

## ***Introduction.***

Ovarian cancer is the second most common gynecologic cancer among women and is the fourth leading cause of cancer death among women, behind lung cancer, breast cancer, and colon cancer.

Compared to most other common cancers, ovarian cancer is more likely to present at an advanced stage when it is first diagnosed. More than 70 percent of women with ovarian cancer have advanced stage disease at the time of diagnosis. For this group, the average 5 year survival rate is estimated to be 20 to 30 percent. In contrast, for women with locally confined disease, the cure rate is estimated to be 70 to 90 percent.

There are different histologic subtypes of ovarian cancer; ovarian epithelial carcinoma is the most common subtype.

For many years, major professional groups did not recommend screening asymptomatic women for ovarian cancer, because of a lack of evidence that screening worked in reducing deaths from this disease. A recent study, however, suggests that women who suffer from certain symptoms (pelvic/abdominal pain, increased abdominal size/ bloating, urinary frequency/urgency, or feeling full with difficulty eating) more than 12 times a month may be at increased risk and should undergo additional evaluation for ovarian cancer (Goff et al., Development of an Ovarian Cancer Symptom Index, *Cancer* 2007; 109:221-7).

The Institute for Women's Health's Dr. Erin N. Marcus interviewed Dr. Joseph Lucci, Director of Gynecologic Oncology and Professor of Clinical Gynecology at the University of Miami Miller School of Medicine, about new developments in the screening, detection and treatment of ovarian cancer.

## ***Question 1.***

Thank you for taking the time to speak with us, Dr. Lucci. The National Cancer Institute estimates that there will be 22,430 new cases of ovarian cancer diagnosed in the U.S. this year and 15,280 deaths from the disease. Has there been much progress made in reducing deaths from ovarian cancer over the past few decades?

## ***Answer.***

Yes, there's been significant progress. We've now come to look at ovarian cancer as a chronic disease. The average survival was about 18 months in the late 1970's, and now it's about 5 years. But it's very important that the initial treatment be managed at centers that have a track record in treating ovarian cancer and that the initial surgery be done by a gynecologic oncologist. The initial surgery is the factor that has the most significant impact on outcome, since the amount of cancer left at the completion of the first surgery predicts a patient's response to chemotherapy and long-term survival. Gynecologic oncologists tend

to be much more successful at tumor debulking than general surgeons or general gynecologists.

**Question 2.**

Who is at increased risk of developing the disease?

**Answer.**

The risk factors are generally related to those things that increase the number of ovulatory cycles during a lifetime, such as early onset of menarche, late menopause, few pregnancies or infertility issues. Additionally, patients who have a family history of ovarian cancer, breast cancer, or colon cancer are at increased risk, as are patients with mutations of BRCA1 and BRCA 2 and other genes that predispose them to ovarian cancer.

**Question 3.** Are women who have undergone fertility treatments involving ovulation induction at increased risk?

**Answer.**

We have a limited amount of data on the association between infertility and the risk of developing ovarian cancer. The information we do have suggests there's a slightly increased risk with ovulation induction – but this data may be confounded by the increased risk from whatever is causing the infertility. The global answer is yes, but to what extent is not well defined.

**Question 4.**

What can women do to reduce their risk of developing ovarian cancer?

**Answer.**

The longer a woman is exposed to birth control pills, the more her risk of ovarian cancer is reduced. Taking birth control pills for 10 years reduces a woman's ovarian cancer risk 50 percent. This applies to women in the general population as well as women at high risk or with a genetic predisposition. The amount of reduction in risk is proportional to the duration of use of birth control pills, and the reduction in risk continues to improve out to 10 years.

Women who have undergone hysterectomy or tubal ligation appear to have some reduction of risk as well. For women who are at very high risk, we often offer removal of the ovaries, fallopian tubes, and uterus. In genetically predisposed women this can reduce the lifetime risk from 50 percent to 2 percent. We offer this to women with a detectable genetic predisposition and women with a family history that is extremely suggestive of ovarian cancer, but for which we cannot identify a specific gene. Before we make any recommendations, however, these women must have a history and screening by a genetic counselor.

**Question 5.**

What role do ultrasound and tumor markers such as CA-125 play in the screening of ovarian cancer?

**Answer.**

For the general population, the use of CA-125 and ultrasound has not been proven to be useful. This is because the false positive rate is high, resulting in too many unnecessary surgical interventions.

However, in women who have been determined to have a genetic predisposition or are at high risk, our recommendation is a gynecologic exam, CA-125, and pelvic ultrasound every 6 months. There are some caveats, but that's our general recommendation.

**Question 6.**

What about the role of screening women for the gene mutations BRCA 1 and BRCA 2? Who should undergo such screening?

**Answer.**

Testing for BRCA1 and BRCA2 can cost up to \$3500, and not everyone is a candidate. But anyone who has had two and more family members with breast or ovarian cancer is a good candidate to see a genetic counselor for further review of their family history and assessment. Seeing a genetic counselor before the test is obtained is important so that patients understand the ramifications of the test.

**Question 7.**

Are there any women in whom you recommend prophylactic oophorectomy to prevent the development of ovarian cancer?

**Answer.**

At our institution we recommend removing the uterus also to further reduce cancer risk. All patients who test positive for a deleterious BRCA1 and 2 mutation and those patients where there is a strong family history are candidates. But again, this is where a genetic counselor is very important so that we can obtain an accurate and complete family history. Once we have a reasonable assessment of a patient's risk we can counsel the patient so that she can make an informed decision.

**Question 8.**

As a primary care physician, I often see patients who complain of bloating. How aggressive an evaluation do such patients need, given the findings in the study by Goff et al. mentioned above?

**Answer.**

If you look at the spectrum of symptoms associated with ovarian cancer, they often are very vague and seldom related to anything in the pelvis. But women who have persistent complaints of bloating that don't respond to appropriate

treatment in a reasonable amount of time, say a month, probably warrant additional evaluation to rule out pelvic disease.

**Question 9.**

Are there any new treatments that show particular promise for ovarian cancer?

**Answer.**

There are a number of new chemotherapeutic agents that are highly effective for treatment of ovarian cancer. There are also a number of biologic treatments, such as Bevacizumab (Avastin), that have activity and we're still learning how to use them for ovarian cancer. There are a variety of other targeted agents that look promising and are currently under investigation. We are making significant progress in the treatment of women with ovarian cancer.

**Question 10.**

Are there any public misperceptions regarding this disease?

**Answer.**

I think there's still a public misperception that the disease of ovarian cancer is a death sentence and that patients don't respond to treatment, when in fact patients do have a high response rate to treatment. We have made substantial advances in the treatment over the past few decades, and our median survival is now 60 months. Certainly, there are selected patients who don't respond to treatment, but they comprise less than 20 percent of the total number of patients. Many women are leading long, happy, healthy, productive lives years after the diagnosis. I have a number of patients who are seven years out and are still working full time and feeling well.

**Question 11.**

What are your specific areas of interest in ovarian cancer research, and do you have any findings you would like to share?

**Answer.**

My particular research interest relates to immunotherapies. We have a number of vaccines that may be beneficial in the treatment or prevention of recurrence of gynecologic cancer. Some are in clinical trials. These are treatments that are not toxic and have very few or no side effects and can effectively treat cancer or its recurrence.

**Dr. Marcus.** Thank you, Dr. Lucci, for taking the time to explain this illness to us.