

Ovulation cycles linked to ovarian cancer

For the female body, ovulation is hard work. An ovary secretes hormones, produces an egg, thrusts it through a wall of tissue, and afterward repairs the rupture. Four weeks later, the process repeats.

Scientists have suspected that the frequency and rigor of tissue rebuilding can lead to ovarian cancer because, after each ovulation, the manufacture of new cells requires synthesis of DNA. This cell proliferation is thought to open the door to mutations in the p53 gene, which produces one of the body's natural cancer fighters.

Now, a new study bolsters this incessant-ovulation theory (SN:10/31/92, p. 298) and its corollary that pregnancy, breast feeding an infant, or taking oral contraceptives lessens a woman's cancer risk by giving her welcome rests from ovulation and easing wear and tear on the ovaries.

The key element in this theory is the p53 gene, which normally blocks cell division when a cell has sustained DNA damage. If the p53 gene itself becomes disabled, however, it allows damaged cells to proliferate, possibly leading to cancer. A sure sign of a mutated p53 gene, researchers have discovered, is overproduction of a distorted p53 protein.

Duke University researchers tested for overproduction of altered p53 protein in malignant tissue from 197 women, averaging 47 years old, with ovarian cancer. They found that 105 had such an overabundance. Moreover, the researchers calculated that these 105 women each averaged 388 ovulation cycles in her life so far, nearly 30 full years' worth, while the ovarian cancer patients without the p53 protein surplus averaged only 342 cycles.

Compared with a group of 3,363 healthy women, the women who had cancer and an overabundance of the telltale p53 protein were nine times more likely to have had high numbers of ovulation cycles. This difference emerged after the researchers statistically accounted for variations in age, menopausal status, and number of children, says Joellen M. Schildkraut, an epidemiologist from Duke University Medical Center in Durham, N.C., and lead author of the study, which appears in the July 2 *JOURNAL OF THE NATIONAL CANCER INSTITUTE*.

The researchers computed the total number of ovulations by using the women's age and their responses to survey questions. The researchers calculated menstruation to start, on average, at age 12. They then multiplied the fertile years by 13 periods per year and subtracted out the months when the women were pregnant, breast-feeding a child, or taking oral contraceptives.

The p53 protein findings lend credence to the incessant-ovulation theory of ovarian cancer: As cells multiply each month to repair the breach in the ovarian wall, mistakes in DNA replication make some mutations more likely. "For years that's been thought to be the mechanism," says Alice S. Whittemore, a Stanford University School of Medicine epidemiologist. "This supports that theory."

Meanwhile, many of the ovarian cancer patients in the study didn't have an abundance of the abnormal p53 protein, which suggests the cancer can use another line of attack besides taking advantage of a mutant p53 gene, Schildkraut says. Whittemore agrees that the study raises an obvious question: "What's causing the other cancers?" So far, no one knows.

Because the average age of an ovarian cancer patient at the time of diagnosis is 59, the patients in the Duke University study, who ranged in age from 20 to 54, may not represent the majority of ovarian cancer patients, Schildkraut says. The findings leave open the possibility that later onset ovarian cancer may have a different cause. For these reasons, the study needs to be replicated on older women, she says.

—N. Seppa