

[MUSIC PLAYING]

**DIMITRY  
LERNER:**

I'm Dimitry Lerner, gynecologic oncologist with John Muir Health, and I will be discussing the role of genetic testing in gynecologic malignancies. Scientific advances are helping us understand the role of genetics and genetic testing in gynecologic oncology. National Comprehensive Cancer Center guidelines issued in 2011 recommend genetic testing for patients with uterine, fallopian tube, and primary peritoneal cancer.

It is based on data that 20% of patients carry an inherited mutation. Most histologic cell types should prompt consideration for genetic counseling and testing. Borderline ovarian tumors and mucinous tumors are the exception. Traditionally, testing has been performed on BRCA1 and 2 genes considered most likely to be involved based on family history.

Recently, multi-gene panels have been developed. The testing looks for germline changes, changes that are in every cell. These panels have the advantage of testing for many potential gene mutations simultaneously. They are a lower cost than traditional testing. Because so many genes in a panel are being investigated, there is a higher likelihood of diagnosing a variant of uncertain significance, which is genetic change without any clear association to health problem.

Changes in genes that are known to be associated with cancer are called deleterious mutation. Survival from ovarian cancer is improved in women who do test positive for BRCA1 or BRCA2 mutation, compared to those who do not have the mutation. BRCA1 and BRCA2-related ovarian cancers may be more sensitive to platinum chemotherapy. This may affect treatment options.

If ovarian cancer recurs, patients may be eligible for treatment with a class of drugs called PARP inhibitors that are particularly effective in women with BRCA1 and BRCA2 mutations. Currently, the PARP inhibitor, olaparib, is FDA approved in the United States for women with recurrence of ovarian cancer after three prior lines of therapy. However, clinical trials with PARP inhibitors might be available for women in other clinical settings, such as mutations in genes other than BRCA1 and BRCA2, fewer prior treatment regimens, or other somatic mutations.

Genetic counseling and testing for individuals at risk for BRCA mutations is considered a preventative service under the Affordable Care Act. For patients who test positive for deleterious BRCA1 and BRCA2 mutation, heightened surveillance and several risk reduction options are available. To lower breast cancer risk, increased surveillance is recommended, including annual magnetic resonance imaging and mammography. Such screening can detect cancer early, but does not prevent cancer. Risk-reducing mastectomy decreases the breast cancer risk by 97%.

Women with BRCA2 mutations who commonly develop estrogen receptor positive breast cancers, can be offered a type of chemo prevention drug called selective estrogen receptor modulator, which are associated with breast cancer risk reduction of up to 50%. For ovarian cancer, risk reduction can be achieved by using oral contraceptives. However, surgical risk reduction with bilateral removal of fallopian tubes and both ovaries is recommended after childbearing is complete.

Removing tubes and ovaries will reduce the risk of ovarian fallopian tube and peritoneal cancer by a more than 80%, and reduce their risk of breast cancer by 50%. There is growing interest in earlier salpingectomies with delayed ovarian removal, in order to delay the onset of menopause. However, clinical trials using this strategy of salpingectomy and delayed oophorectomy are not yet complete, so the degree of risk reduction is not known.

Patients with known BRCA1 mutation should consider removing tubes and ovaries after childbearing between ages 35 and 40. For women with BRCA2 mutation, the risk of ovarian cancer occurs later. They may delay removal of tubes and ovaries to 40 to 45 years of age. Estrogen replacement therapy is safe and reasonable if breast cancer has not been previously diagnosed. I am Dimitry Lerner, gynecologic oncologist with John Muir Health.