

## Vitamin D protects against obesity-induced endometrial cancer, researchers say

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Findings from an animal study suggest that obese women can reduce their increased risk of endometrial disease if they take vitamin D supplements, say researchers at the Georgetown Lombardi Comprehensive Cancer Center.

The scientists report in *Cancer Prevention Research* published online today that 25 percent of obese mice fed a vitamin D supplemented diet developed endometrial cancer, while 67 percent of obese mice not treated with the vitamin developed cancer. They also report that vitamin D offered no protective effects for normal weight mice; whether or not they used the vitamin, about 60 percent of these mice developed cancer.

All of the mice were genetically predisposed to develop endometrial cancer, because they were missing one of their two PTEN tumor suppressor genes, loss of which is strongly linked to development of human endometrial cancer. Obesity is also a strong known risk factor, researchers say.

"Vitamin D has been shown to be helpful in a number of cancers, but for endometrial cancer, our study suggests it protects only against cancer that develops due to obesity," says the study's lead investigator, Leena Hilakivi-Clarke, PhD, a Professor of Oncology. "Still, if these results are confirmed in women, use of vitamin D may be a wonderfully simple way to reduce endometrial cancer risk.

"Until further studies are done, I think the best advice for women



concerned about their risk is to take vitamin D supplements or spend a few more minutes each week in the sun. This vitamin has shown many health benefits in addition to the promise suggested by our mouse study," she says.

Best for women, of course, is to attempt to keep a normal weight, because it offers many other health benefits besides endometrial cancer prevention, Hilakivi-Clarke says. "However, since over 50% of women in the US are overweight or obese, and loosing weight is difficult, other means are needed to prevent endometrial cancer in these women. One way is to use progesterone, but it increases breast cancer risk. Vitamin D supplements are likely to be safer than, for example, progesterone."

While previous studies of women have demonstrated that <u>obesity</u> increases endometrial cancer risk by 2-fold or more and recurrence by up to 6-fold, recent research published by the National Institutes of Health on the protective effects of vitamin D on endometrial cancer showed no overall benefit. But the study did not investigate whether vitamin D was effective in <u>obese women</u>, Hilakivi-Clarke says.

Therefore, in this study, researchers keyed in on a potential link between weight, a known endometrial cancer risk factor, and vitamin D, a potential reducer of risk in many cancers.

They used the best animal model available to look at endometrial cancer - the PTEN knock-out mice. "Loss of PTEN is a common event in endometrial cancer in women," Hilakivi-Clarke says.

The research team, which included investigators from the National Cancer Institute, Northwestern University, Wake Forest University School of Medicine, and Walter Reed Hospital, divided their PTEN-mice into four groups. One group was fed a normal diet and one received a normal diet with supplements of vitamin D. Another group



was fed a high-fat diet, and the fourth group received a high fat diet plus vitamin D.

They found that in the mice fed a normal diet, the use of vitamin D had no effect on the development of endometrial cancer - about 60 percent of mice in both groups developed the cancer. And 67 percent of mice that became obese from a high fat diet developed the cancer, while only 25 percent of obese mice that also received vitamin D developed endometrial cancer.

"In the obese mice, vitamin D offered a very strong, very significant protective effect," Hilakivi-Clarke says.

She adds that researchers at this point do not know why vitamin D reduces <u>endometrial cancer</u> risk only in obese animals, but says data from the study suggests that these mice produce less osteopontin, which pushes cancer to be aggressive, and more E-cadherin, which stops cancer from metastasizing. Insulin resistance is also reduced in these mice, and that is important because fat cells produce inflammatory cytokines causing insulin resistance, and they also drive cancer development.

"But we really don't know why dietary <u>vitamin D</u> works so well in our obese mice," Hilakivi says. "We are currently investigating the mechanisms, and we are hopeful that we can find an answer."

## Provided by Georgetown University Medical Center

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