

HEALTH JOURNAL

Toward Earlier Detection of Ovarian Cancer

Two new studies offer a glimmer of light into the dark puzzle of ovarian cancer, which remains one of the most deadly cancers because it is so difficult to detect early.

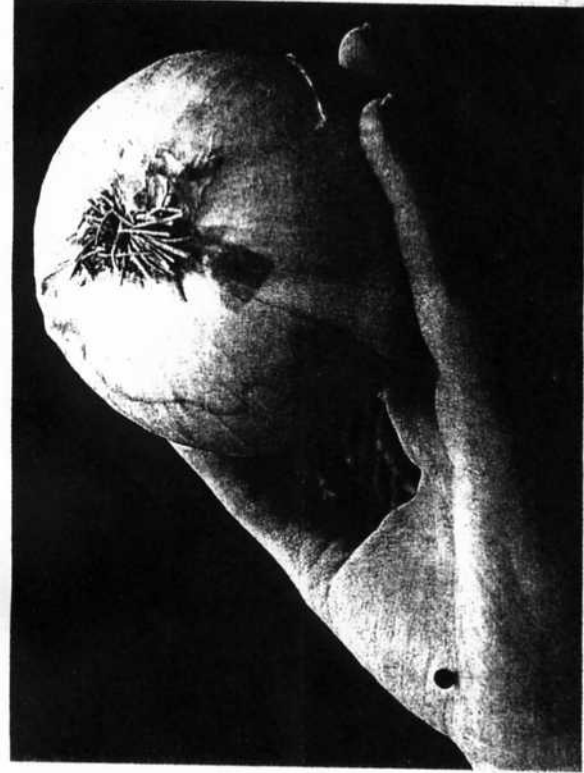
Researchers in the United Kingdom have identified a new genetic variation that appears to raise a woman's risk of developing ovarian cancer.

BRCA2, as the gene is called, is far more common than the previously identified genes, BRCA1 and BRCA2, and it doesn't raise the risk of ovarian cancer nearly as much, according to the study, which was published in *Nature Genetics*. But it's the first of what scientists believe will be many common gene variations linked to ovarian cancer that, when combined, may raise the risk significantly.

"This study confirms that ovarian-cancer risk is partly determined by genetic variants present in a large number of women," said Andrew Berchuck, a gynecologic oncologist at Duke University and head of the Ovarian Cancer Association Consortium, which enables researchers world-wide to work together to speed up discoveries.

The second study, published in the online journal *PLoS* last week, provides new insights into what ovarian tumors typically look like before they are discovered. Researchers at Stanford University School of Medicine and the Canary Foundation, a nonprofit group dedicated to early cancer detection, analyzed reports of tumors found in ovaries and fallopian tubes that were removed as a precaution from women who had the BRCA1 mutation. Even though all the women were believed healthy at the time, about 8% had undiagnosed serious ovarian tumors, the most deadly kind.

Using a mathematical model, the researchers determined that most such tumors remain extremely small—less than 1 centimeter in diameter—for about four years before metastasizing, and about half of them were still



Patrick Brown

"If I hadn't opened that envelope, I would have passed away years ago," says Donna Lackey, 42, of Southlake, Texas. Her mother and grandmother died of breast cancer in their 40s, and in 2002, a cousin wrote to say that she and her siblings had tested positive for BRCA1. Ms. Lackey tested positive too and scheduled what she thought would be a preventative double mastectomy and oophorectomy (removal of the ovaries). But the surgeons found that ovarian cancer had already spread throughout her abdomen and lymph nodes, even though she had no symptoms whatsoever.

Ms. Lackey has since had seven cancer recurrences and has been on chemotherapy continuously for the past year. Still, she has beaten the five-year odds and is grateful she had the surgery. "If I hadn't, my boys would have lost their mom in second and fifth grade. Their whole lives would have been different," she says.

To date, only about 25% of ovarian-cancer cases appear to have a family connection. The rest are probably related to unknown genetic problems or to environmental causes, or an interplay of both. "We don't be-

Telltale Symptoms

See your doctor if you experience any of these for more than three weeks:

- Abdominal bloating
- Vague but persistent gastrointestinal complaints
- Change in bowel habits
- Frequency or urgency of urination
- Unexplained weight gain or loss
- Abnormal vaginal bleeding

—Source: Ovarian Cancer Research Fund

lieve that anybody inherits cancer. What you may inherit is a predisposition to it," says Thomas Sellers, a genetic epidemiologist at Moffitt Cancer Center in Tampa, Fla., who expects his group to identify several more gene variations—called

SNPs, for single-nucleotide polymorphism—linked to ovarian cancer within the year.

Other doctors at Moffitt are analyzing the gene expressions in tumors themselves, rather than the DNA of patients. "The SNPs study is looking at the individual components of the engine," says Johnathan Lancaster, head of women's oncology at Moffitt. "We're looking at differences in the speed the cars go." In a pilot study, he is using those genetic fingerprints in tumors to select chemotherapy drugs for patients with recurrent ovarian cancer—a major step toward individualized cancer treatment.

Researchers also have high hopes for preventing ovarian cancer in the first place. Bearing children, breast-feeding them and taking birth-control pills for at least five years all seem to lower the risk significantly—probably because each suppresses ovulation temporarily. Maintaining a healthy weight is also recommended.

Doctors often recommend that women at high risk who have completed their families have their ovaries and fallopian tubes removed, which can cut the cancer risk dramatically. That does put them into immediately "surgical" menopause, and in rare cases, ovarian cancers can still occur in the lining of the abdominal cavity. But Carmel Cohen, a gynecological oncologist at Mount Sinai School of Medicine in New York and vice chair of the Ovarian Cancer Research Fund, says he knows of no data to suggest that taking low-dose estrogen raises the risk of cancers after ovaries have been removed.

Researchers are also looking for more specific markers that might be evident in blood, in vaginal fluid or even the breath of women with early cancers.

Experts advise women to check their family history and look out for symptoms. As Dr. Cohen says: "If a woman has symptoms that are recent, persistent and otherwise unexplained, she should go to her provider and say, 'Prove to me I don't have ovarian cancer.'"

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