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### Cancer Causing Fat- Why Postmenopausal Obese Women Are in Danger

The obesity epidemic in the United States is well publicized, evidenced by hit shows like *The Biggest Loser* and endlessly advertised weight-loss programs like Weight Watchers, the Atkins Diet, and Nutrisystem. Magazines and advertisements constantly entice us with magical new workouts and diets that will help us shred ten pounds instantly. From Zumba to Barre to Soul Cycle, there is always a new type of exercise to try, a new way to lose weight to achieve that perfect body. These trends and fads reflect our need to lose weight, given our country's 38% obesity rate according to NHANES 2014 data.

We all know that losing weight is healthy for our body in order to prevent avoidable health conditions. The 1991 *Scientific American* article, "Gaining On Fat," proves that we have known for decades that obesity increases risk of heart disease, osteoarthritis, and high blood pressure. The association between obesity and these risk factors is common knowledge since most of us have heard stories and testimonials of people who suffer these conditions due to their weight.

But many of us do not associate obesity with cancer.

Recently though, scientists have found evidence that obesity actually causes cancer. This information is not as well known; in fact, less than half of us realize that obesity and cancer are linked according to the American Institute of Cancer Research. Up until the 1990s, even scientists did not think they were related. They thought that fat did not have much purpose besides storing and releasing fatty acids. It is obvious that obese people have excess body fat, but scientists did not think this extra tissue had any significant function. After many studies and

experiments, scientists now know that this tissue is highly active in hormone regulation and sugar balance, both of which regulate cell division and can cause cancer. The tissues are more than energy storage; they actually emit molecules and signals that cause cancer.

It is not obvious that cancer and obesity are related. After all, they generally occupy two separate realms in our minds. Like obesity, we are intimately familiar with cancer, especially since half of all adults will get a cancer diagnosis according to Cancer Research UK. Sadly though, a high percentage of these cancers are completely preventable by simply weighing less; around 15% of cancers, or 85,000 cases of cancer a year, are caused by excess fat according to the American Institute of Cancer Research.

While there are many types of cancers that are impacted by obesity, postmenopausal breast cancer is especially affected by obesity. Postmenopausal obese women are more susceptible to breast cancer due to their hormonal levels, and they're susceptible to cancer in general because of their weight. In all of our bodies, fat tissue produces estrogen, a hormone that postmenopausal women have stopped producing due to their age. Their fat is their main source of estrogen, but their estrogen levels are significantly elevated due to excess body fat. Many breast cancer tumors have many estrogen receptors that help the tumor grow and multiply, so as a result, postmenopausal women are vulnerable to these breast tumors due to high levels of estrogen from their fat.

Knowing this information, it makes sense that over 70% of postmenopausal women diagnosed with breast cancer were obese. In 2002, after over a decade of research in obesity and cancer, the International Agency for Cancer Research officially stated that "excess body weight is an avoidable cause of post-menopausal breast cancer." Once these women have breast cancer, their weight also causes far worse outcomes than their leaner counterparts. A study of 1436

women diagnosed with breast cancer in 1996-1997 showed that women who gained weight after diagnosis had a significantly worse survival rate than women who did not gain weight. Research from Michigan State University in 2005 by a researcher named EM Velie proved that there is a two-fold increase in risk for death from breast cancer in obese women. Being overweight or obese not only increases your risk for cancer, but it also significantly increases your risk for death once you have breast cancer. Obesity does not just cause high blood pressure and diabetes; it causes life-threatening cancers and death.

But what exactly happens in fat tissue that makes obese people susceptible to cancer? What else is different in postmenopausal women that make these women susceptible to breast cancers? Scientists have been continuously researching this topic since the 1990s and are still trying to understand the science behind these findings, but they have found a few discoveries that explain this phenomenon.

### Increased Insulin Levels

One reason for the link between obesity and cancer is that excess fat in obese and overweight people leads to resistance to insulin, a hormone used by our bodies to convert sugar into energy or storage. Insulin is needed to process sugar; without insulin, there will be high blood sugar levels of unused, unprocessed sugar. The term insulin resistance hopefully sounds familiar because it causes diabetes, a condition that is commonly associated with obesity.

Though insulin resistance is incredibly common, we still do not know what exactly causes this insulin resistance in obese people. One theory is that cells basically become poisoned by fat. This hypothesis states that when fat tissue cannot store excess fat, fat accumulates inappropriately in muscle and liver cells. The accumulation of fat damages the functionality of these cells and prevents the cells from using insulin, which results in excess, unused insulin and

unconverted sugar floating around in the bloodstream. This extra sugar is dangerous because malignant, cancer tumor cells use this sugar to replicate. Our body essentially feeds this sugar to cancer cells since it lacks the ability to use insulin to convert the sugar into usable energy.

Another theory states that our fat releases products that can block the insulin-signaling process. When that happens, no matter how much insulin we have in our blood, our cells will not be able to use insulin since the signaling pathway is muted by these products. Insulin will try to communicate with cells to help process the sugars, but the cells will not be able to “hear” the insulin because of the products from fat that interfere and silence this communication. This silencing subsequently causes blood sugar levels to build up in the blood since insulin is not being used to breakdown these sugars, and thus cancer cells are supplied food.

We have established that insulin resistance exists in obese people, but this resistance does more than create food for cancer cells. It also increases the amount of growth factors in the bloodstream according to Ruth Patterson and her team from Moores USCD Cancer Center. These growth factors are signals that tell cells to duplicate. More insulin in the blood stream leads to more growth factors telling cancer cells to multiply.

So in other words, obese people experience insulin resistance, which results in too much insulin and sugar in our bodies. The sugar gives nutrients for cancer cells to grow, and the insulin tells these cancer cells to grow. Researchers are looking at drugs to target these high insulin levels, specifically with metformin, a drug used to treat type 2 diabetes. Research so far has shown that metformin has reduced growth of most breast cancer cells, but we need to know more about long-term usage of this drug.

#### Affected Reproductive Hormone Levels

All overweight and obese people are susceptible to insulin resistance and the uncontrolled cell division that results from it. However, fat tissue not only affects insulin levels, but also estrogen levels. The effects on estrogen levels lead to consequences that mainly obese postmenopausal women experience. The exclusiveness of this effect is due to the fact that postmenopausal women have stopped releasing eggs and producing estrogen in ovaries, so their fat is their only source of estrogen. As a result, excess fat in obese women means that their levels of estrogen are abnormally high. An abnormally high level of estrogen is very dangerous because estrogen is a driving force behind most breast cancers. Research by Neil Iyengar from Memorial Sloan-Kettering Cancer Center has shown that postmenopausal women are at a much higher risk of developing tumors that express estrogen receptors. These tumors account for about 60% of breast cancers according to research conducted in Sirai Hospital, Italy. Essentially, obese postmenopausal women have far higher than normal levels of estrogen, and this estrogen causes cancer.

Estradiol is the specific estrogen that is thought to stimulate the reproduction of breast cells and mutations. However, there is confusing research on estradiol that researchers are trying to understand. Postmenopausal women have higher rates of breast cancer than premenopausal women, so it would make sense that they must have high levels of estradiol since this hormone helps replicate breast cells. But compared to premenopausal women, estradiol levels in postmenopausal women are much lower since ovaries no longer produce substantial amounts of estrogen. Postmenopausal women have less estradiol in their bodies, but they are the most susceptible to their effects. Researchers do not know why. Though it hasn't been directly proven that estrogen causes breast cancer, it has been shown by Ruth Patterson from UCSD that women with hormonal levels in the top 20% have two to three times higher risk of breast cancer

compared to the bottom 20%. Therefore, despite not knowing exactly how estradiol or estrogen causes cancer cell replication, researchers know for certain that hormones are responsible for cancer proliferation.

### Chronic Inflammation

In addition to high insulin levels and excess estrogen, a last cause of postmenopausal cancer in obese patients is chronic inflammation, a biological process that occurs when our bodies' white blood cells are released into blood and tissues to protect our body from foreign substances. We feel this inflammation when we have a sore throat, a stuffy nose, a swollen ankle, or arthritis, but it is also caused by daily activities like eating too much and being stressed. Diets that are high in saturated fat and trans fats can also induce inflammation, and these diets are common in obese and overweight people. Obese people as a result experience high levels of inflammation, and many cancers arise at sites of chronic inflammation. In fact, inflammatory response is linked to 15% to 20% of all cancer-related deaths worldwide according to Dr. Neil Iyengar, a researcher from Memorial Sloan-Kettering Cancer Center at Weill Cornell Medical College in New York. The release of chemicals by our immune system is meant as a protective process, but it turns out that too much inflammation has an opposite effect.

Naturally due to the extra fat in obese patients, levels of adipokines, a signal released by fat that is involved in inflammation, are significantly higher. Fat releases these adipokines in the same way that it releases estrogen. Many studies show worse prognosis or increased breast cancer risk in women with higher circulating levels of adipokines. It has not been established yet how exactly the higher levels of adipokines directly cause cancer, but it's known that adipokine is one of many indicators of inflammation that are present in breast cancer tumors. Our fat also secretes cytokines, which induce an inflammatory response. Cytokines decrease insulin

sensitivity and thus contribute to insulin resistance and all the consequences of insulin resistance like uncontrolled cell growth.

In exploring the causes of cancer in obese people, we are constantly reminded that there is so much to be discovered. We do know from the past 25 years of research that excess fat results in too much insulin and sugar in our bloodstream, which feeds cancer cell growth. We know that excess fat also produces extra estrogen, which induces breast cancer in postmenopausal women because many breast cancers have estrogen receptors. We also know that breast cancers often grow in sites of inflammation that are caused by poor diet. We have made significant progress, but much work needs to be done.

Luckily, the scientific community recognizes this issue as a major health risk, so they are frantically finding new research models to get more information about obesity and cancer. The National Cancer Institute is driving this movement by funding many new research centers that foster collaboration among disciplines on this research. Several human trials are in progress today. One study in obese women examines the effectiveness of diets that have high carbohydrates or high fat. Another study looks at how metformin and exercise can impact breast cancer mortality among the overweight and obese. A different clinical trial will monitor obese women with heart rate monitors, accelerometers, and GPS devices to analyze the effects of physical activity energy expenditure on insulin levels. These trials are looking at the best way to help us lose weight and prevent these cancers, and hopefully in another 25 years, we will have more answers.

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## Works Cited

- Fischetti, Mark. "Dying to Eat: A Graphical View of U.S. Obesity." *Scientific American*.  
Scientific American, 13 Sept. 2010. Web. 08 Nov. 2016.
- Fox, Maggie. "America's Obesity Epidemic Hits a New High." *NBC News*. NBC7, 7 June 2016.  
Web. 08 Nov. 2016.
- Iyengar, Neil M., Clifford A. Hudis, and Andrew J. Dannenberg. "Obesity and Inflammation:  
New Insights into Breast Cancer Development and Progression." *American Society of  
Clinical Oncology Educational Book* 33 (2013): 46-51. Web.
- Kwon, Hyokjoon, and Jeffrey E. Pessin. "Adipokines Mediate Inflammation and Insulin  
Resistance." *Frontiers in Endocrinology* 4 (2013): 71. *PMC*. Web. 8 Nov. 2016.
- "Lifetime Risk of Cancer." *Cancer Research UK*. N.p., 13 June 2016. Web. 16 Nov. 2016.
- Liu, Li-Yuan et al. "The Role of Adiponectin in Breast Cancer: A Meta-Analysis." Ed. Seema  
Singh. *PLoS ONE* 8.8 (2013): e73183. *PMC*. Web. 8 Nov. 2016.
- Neuhouser ML, Aragaki AK, Prentice RL, Manson JE, Chlebowski R, Carty CL, Ochs-Balcom  
HM, Thomson CA, Caan BJ, Tinker LF, Urrutia RP, Knudtson J, Anderson GL.  
Overweight, Obesity, and Postmenopausal Invasive Breast Cancer Risk: A Secondary  
Analysis of the Women's Health Initiative Randomized Clinical Trials. *JAMA  
Oncol.* 2015;1(5):611-621.
- "SEER Stat Fact Sheets: Cancer of Any Site." *Surveillance, Epidemiology, and End Results  
Program*. National Cancer Institute, n.d. Web. 07 Nov. 2016.
- Velie EM, Nechuta S, Osuch JR. Lifetime reproductive and anthropometric risk factors for breast  
cancer in postmenopausal women. *Breast Dis.* 2005; 24:17-35.



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