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Breast Cancer Vaccine

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Abstract

Breast cancer, just reading those words can make many women worry, as breast cancer is the most common cause of cancer death in women worldwide. Investing in breast cancer prevention is cost effective on both the social and economic levels [1]. The word vaccine is classically used to define the material used for prevention of infective diseases, but we can use it to refer to the methods proved to be effective in preventing breast cancer. An experimental vaccine against breast cancer safely generated a strong immune response to a key tumor protein, researchers from the University of Washington School of Medicine in Seattle report in a paper published by the journal JAMA Oncology. The findings suggest the vaccine may be able to treat different types of breast cancer [2]. "Because this was not a randomized clinical trial, the results should be considered preliminary, but the findings are promising enough that the vaccine will now be evaluated in a larger, randomized clinical trial," said lead author Dr. Mary "Nora" L. Disis, a UW professor of medicine, Division of Medical Oncology, and director of the Cancer Vaccine Institute [2].

Keywords: Cancer Vaccine; Ductal Carcinoma; Ductal Hyperplasia; Lobular Hyperplasia; Breast Cancer

Abbreviations: DCIS: Carcinoma in Situ; LCIS: Lobular Carcinoma in Situ; DCIS: Ductal Carcinoma in Situ; LCIS: Lobular Carcinoma in Situ; ADH: Atypical Ductal Hyperplasia; ALH: Atypical Lobular Hyperplasia; DCIS: Ductal Carcinoma in Situ

Background

Nearly everyone knows someone touched by the disease. A risk factor is anything that raises your risk of getting a disease. Your risk factors will need to be assessed to find out if you are at higher-than-average risk for breast cancer. But keep in mind that having risk factors does not mean that you will develop breast cancer. In fact, most women who have one or more risk factors never develop breast cancer.

[3,4].

Some important risk factors for breast cancer include:

i. Getting older

ii. Having close relatives who have breast cancer

iii. Having a longer menstrual history (more total menstrual cycles)

iv. Having had invasive breast cancer or ductal carcinoma in situ (DCIS) before

v. Being diagnosed with lobular carcinoma in situ (LCIS)

vi. Being diagnosed with atypical ductal hyperplasia (ADH) or atypical lobular hyperplasia (ALH)

vii. Having a gene mutation linked to a family cancer syndrome (such as a BRCA mutation)

Researchers have built some statistical models to help predict a woman's risk of getting breast cancer. For example, the Breast Cancer Risk Assessment Tool (based on the modified Gail Model) is commonly used to assess risk. It can estimate your risk of getting breast cancer in the next 5 years and over your lifetime, based on many of the factors listed above. This tool only looks at family history in close relatives (like siblings, parents, and children), though. And it can't be used to estimate risk if you have a history of ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), or breast cancer, or if you have a family cancer syndrome.

Also, the data that this tool is based on didn't include American Indian or Alaskan Native women, so estimates for these women may not be accurate [5]. Other risk assessment tools, such as the Tyrer-Cuzick model and the Claus model, are based largely on

family history. These tools are used mainly by genetic counselors and other health care professionals. These tools can give you a rough estimate of your risk, but no tool or test can tell for sure if you'll develop breast cancer [6].

Discussion

There is a lot of good news about breast cancer these days. Treatments keep getting better, and we know more than ever about ways to prevent disease. Breast cancer prevention starts with healthy habits such as limiting alcohol and staying physically active. Understand what you can do to reduce your breast cancer risk [7]. If you're concerned about developing breast cancer, you might be wondering if there are steps you can take to help prevent breast cancer.

Some risk factors, such as family history, can't be changed. However, there are lifestyle changes you can make to lower your risk. Research shows that lifestyle changes can decrease the risk of breast cancer, even in women at high risk [8]. These simple steps can help lower the risk of breast cancer. Not everyone applies to every woman, but they can have a big impact.

Keep Weight in Check

Ideal BMI is 25. It's easy to ignore because it gets said so often, but maintaining a healthy weight is important for everyone. Being overweight can increase the risk of many different cancers, including breast cancer, especially after menopause [9].

Be Physically Active

Exercise is as close to a silver bullet for good health as there is. Women who exercise for at least 30 minutes a day have a lower risk of breast cancer. Regular exercise is also one of the best ways to help keep weight in check [10].

Eat Your Fruits & Vegetables – and Limit Alcohol (Zero is Best)

A healthy diet can help lower the risk of breast cancer. Try to eat a lot of fruit and veggies and limit alcohol. Even low levels of drinking can increase the risk of breast cancer. And with other risks of alcohol, not drinking is the best choice overall for your health. Women who eat a Mediterranean diet supplemented with extra-virgin olive oil and mixed nuts might have a reduced risk of breast cancer. The Mediterranean diet focuses mostly on plant-based foods, such as fruits and vegetables, whole grains, legumes, and nuts. People who follow the Mediterranean diet choose healthy fats, such as olive oil, over butter and eat fish instead of red meat [11].

Don't Smoke

On top of its many other health risks, smoking causes at least 15 different cancers – including breast cancer. If you smoke, try to quit as soon as possible. It's almost never too late to get benefits. You can do it [12].

Breastfeed, If Possible

Breastfeeding for a total of one year or more (combined for all children) lowers the risk of breast cancer. It also has great health benefits for the child [13].

Avoid Birth Control Pills, Particularly After Age 35 or If You Smoke

There's some evidence that hormonal contraception, which includes birth control pills and IUDs that release hormones, increases the risk of breast cancer. But the risk is considered very small, and it decreases after you stop using hormonal contraceptives. Birth control pills have both risks and benefits. The younger a woman is, the lower the risks are. While women are taking birth control pills, they have a slightly increased risk of breast cancer.

This risk goes away quickly, though, after stopping the pill. But long-term use can also have important benefits, like lowering the risk of ovarian, colon and uterine cancers. Birth control pills also prevent unwanted pregnancy, so there's also a lot in their favor. If you're very concerned about breast cancer, avoiding birth control pills is one option to lower risk. A recent study that showed an association between hormonal contraceptive use and breast cancer determined one additional breast cancer could be expected for every 7,690 women who use hormonal contraception for at least one year [14].

Avoid Hormone Therapy for Menopause

Hormone therapy in menopause shouldn't be taken long term to prevent chronic diseases. Studies show its mixed effects on health, raising the risk of some diseases and lowering the risk of others. Whether estrogen is taken by itself or it's combined with progestin, hormones increase the risk of breast cancer. If women do take hormone therapy during menopause, it should be for the shortest time possible [15].

Tamoxifen and Raloxifene for Women at High Risk

Although not commonly thought of as a "healthy behavior," taking the drugs tamoxifen and raloxifene can greatly lower the risk of breast cancer in woman at high risk of the disease. Approved by the FDA for breast cancer prevention, these powerful drugs can have side effects, so they aren't right for everyone [16].

Methods

- Women with a strong family history of cancer can take special steps to protect themselves. That's why it's key for women to know their family history. You're at higher risk if you have a mother or sister who had breast or ovarian cancer. This risk is even higher if your relative was diagnosed at an early age. Having multiple family members (including males) who had breast, ovarian or prostate cancer also raises your risk. A doctor or genetic counselor can help explain your family history of the disease [17].

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- Breast cancer screening with mammograms saves lives. It doesn't help prevent cancer, but it can help find cancer early when it's more treatable. Most women should get yearly mammograms starting at age 40.

- Women at higher risk for breast cancer may need to start getting screened earlier. It's best to talk to a doctor by age 30 about your risk and whether you'd benefit from earlier screening [18].

- Because regular breast self-exams haven't proven to be beneficial, they aren't recommended for screening. Still, knowing your breasts is key. Tell your doctor right away if you notice any changes in how your breasts look or feel.

Be vigilant about breast cancer detection. If you notice any changes in your breasts, such as a new lump or skin changes, consult your doctor. Also, ask your doctor when to begin mammograms and other screenings based on your personal history [19]. 5-Your level of risk is determined by factors such as your age, your family's medical history, and the results of genetic tests. If you have an increased risk of developing breast cancer, treatment is available to reduce your risk. You'll usually be referred for specialist genetic testing if it's thought you have an increased risk of breast cancer. Healthcare professionals at these services should discuss treatment options with you [20].

Prophylactic Treatment

The 2 main treatments are surgery to remove the breasts (mastectomy) or medicine. 1-Mastectomy: A mastectomy is surgery to remove the breasts. It can be used to treat breast cancer and can also reduce the chances of developing the condition in the small number of women who have a high risk [21]. By removing as much breast tissue as possible, a mastectomy can reduce your risk of breast cancer by up to 90%. However, like all operations, there's a risk of complications, and having your breasts removed can have a significant effect on your body image and sexual relationships.

If you want to, you can usually choose to have breast reconstruction either during the mastectomy operation, or later [22]. During breast reconstruction surgery, your original breast shape is recreated using either breast implants or tissue from elsewhere in your body. An alternative is to use breast prostheses. These are artificial breasts that can be worn inside your bra. An alternative to mastectomy is a nipple-sparing mastectomy, where the whole mammary gland is removed, but the skin of the breast is preserved. This is not widely available now, but it's being used more often and can achieve excellent results [23].

Medicine

For women with a higher-than-average risk of breast cancer, some medicines can help reduce this risk. But these drugs can also have side effects, so it's important to weigh their pros and cons before deciding to take one. Taking medicines to help lower the risk of getting a disease is called chemoprevention. The most used medicines to lower breast cancer risk are tamoxifen and raloxifene. Other medicines called aromatase inhibitors (such as anastrozole and exemestane) might also be options [24].

There are 3 medicines available on the NHS for women who have an increased risk of breast cancer:

tamoxifen – for women who either have or have not been through the menopause anastrozole – for women who have been through the menopause raloxifene – for women who have been through the menopause. These medicines are usually taken once a day for 5 years. They can reduce the risk of breast cancer while taking them and possibly for several years afterwards. Side effects of these medicines can include: hot flushes, sweating, feeling sick, tiredness, leg cramps. There's also a small risk of more serious problems, such as weakened bones (osteoporosis), blood clots or womb cancer [25].

If the doctor suggests taking medicine to reduce the risk of breast cancer, ask them about the benefits and risks of each medicine. The first step in deciding if you should take a drug to help lower your chances of getting breast cancer is to have a health care provider assess your breast cancer risk [26]. Most experts say that your breast cancer risk should be higher than average for you to consider taking one of these drugs. If you do have a higher-than-average risk, you need to compare the benefit of possibly reducing your chance of getting breast cancer with the risk of side effects and other problems from taking one of these drugs [27].

Breast Cancer Genes

Genetic testing for hereditary breast and ovarian cancer looks for mutations in the BRCA1 and BRCA2 genes. The breast cancer 1 (BRCA1) and breast cancer 2 (BRCA2) genes are the genes most commonly affected in hereditary breast and ovarian cancer. Normally, the BRCA1 and BRCA2 genes protect you from getting certain cancers. But certain mutations in the BRCA1 and BRCA2 genes prevent them from working properly, so that if you inherit one of these mutations, you are more likely to get breast, ovarian, and other cancers. You and your family members are more likely to have a BRCA1 or BRCA2 mutation if your family has a strong history of breast or ovarian cancer. Because BRCA1 and BRCA2 mutations are inherited, family members with BRCA1 or BRCA2 mutations usually share the same mutation [28].

The genetic counselor can help you determine the best testing strategy for you and your family. Whenever possible, the first person tested in your family should be someone who has breast, ovarian, or another BRCA-related cancer. If none of your family members who have had one of these cancers are available for genetic testing, then genetic testing can start with an unaffected person. However, the test results might not be as helpful. Genetic counseling after genetic testing is important to help you understand your test results and decide the next steps for you and your family. If you have a positive test result, the test showed that you have a mutation known to cause hereditary breast and ovarian cancer. You can take steps to make it less likely that you

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will get cancer or to find cancer early if you do get it.

If you have already had breast or ovarian cancer, a positive test result can help guide your treatment decisions. If other family members decide to get genetic testing, their test should check for the same mutation you have. Your parents, children, sisters, and brothers each have a 1 in 2 (50%) chance of having the same mutation. If you have a negative test result, the test didn't find a mutation. However, what this means for you depends on whether you have already had breast or ovarian cancer and whether another relative is known to have a mutation. A negative result means that the test did not find a mutation that caused your cancer, the breast and ovarian cancer in your family is less likely to be due to an inherited mutation, unless another relative is known to have a mutation [29].

Genetic testing in your family members who have not had breast or ovarian cancer is unlikely to be helpful, unless another relative is known to have a mutation. In some cases, testing might still be helpful for another family member who has breast or ovarian cancer. This is because it is still possible that there is an inherited mutation in your family, but you did not inherit it. If a mutation has not already been found in another family member, a negative test result is considered uninformative because the result could mean that the breast and ovarian cancers in your family are caused by one of the mutations included in the genetic test but you did not inherit the mutation, or the breast and ovarian cancers in your family were not caused by a mutation that was included in the genetic test.

You are still considered at increased risk for the cancers that run in your family. The level of risk, appropriate screening and prevention options, and need for additional genetic testing will vary for each person and each family. If a mutation has already been found in another family member and the test showed you do not have the mutation, you are not at higher risk than the average person for breast or ovarian cancer. You also cannot pass the mutation on to your children. If you have a variant of uncertain significance (VUS) result, the test found a mutation in one of the genes associated with hereditary breast and ovarian cancer, but whether that specific mutation causes cancer is unknown. Some mutations prevent genes from working properly, while others have no effect.

It is not always easy to tell whether a mutation in a gene has a harmful effect. If you have already had breast or ovarian cancer, it is unclear whether the mutation found in the test caused your cancer. Further testing might be available. Whether or not you have already had breast or ovarian cancer, you are still considered at increased risk for the cancers that run in your family. The level of risk, appropriate screening and prevention options, and need for additional genetic testing will vary for each person and each family [30]. Having a strong family health history of breast and ovarian cancer does not mean that you definitely have an inherited mutation. In fact, most women identified as being at increased risk for BRCA1 and BRCA2 mutations based on family health hihaveve BRCA1 or BRCA2 mutations. Using family health history information will not find anyone with BRCA1 or BRCA2 mutations. Not everyone with a BRCA1 or BRCA2 mutation has a strong family health history of breast and ovarian cancer. Some even have no known family health history of breast and ovarian cancer [31].

Genetics

A trial was designed to evaluate the safety of a vaccine that targets a protein called human epidermal growth factor receptor 2 (HER2) and to see if it generated an immune response to the protein. HER2 is found on the surface of many cells, but in as many as 30% of breast cancers, HER2 is overproduced by as much as hundred times the amount seen in normal cells. These "HER2-positive" cancers tend to be more aggressive and more likely to recur after treatment, but the overproduction of HER2 also triggers an immune reaction that can be beneficial [32].

Specifically, patients with HER2-positive breast cancers who mount a type of immune response called cytotoxic — or cell-killing — immunity are less likely to see their cancer recur after treatment and have longer overall survival than those who do not mount such an immune response [33]. To stimulate this kind of response, the scientists created a DNA vaccine. Unlike protein vaccines, which typically contain a protein or part of a protein that you want the immune system to target, DNA vaccines contain the DNA instructions for the target protein [34].

Vaccine

Once injected, this DNA is taken up by cells at the injection site, which then start to produce the protein encoded in the vaccine's DNA instructions. The cells will then present protein to the immune system, a process more likely to generate a strong, cytotoxic immune response [35]. The vaccine used in this trial contained the DNA instructions for a part of the HER2 that is usually located within the cell. This intracellular portion is known to provoke stronger cytotoxic immune responses [36]. Sixty-six women who had metastatic cancer were enrolled in the study. All the women had completed a standard course of therapy and had either achieved complete remission or only had tumor remaining in their bone, which tends to grow slowly [37].

The study participants were divided into three groups with each participant receiving three injections. One group received three low-dose injections (10 mcg) of the vaccine, one group got three injections with an intermediate dose of 100 mcg, and one group, three injections of a high dose, 500 mcg. They also received the immune-stimulating drug granulocyte-macrophage colony-stimulating factor (GM-CSF), which promotes cytotoxic immunity [38]. The participants were then followed for three to 13 years (median follow-up was nearly 10 years). A long follow-up was important because HER2 is found on many other cell types. The researchers wanted to ensure the vaccination did not, over time,

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trigger an autoimmune response against other healthy tissues bearing HER2.

The results showed that the vaccine was very safe. In fact, the most common side effects that we saw in about half the patients were very similar to what you see with COVID vaccines: redness and swelling at the injection site and maybe some fever, chills and flu-like symptoms [39]. The vaccine also successfully stimulated the desired cytotoxic immune response without triggering severe side effects, with strongest immune response appearing in patients who received the middle dose. Although the study was not designed to see if the vaccine could slow or prevent progression of the cancer, the researchers noted that the participants have done much better than would be expected in patients with similar stages of breast cancer, about half of whom would be expected to die within 5 years of treatment. These women were followed for ten years and 80% of them were still alive [40,41].

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