majority of women with ovarian cancer are diagnosed when the disease has already advanced beyond the ovaries. And most die from their cancer within five years.

But there is hope. Significant strides have been made in treatment and even in prevention. Although there has not yet been a dramatic change in the cure rate for advanced ovarian cancer, improved chemotherapy is helping patients to live longer.

The most encouraging news is that if ovarian cancer is diagnosed and treated early, when the cancer is confined to one or both ovaries, at least 90% of all patients survive for five years or more, and many need not undergo chemotherapy.

Suspicious symptoms

As with all cancers, early detection is vital. That's easier said than done, however. Cancer occurs when cells become abnormal and divide rapidly, forming a mass of extra tissue (a tumor). When an ovarian tumor develops and grows, it takes up extra space in the abdominal cavity. This can cause vague feelings of bloating or discomfort. It's easy to attribute these symptoms to gastrointestinal problems, menstrual changes, weight gain, or other minor conditions. That's why ovarian cancer is often called a "silent" disease — the symptoms are so mild or vague that they are easily ignored.

Suspicion is your best protection. If any of the following symptoms persists for more than a few weeks, it could be an early sign of ovarian cancer:

• Feelings of abdominal bloating or swelling
• General discomfort in the pelvic area (lower abdomen)
• Loss of appetite or feelings of fullness, even after a light meal
• Gastrointestinal symptoms such as gas, indigestion, or nausea
• Change in bowel movements or urination
• Abnormal vaginal bleeding
• Pain during sexual intercourse
• Unusual fatigue.

See your doctor to investigate the cause of any persistent symptoms, but don't be surprised if you are the one who has to mention the possibility of ovarian cancer. Even for doctors, it is often low on the suspicion list. "We have to emphasize among the medical community that when a woman visits her doctor with complaints of abdominal distress or anything that may be associated with ovarian cancer — even vague complaints — ovarian cancer is one of the things that should be thought of immediately, right up front, by all doctors, not just gynecologists," declares Thomas A. Caputo, M.D., Director of Gynecologic Oncology at New York Presbyterian Hospital and professor of clinical obstetrics and gynecology at Weill Medical College of Cornell University.

Diagnostic tests and surgery

To investigate the cause of any symptoms, women need a full physical examination and a pelvic exam in which the doctor feels the vagina, rectum, and lower abdomen for masses or growths. Tests for gastrointestinal problems may be ordered next, but even while this workup is continuing, Dr. Caputo advises women to undergo two specific tests for ovarian cancer. The first is transvaginal pelvic ultrasound, in which high-frequency sound waves are used to produce computer images (a sonogram) of the vagina, uterus, ovaries, fallopian tubes, and bladder. Ultrasonography can often — though not always — differentiate between

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malignant (cancerous) tumors and benign (noncancerous) growths, such as ovarian cysts.

The second test is a CA-125 blood serum test. CA-125 is a tumor marker — a substance often found in increased amounts in the blood or tissues when cancer is present in the body. Although a very high level of CA-125 often indicates cancer, CA-125 is not always present in women with ovarian cancer, and it may be found in women who have benign ovarian conditions.

Results of these two tests in combination indicate whether ovarian cancer is likely to be present, but neither of these tests is accurate enough to make a definitive diagnosis.

There have been tests of other tumor markers, such as lysophosphatidic acid, but results are still preliminary. Research has also shown that it is harmful to make a diagnosis by extracting some ovarian tissue with a needle (a needle biopsy), as the procedure can spread ovarian cancer cells to surrounding structures.

The only sure way to know if ovarian cancer is present is exploratory surgery, with an incision into the abdominal cavity. This permits removal of fluid and tissue samples (a biopsy) from the ovary, diaphragm, and other structures in the abdomen, allowing them to be microscopically examined for cancerous cells.

Initial surgery also involves two crucial procedures. The first is removal of the cancerous tumors. Both ovaries are usually removed in postmenopausal women. It is often possible to remove only one ovary in a young woman who has not completed childbearing, if cancer is found at an early stage. Unfortunately, most ovarian cancers are discovered at an advanced stage, which necessitates extensive surgery (debulking) to remove all areas of cancerous tissue.

Initial surgery also involves staging. Examination of biopsy samples shows what kind of cancer cells are present (epithelial-cell cancers from the outer lining of the ovary are the most common) and how far the cancer has spread. Staging determines whether more extensive surgery or other treatments may be needed.

There are four basic stages of ovarian cancer:

Stage I – Cancer growth is limited to one or both ovaries.

Stage II – Cancer has spread beyond the ovary but is limited to the pelvic cavity (uterus, fallopian tubes, or other structures in the pelvis).

Stage III – Cancer is found in one or both ovaries, in the pelvis, and also in the abdominal cavity and/or nearby lymph nodes.

Stage IV – Cancer has spread outside the ovary and abdomen (called distant metastases) or to the liver.

"Proper initial surgery is very, very important," Dr. Caputo emphasizes. If the surgery is performed skillfully and effectively, it provides the key window of opportunity to improve a patient's prognosis. As with most complex operations, board-certified specialists at major medical centers and teaching hospitals (those affiliated with medical schools) who perform a high volume of these surgeries generally have the best success rate. In one study, for example, researchers found that proper staging was performed in 97% of ovarian cancer surgeries performed by gynecologic oncologists, but in only 52% of surgeries done by general obstetrician gynecologists, and in just 35% of those performed by general surgeons. "It just makes sense to choose skilled doctors who have the most experience," says Dr. Caputo.

Progress in treatment

Although most ovarian cancers have reached Stage III by the time they are detected, patients' chances of longer survival and good quality of life have improved significantly, thanks to recent significant advances in chemotherapy.

Chemotherapy is used immediately following surgery to kill any cancer cells that may remain in the body, and also for any recurrences of cancer. Extensive studies completed in just the past five years have shown that a two-drug combination of intravenous platin (carboplatin or cisplatin) plus Taxol (paclitaxel) is the most effective initial therapy, as measured by the percentage of patients who are helped, whether recurrences develop, and how long patients live after treatment. Radiation therapy is not routinely used but may help to relieve pain in late-stage ovarian cancer.

Several new drugs have also shown very promising results, notably topotecan, doxorubicin, and gemcitabine. Clinical trials of these drugs and others, including Herceptin (the first of a new class of drugs known as monoclonal antibodies), vaccines, and hormonal agents such as tamoxifen, are now under way. For information about participating in such trials, call the National Cancer Institutes' information line at 800-4-CANCER.

How to protect yourself

Every woman who has ovaries is at risk for ovarian cancer, but your own personal risk may be higher or lower than average, depending on your age, heredity, and reproductive history.

Risk increases with age. Ovarian cancer is most common in menopausal women, with an average age of onset of 61 years. Anything that suppresses ovulation in the premenopausal years reduces ovarian cancer risk, such as more than one full-term pregnancy, breast-feeding, use of oral contraceptives, tubal ligation, and removal of the ovaries.

Other factors, some of which you cannot control, tend to increase your risk. These include early age at first menstruation; late age at menopause; never having children or not having children until late in life; use of talcum powder in the genital area (cornstarch powder is a safe alternative); and a family history of ovarian and/or breast cancer, especially in a first-degree relative (mother, sister, daughter).

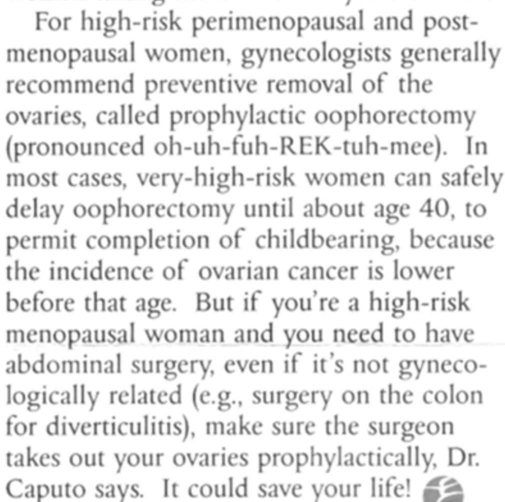
Concern about family history and genetic predisposition to ovarian and breast cancers was greatly heightened by the recent identification of the BRCA1 and BRCA2 genes, commonly known as the breast-cancer susceptibility genes. These genes are responsible for most hereditary ovarian cancers, particularly in white women of eastern European Jewish descent. "We are taking more-detailed family histories now and doing more gene testing," says Dr. Caputo. "But it's still very con-

troversial, and there are great implications for families. If you are a young woman at high risk, it can open up a whole range of devastating anxieties, such as 'What about my daughters or my sisters?'" That's why genetic testing should include proper counseling and support.

Only 5–10% of all ovarian cancer patients have these hereditary factors, but if you do, it's important to determine if preventive measures are appropriate. According to Dr. Caputo, having a single relative with breast or ovarian cancer does not correlate with very high risk. But if you have two affected first-degree relatives, or if you are BRCA1 or BRCA2 positive, you are at high risk.

What should a high-risk woman do? Unfortunately, easy preventive measures, such as a low-fat diet or eating lots of green vegetables, have not been proven in research studies. Some experts recommend regular ultrasonography and CA-125 screening tests, although many early cancers may still be missed.

Dr. Caputo recommends that high-risk premenopausal women go on birth-control pills. Studies show that the risk of ovarian cancer is reduced by 50% in women who take the Pill for five years, and by 75% in women taking the Pill for 10 years or more.



For high-risk perimenopausal and postmenopausal women, gynecologists generally recommend preventive removal of the ovaries, called prophylactic oophorectomy (pronounced oh-uh-fuh-REK-tuh-mee). In most cases, very-high-risk women can safely delay oophorectomy until about age 40, to permit completion of childbearing, because the incidence of ovarian cancer is lower before that age. But if you're a high-risk menopausal woman and you need to have abdominal surgery, even if it's not gynecologically related (e.g., surgery on the colon for diverticulitis), make sure the surgeon takes out your ovaries prophylactically, Dr. Caputo says. It could save your life!

For more information

The Gilda Radner Familial Ovarian Cancer Registry at Roswell Park Cancer Institute, Buffalo, NY

800-OVARIAN (800-682-7426)

http://rpci.med.buffalo.edu/departments/gynonc/grwp.html

The National Ovarian Cancer Coalition

888-OVARIAN (888-682-7426)

www.ovarian.org