Ovarian Cancer: Lowering an Unacceptable Risk

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Ovarian cancer is the 11th most common cancer among women in the United States but it is the 5th leading cause of cancer-related deaths. 1 woman out of every 91 will develop ovarian cancer during her lifetime and the lifetime risk of dying from it is 1 in 143. The 5 year survival estimate is about 50%. These uncomfortable statistics are related to several things: abdominal symptoms are usually attributed to other causes leading to late diagnosis, more than half of cases are diagnosed at advanced stages, there is no reliable screening tests for the general population, and there are accumulating environmental and lifestyle risk factors. There is also an increase in both the incidence and mortality from ovarian cancer in the under 39 year old age group – especially in the ages 20 – 24 years old. This condition still remains mostly an older woman's cancer with the average age at diagnosis being 63 years. Only about 5% of all cases are seen in under 35 year olds. But still, it is an ominous trend that incidence rates of 14 out of 33 cancer types studied have been increasing in incidence in younger people. The May 2025 Cancer Discovery study also reported that 9 of these cancer types had increased incidence rates in older age groups as well. Specific to ovarian cancer, the incidence increases sharply after age 45 and peaks in the 55–64 age group (24.2% of cases), and remains significant well into advanced age (21.3% of cases in 65 – 74, 15.9% in 75 - 84, 8% in over 85). This feels so unacceptable.

Risk Factors for Ovarian Cancer

The strongest known risk factors for ovarian cancer are age and genetic factors. Women with BRCA1, BRCA2, and other mutations (e.g., RAD51C, RAD51D, BRIP1) are known to have higher risk. But environmental and lifestyle exposures are also playing a role. One would have to be living under a rock for the past 50 years not to see the myriad of environmental toxins and lifestyle choices that have been accumulating to make us sick. It was way back in 1977 when the epidemiologic evidence showed 80% of all cancers were caused by environmental factors that damage DNA. More recent research has shown the biologic mechanisms of disrupted cellular signaling and dysfunctional cellular protective pathways that allow this DNA damage. As a country (and a world), we continually refuse to invest money and talent into real prevention – understanding and removing sources of risk. For ovarian cancer, we know very little about these risks.

Environmental and Lifestyle Risk Factors

The most well-known environmental risk factor for ovarian cancer is long term use of talcum powder in the perineal area. There is biologic plausibility that these tiny particles can migrate through the genital tract causing chronic inflammation leading to cancer and there is epidemiological evidence showing a 20 – 30% increase in risk with long term talc use but there has been no causality established. Additionally there are endocrine disrupting chemicals that have been shown to increase risk in animal studies, most notably the plasticizers BPA and phthalates. Other endocrine disrupting chemicals that need to be studied as risk factors include herbicides (atrazine), non-stick containers, pots and pans (PFAS), personal care products (parabens), industrial chemicals (dioxins, PCBs) among others. Besides being sold to us in consumer goods, these chemicals persist in our environment and contaminate our food and water. There is also evidence that asbestos exposure (through occupation or via use of contaminated talcum powder) is also a possible ovarian cancer risk factor. High dose pelvic or abdominal radiation (once a treatment used for cancer) is another possible risk factor.

Lifestyle factors that appear to be associated with ovarian cancer risk include smoking and obesity. Smokers have a 2 times increased risk of mucinous ovarian cancer but not other subtypes. Obesity is associated for several reasons: fat tissue produces a high quantity of Estrogen and Insulin-like Growth Factor - both of which have been associated with cancer risk. Inadequate physical exercise is a known cancer risk factor while ovarian cancer symptoms and diagnosis on physical exam may be more difficult in the context of obesity.

Protective Lifestyle and Environmental Factors

—include long term use of oral contraceptive pills (at least 5 years), pregnancy, and breast feeding as these reduce the lifetime number of ovulations. Having a tubal ligation or hysterectomy has been shown to reduce risk by interrupting the cancer pathway. Maintaining a healthy weight and diet would reduce chronic inflammation that can lead to cancer.

Reducing modifiable risk factors is one strategy for lowering one's risk of ovarian cancer, but there is not a lot of strong evidence what these risk factors may be. Determining one's personal risk based on genetics or reproductive function (see Side Bar) can help drive motivation for risk reduction as well – if we knew more what to do.

But what about screening?

Women who present to their doctor complaining of bloating, abdominal discomfort, early satiety and urinary frequency are usually evaluated for gastrointestinal or urinary conditions. If a woman has a higher risk for ovarian cancer, she might be screened with a blood test (CA125) and a transvaginal pelvic ultrasound whether she has these vague symptoms or not. But this combination test lacks the specificity and sensitivity needed to detect early-stage ovarian cancer reliably.

Screening tests for ovarian cancer being studied include:

- The ROCA test – an algorithm that considers age, menopausal status, and trends in CA125 over time often with a transvaginal pelvic ultrasound to calculate a risk score. The large UK study on using ROCA testing in over 200,000 women was started in 2001 and did not show a statistically significant reduction in deaths and led to some unnecessary surgeries in women with false positive results.
- Liquid biopsies - blood tests that detect:
  - circulating tumor cells (ctDNA). These are already on the market
  - exosomes or other biomarkers
- Proteomics and Biomarker panels - combinations of proteins or genetic markers that may improve accuracy of screening
- Artificial Intelligence in the interpretation of imaging or clinical data may enhance risk prediction
- The EVA test (Early oVArian cancer test) evaluates vaginal fluid (taken by swab during a routine PAP test) for DNA copy number profile abnormalities associated with pelvic organ cancer (ovarian, fallopian tube, endometrial) and detectable up to 9 years before an ovarian cancer diagnosis. Studies from Johns Hopkins and others have shown that the EVA method can detect up to 90–95% of endometrial cancers. For ovarian cancer, the 75% sensitivity and a 96% specificity is identical to that for the CA 125 blood test but EVA is equivocal in about 14% of cases. It is promising but not yet accurate enough for universal screening.
- PAPSEEK is a multi-target genetic test analyzing DNA from PAP (cervical fluid) and/or Tao brush (endometrial fluid) samples looking for mutations in 18 genes which are highly or commonly mutated in endometrial or ovarian cancers, and aneuploidy (an abnormal number of chromosomes in cells). Early research showed PAPSEEK was 99% specific for cancer, and it detected 81% of endometrial cancers and 33% of ovarian cancers. Again, this is promising but not yet accurate enough for universal screening

Determining risk for ovarian cancer is mostly genetic.

Higher risk includes a positive family history:

- First-degree relatives (mother, sister, daughter) with ovarian, breast, or related cancers
- Multiple family members with:
  - Ovarian cancer
  - Early-onset breast cancer (before age 50)
  - Male breast cancer
  - Pancreatic or prostate cancer
- Three or more affected relatives across generations raises concern for hereditary cancer syndromes (Ovarian cancer is associated with BRCA1, BRCA2 and Lynch syndrome.)

Other associations conferring a higher risk for ovarian cancer include:

- A personal history of breast cancer (especially before age 50)
- Ashkenazi Jewish ancestry (1 in 40 BRCA mutation carriers)
- Infertility /No childbirths
- Endometriosis (linked to clear cell and endometroid subtypes)
- Hormone replacement therapy (long term use of conventional HRT has shown a slight risk in some studies)

Women in the above categories should consider genetic screening and counseling

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A New Way to Reduce Risk

Ovarian cancer has several types and subtypes but 85 – 90% of all ovarian malignancies are the type called epithelial ovarian cancer (EOC) which typically affects postmenopausal women usually in their 50s through 70s. High grade serous ovarian carcinoma (HGSOC) is the most aggressive subtype accounting for 70% of all EOCs. Recently it has been recognized that the primary source of serous ovarian cancer is the fallopian tube and a strong risk reduction strategy would be to have both tubes removed (bilateral salpingectomy). This procedure reduces ovarian cancer risk by 80 – 90%. It is being recommended to women between the ages of 35 – 45 who are BRCA1/2 carriers. It also reduces their risk of breast cancer (especially for BRCA1). Women with one or more first degree relatives with ovarian cancer with or without known genetic mutations should also consider this surgery. "Opportunistic risk-reducing salpingectomy" is a generally safe procedure and women should be offered this choice when having a hysterectomy or a tubal ligation for permanent contraception. Any women 45 years or older, having any abdominal or pelvic surgery (gall bladder removal, hernia repair, bowel surgery…) should discuss having an opportunistic salpingectomy to reduce ovarian cancer risk. It will not eliminate all ovarian cancer risk but it will reduce one's risk substantially. Removing the ovaries as well in higher risk women is recommended but the option to preserve the ovaries avoids immediate menopause, long term health risks of early menopause (osteoporosis, heart disease, cognitive decline), and loss of fertility. A 2025 Johns Hopkins study published in JAMA, reported 24% of women with high grade serous ovarian cancer had missed opportunities for risk reducing fallopian tube removal during a surgery prior to their cancer diagnosis.

Seems to me we are at least going to get some improved early screening and prevention options soon. Understanding the causes and eliminating them (true prevention) is still not on the agenda.

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