

## ENDOMETRIOSIS AND OVARIAN CANCER REVIEW

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Farr Nezhat, M.D., St. Luke's-Roosevelt Hospital Center, New York city, and colleagues have published an excellent review on the relationship of endometriosis (endo) and ovarian cancer in the November, 2008, issue of *Fertility and Sterility* (Vol. 90, No. 5). Nezhat became a gyn oncologist (physician specializing in gynecologic cancers) after becoming interested in how endometriomas (endometriosis cysts) develop and then sometimes further develop into ovarian cancer.

The Endometriosis Association is grateful for Farr Nezhat's continuing interest and work to bring endo and ovarian cancer to the attention of physicians who, no doubt like many patients, do not want to know that endometriosis can be a risk factor for such a deadly cancer. As one gyn said at an ESHRE (European Society of Human Reproduction and Embryology) meeting recently after new data on the risk of cancers in women with endo was presented, "Does this mean we have to take endometriosis seriously now?" (In the Endometriosis Association's Vol. 28, No. 6 newsletter, summaries were given for four recent studies that found an increased risk for endocrine, ovarian, kidney, thyroid, brain, breast and colon cancers, and non-Hodgkin's lymphoma and melanoma.)

Nezhat's review article is thorough, covering what's known about endo and ovarian cancer links, including the fact that endo is associated with a chronic inflammatory state, known to be a risk for cancer.\* Dr. Nezhat and his colleagues also provide an excellent review of the immune and endocrine dysfunction elements of endo and how that may play into the development of cancer. Recent endo-cancer studies are described — the growing number of these alone should alert healthcare providers about the link between endo and cancer. Studies are again finding that the appearance of cancer, is, on average, at a younger age in women with endo than in women without, which means we must be all the more vigilant for our health or that of family members since physicians won't be expecting these cancers in younger women. These studies also have been finding that women with long-standing endometriosis have higher risk. Unfortunately, the article fails to note that dioxin, now being linked so strongly to endo, is a potent cancer-causing agent.\*\*

Of all the cancers for which women with endo are at greater risk, the most deadly is ovarian. The most common types of ovarian cancer rising from endo are endometrioid (60 percent) and clear cell (15 percent). Nezhat notes that "about 60 to 80 percent of cases of endometrioid endometriosis-associated ovarian cancers arise in the presence of atypical endometriosis." This important observation begs the question, why aren't surgeons more vigilant about sending tissue samples to the pathology lab to determine if they are atypical so that those at greatest risk could be watched more closely?

Another way to look at the risk: "Several studies support the pathologic malignant transition of endometriosis in about 5 to 10 percent of women found to have ovarian endometriomas at surgery versus 1.5 percent in the general population." It is often noted by practitioners that the risk for ovarian cancer is small, but it is likely they are thinking of the overall population versus those at much higher risk, that is, women with endo. Five to ten percent of women with endo at risk for a highly deadly cancer is not a small number. On the plus side, Nezhat and colleagues note that some of the studies found that women with endo were diagnosed with ovarian cancer earlier than women without endo and therefore had somewhat better survival. Endometriosis is indeed the great teacher to be vigilant for our health.

Nezhat and his colleagues conclude that "the malignant potential of endometriosis holds serious implications for management, such as the need for earlier and more meticulous surgical intervention for complete disease treatment." The authors also note, "special consideration should be given toward bilateral oophorectomy [removal of both ovaries] in women with endometriosis undergoing hysterectomy near the age of menopause, especially those with a history of infertility, a family history of ovarian and breast cancer, or ovarian hyperovulation stimulation." \*\*\*

A sure sign of the growing awareness in medicine generally of endo is a review article by Endometriosis Association Advisor, Serdar Bulun, M.D., in the *New England Journal of Medicine* (360; 3). Dr. Bulun is the scientist who headed up the team discovering that endometriosis makes its own estrogen (estrogen is also produced in fat and skin tissue as well as from the ovaries), and discovered important scientific information leading to the potential use down the road of aromatase inhibitors for treatment of endo. \*\*\*\*

Dr. Bulun's article provides an extensive, in-depth discussion on the role of various hormones in endo. Most interesting in his article is a model of how impact on the female embryo by genetic influences or environmental toxins ("epigenetics") could cause molecular abnormalities predisposing girls and women to endometriosis. His article elucidates many of the hormonal complexities in endo and makes the old thinking — that estrogen simply caused the growth of the disease and progesterone reduced the growth — seem incredibly simplistic.

Also, we now see the new emphasis being placed, not only in his article but elsewhere, on prostaglandins in endometriosis. It was well known more than twenty years ago that an imbalance of prostaglandins played a major role in promoting inflammation and pain but the field was all but abandoned for many years, at least as it related to endometriosis. "Endometriotic stromal cells produce large quantities of prostaglandin E<sub>2</sub>, which induce local estrogen biosynthesis and pelvic pain," Bulun notes.

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\*Often women with endo and healthcare providers ignore the all-important immune dysfunction and inflammation in endo while focusing almost exclusively on the lesions. Many women utilize immune-modulating approaches, perhaps along with gyn approaches, to achieve better health. Endometriosis Association books cover some of these approaches including immunotherapy, atopic disease management (allergy, asthma, and eczema), preventative approaches, and nutritional approaches that help reduce the load on the immune system. Dioxin is also a potent inflammatory agent.

\*\*Another, more surprising, risk factor for ovarian cancer was uncovered by Endometriosis Association Advisor Roberta Ness, M.D., M.P.H., TX, who has published her studies showing that danazol, the drug used so often in the 80s for endo, increases the risk for ovarian cancer. Lupron did not increase risk in her studies.

\*\*\*Information on ovarian cancer symptoms and a short article by Dr. Nezhat appears in the Endometriosis Association's Vol. 28, No. 4-5 newsletter. A full discussion of preventative approaches for endo-related cancers appears in *Endometriosis: The Complete Reference for Taking Charge of Your Health*.

\*\*\*\*See *Endometriosis: The Complete Reference for Taking Charge of Your Health* for background.