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Breast Cancer Metastasis Increases After Estrogen and Progestin Hormone Therapies, Study Finds

After menopause, 6 to 10 million women take hormone therapies, which are often a combination of estrogen and progestin, to replace hormones lost from inactive ovaries. Progestin is a hormone that is used to counteract the potentially negative effects of estrogen therapy on the uterus. In studies sponsored by the National Institutes of Health, evidence has been found that estrogen and progestin in hormone therapies increase the risk of breast cancer in post-menopausal women. Now, a University of Missouri study has found that progestins can also increase the chance of the cancer metastasizing, or spreading to the lymph nodes.

"In our study, we found that progestins increase the number of blood vessels that are responsible for transporting existing cancer cells," said Salman Hyder, the Zalk Endowed Professor in Tumor Angiogenesis and Professor of Biomedical Sciences in the College of Veterinary Medicine and the Dalton Cardiovascular Research Center. "The more the blood vessels increase, the higher the chance of cancer cell metastasizing. Progestins could even be more harmful to women, who have functionally abnormal p53, a protein that acts as a tumor suppressor. In the absence of p53, progestins increase the release of a protein from tumor cells that allows formation of new blood vessels within tumors."

In the study, researchers compared the effects of several types of commonly used progestins on breast cancer tumors in an animal model. Researchers found that all types of progestin tested act in the same way and increased the risk of metastasis. Also, results showed that estrogen and progestin acted the same way whether taken together or separately. Although Hyder said that the study was independent of whether or not the ovaries were intact, it's

still unclear whether progestins have the same effects in pre-menopausal women.

"Especially if there's a family history of breast cancer, it's advisable not to take progestins. It's a difficult call that must be made on an individual basis by a physician," Hyder said. "The next step for this research is finding a type of progestin that does not cause tumor progression but still protects the uterus. Also, we're trying to see if it's possible to give patients something in addition to estrogen and progestin that can protect the breast."

Hyder's study has been accepted for publication in *Menopause: The Journal of The North American Menopause Society*. It was co-authored by Hyder's colleagues at MU: Yayun Liang, Research Assistant Professor in the Dalton Cardiovascular Research Center; Cynthia Besch-Williford, associate professor in the College of Veterinary Medicine; Indira Benakanakere, research scientist; Ryyan Hyder, Undergraduate Assistant in the Dalton Cardiovascular Research Center; and Mark Ellersieck, Research Professor in the College of Agriculture, Food and Natural Resources.