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## Updates on Breast Cancer Treatment

**Guest Expert:**

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*Associate Professor of Medical Oncology*



**Yale Cancer Center Answers**

is a weekly broadcast on

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Sunday Evenings at 6:00 PM

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*Welcome to Yale Cancer Center Answers with Drs. Ed Chu and Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center. Dr. Miller is an Oncologist who specializes in pain and palliative care. If you would like to join the discussion, you can contact the doctors at [canceranswers@yale.edu](mailto:canceranswers@yale.edu) or 1-888-234-4YCC. This evening we take a look at the prevention and treatment of breast cancer with Dr. Michael DiGiovanna, Associate Professor of Medical Oncology at the Yale Cancer Center.*

Miller Mike, let's start by talking about some of the myths that are out there. Does breast cancer only effect women who have a family history?

DiGiovanna It certainly does not. Having a family history is only one of the well known risk factors for developing cancer. Many people know that the tendency to develop cancer can be genetically inherited, but only about 5% of breast cancers seem to be genetically inherited, and the other 95% seem to be random.

Chu In what situation would you be more concerned about a genetic family history of breast cancer?

DiGiovanna The situation would be primarily if there is a first-degree relative with the cancer, and by first-degree relative we mean your mother, your sister or your daughter. The next kind of factor that plays a role is how many people in the family have had breast cancer. The more people in the family that have had it, the higher the odds that there is something genetically inherited in the family. Another factor is the age of onset within a family. The average age at which breast cancer strikes is 58 to 60. When it strikes in the premenopausal range, someone 40 or younger, that is a tip off that it can be genetically inherited. Finally, there are certain syndromes that run in groups of cancer. One of the primary ones for breast cancer is a relationship between breast cancer and ovarian cancer. So if those two cancers are in a family, that is a risk factor that could indicate a genetically inherited syndrome.

Miller Talking about risks, there is something called the Gail model that can help a woman, or help a doctor counsel women, in terms of her risk. Can you tell us about the Gail model, or in general, about how you give advice to women in terms of their risk?

DiGiovanna The way I advise women is tell them to run down the list of primary risk factors for breast cancer. I start by saying that the number one risk factor is being female, because almost one out of eight women, statistically in the United States, at some point will develop breast cancer. The next strongest risk factor is one we mentioned, family history. Then there are

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other risk factors that have to do with reproductive issues such as the age at which a woman first has a child, whether a woman has had a child or not, whether a woman breastfed, the age at which her menstrual periods began as a teenager and the age at which she reaches menopause. There are some benign breast conditions that can be seen on biopsies, and some of these benign conditions can be associated with a higher incidence of breast cancer. The Gail model, the one that you mentioned, is one of several available models that can plug all of these factors into an equation and give someone their estimated risk of developing breast cancer. This is actually available online for people on the National Cancer Institute website.

Chu We know that early detection screening is the key for this disease. At what age do you recommend women begin with self exams and having mammograms?

Michael The principal screening test is mammogram and we recommend that all women begin having mammograms at age 40. However, if there is a family history or a genetically inherited syndrome within the family, we may recommend that they begin at an even younger age; perhaps 10 years younger. As well, when there is early-onset breast cancer within a family, we recommend that the other women in that family begin having mammograms at least 10 years earlier than the earliest age of onset of somebody afflicted with the cancer. For example, if a family member was afflicted with breast cancer at age 35, we would recommend mammographic screening beginning at age 25. The other two components of screening are the ones you mentioned, self-breast examination and clinical breast examination. What we mean by that is having a doctor do a breast exam and checkups. All women, once they reach adulthood, should be educated to examine their own breasts with self-breast examinations at least once a month. For pre-menopausal women, this should be done preferably after the menstrual period has ended because prior to that the breasts may naturally have some lumpy consistency to them.

Miller Let us focus a little bit on women who are at higher risk. Let's say they have one of those factors that you mentioned, a family history, etc. Are there other forms of surveillance, such as MRI which has been talked about? How would their surveillance be different than a woman who did not have a risk factor?

Michael MRI scans are another way that the breast can be screened for breast cancer. They actually seem to be even more sensitive than mammograms at picking up cancers. The problem with applying them to the general population is that they are so sensitive, they are somewhat over sensitive.

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Therefore we have many false positives using MRI for screening. If we used it in the general population it is estimated that about one out of four women would be sent for a biopsy that would turn out to be something insignificant. They would have to go through the anxiety and the procedure of a biopsy. Where we recommend it is for women who have the very highest risk. It is most definitely recommended for women who carry known genes that predispose them to hereditary breast cancer. Those genes also predispose women to early-onset breast cancer at an earlier than average age. In addition, in very young women, that is the age group where mammograms are less effective because younger women have much denser breasts which can hide cancer within the dense breast tissue. This also leads to false positives because of naturally dense tissue in the breasts.

- Chu A question for our listeners out there, is screening using mammography covered by all insurances?
- Michael Mammograms are absolutely covered by insurance companies and almost all of them on an annual basis.
- Chu For those women who may not have insurance, and need a mammogram, are there support services that allow them to receive those mammograms?
- Michael Many communities have things like screening vans that can go around to places of employment and offer very inexpensive mammographic screening. Anyone who is concerned and does not have insurance should ask their doctor or their local cancer center and find out about that.
- Miller For women that are at high risk, are there any interventions, any medicines that they can take that will reduce the risk?
- Michael That is a very good question. Just identifying risk is not enough and of course screening can catch the cancer early, but we would rather prevent it. There are essentially two ways that the risk of developing breast cancer can be prevented. One is surgical and one is with medicine. Some women who know that they are at extremely high risk of developing breast cancer, for example some of the genetically inherited syndromes can give a women an 85% chance of developing breast cancer some time in her life, will choose to have prophylactic surgery; prophylactically having a bilateral mastectomy to reduce the risk of breast cancer. There is a medical intervention that is not quite as effective, but somewhat effective, and that is a medicine that can be used to lower the risk of breast cancer. This arose because we were using this medicine to treat breast cancer and realized that when we used it to treat breast cancer, it reduced the odds of

getting a breast cancer in the opposite breast. That medication is called tamoxifen and just in the past year we did an additional study that has shown another medication, actually used to treat osteoporosis and is a cousin of tamoxifen, raloxifene, or Evista, can also reduce the risk of developing breast cancer. These medications seem to reduce the risk by about 50%. They are not a guarantee, but for someone at high risk that is a big chunk of risk that can be eliminated.

Chu How do these two medicines work to reduce the risk of a woman developing breast cancer?

Michael These medications are what we call antiestrogens. That leads to the connection between estrogen, the female sex hormone, and breast cancer. Estrogen is the female sex hormone and that is essentially what makes girls, girls. The parts of the body that contain what is called the estrogen receptor will grow in response to estrogen. Normal breast tissue contains estrogen receptors and that is the reason why when a little girl hits puberty and her estrogen levels go up, she will grow breasts. That does not happen to a boy because boys do not have that surge of estrogen at puberty. When a breast cancer arises in the breast, at least half the time, the cancer also contains the estrogen receptor. If that is the case, then the cancer requires estrogen to grow and the cancer is fed by estrogen. One way that we treat these types of breast cancer is with these antiestrogen drugs like tamoxifen. The mechanism of tamoxifen reducing the risk of developing breast cancer in the first place is exactly the same, by antagonizing estrogen in a woman's breast.

Miller You have done some wonderful laboratory research on breast cancer that we are going to talk more about later, but for women where the tumor is not sensitive to estrogen, what seems to be fueling the cancer in that case?

Michael There is at least one other broad class of breast cancer, and that is the type of breast cancer that contains a different receptor called HER-2. This type of receptor is a little bit different, but it picks up signals from the blood stream to help the cancer grow. For about 20%-25% of all breast cancers that have an abundance of HER-2 receptor, there is a new, very effective therapy for helping to treat those cancers and reducing the risk of relapsing. That therapy is known as Herceptin and in the last year, for patients with advanced cancer that have HER-2, there is a second drug that also works at the HER-2 receptor, and that can work after Herceptin has stopped working.

Miller There has been some research on insulin growth factor. How does that play into the worry about breast cancer?

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Michael That is another type of receptor that is not at all in the realm of treating patients with breast cancer yet. This is still in laboratory research and very early clinical trials, but there is another receptor known as the insulin-like growth factor receptor. The experiments that were done 15 or 20 years ago in the laboratory showed that if you have cells that do not have this receptor, you cannot turn them cancerous. It is a very critical receptor in cancer being cancer and there are drugs that are just coming through the pipeline from some of the pharmaceutical companies that can specifically inhibit this receptor, and as you alluded to, in my laboratory research these types of drugs can really complement some of the types of drugs that we use now, such as tamoxifen and Herceptin. Maybe one day in the near future, we will have a clinical trial to test that type of treatment.

Chu In addition to the new medicines that you just talked about, in terms of trying to either prevent the breast cancer from happening or reduce the risk of the breast cancer from returning, are there any other lifestyle and/or dietary changes that can be made to try to also reduce the potential risk?

Michael Some of the lifestyle factors related to breast cancer are ones that I talked about earlier, and that is the age at which a woman bears her first child and whether or not she breastfeeds. So, a woman who has her first child before age 24 significantly reduces her risk of developing breast cancer. On the other hand, a woman who never has a baby or has a baby later in life, after age 35 or 40, that can actually increase her risk of breast cancer. Now this is not a very modifiable type of risk factor because it is hard for us to go into the public and start telling women in their early 20s that they should all run out and have a baby as quickly as they can. That is not very modifiable. Some of the factors that might perhaps be modifiable are that exercise and a low fat diet might reduce the risk of developing breast cancer. In some very interesting recent research, a low fat diet may also help a woman who has had breast cancer from relapsing. That is something that is of interest as well.

Bruce We would like to remind you to e-mail your questions to [canceranswers@yale.edu](mailto:canceranswers@yale.edu). We are going to take a short break for a medical minute. Please stay tuned to learn more information about breast cancer with Dr. Michael DiGiovanni from the Yale Cancer Center.

### *Medical Minute*

*You know there are over 10 million cancer survivors in the US and the numbers keep growing. Completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life changing experience. Following treatment, the return to normal activities and relationships can be difficult and cancer survivors may face other*

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*longterm side effects of cancer including heart problems, osteoporosis, fertility issues and an increased risk of second cancers. Resources for cancer survivors are available at federally designated comprehensive cancer center such as the Yale Cancer Center to keep cancer survivors well and focused on healthy living.*

*This has been a medical minute and you will find more information at [yalecancercenter.org](http://yalecancercenter.org). You are listening to the WNPR health forum from Connecticut public radio.*

Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller and I am here with my co-host Dr. Edward Chu, and Dr. Michael DiGiovanna discussing treatment for breast cancer. Mike, we finished the first segment talking about what happens after breast cancer in terms of reducing risk and recurrence, can you say a little bit more about that?

Michael: In terms of the treatment for it?

Miller: In terms of lifestyle.

Michael: One of the things I mentioned was that some recent studies have shown that women who adopt a very low fat diet after their treatment of breast cancer can reduce their risk of relapsing. We expected that this would most affect the women who have the estrogen receptor positive types of breast cancer because we know that estrogen can come from fat, so if you reduce your fat intake and lose weight, we thought it might reduce the risk of relapsing in the women with the estrogen receptor positive type of breast cancer. As in science, we are always surprised, and the results actually showed that it was more effective in the women with estrogen receptor negative breast cancer. This is important because they do not have the antiestrogen drugs for protection like the estrogen receptor positive women do. It is postulated that this effect of fat, reducing the estrogen receptor negative cancers from relapsing, could be related to what we were speaking about a few minutes ago, which is insulin-like growth factor that also is related to diet.

Chu Are there nutritional factors that are important to reduce risk, such as fruits and vegetables? The ACSNCI recommendation is to have at least 5 different servings of fruits, vegetables, high fiber and low fat.

Michael: There was that recommendation from the NCI to help reduce the risk of cancer in general. How potent the effect is on breast cancer specifically is still not very clear, but it is certainly advisable for reducing ones risk of any type of cancer, as well as general health in other areas.

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- Chu As we've talked about on this show before a healthy lifestyle can prevent the risk of cardiovascular disease and cerebrovascular disease, so they are good things for our listeners out there to pay attention to.
- Michael: That is right. Some recent research has also suggested that a very important period of life in terms of diet and exercise might actually be in the teenage years. It could have an impact on the risk of developing breast cancer later on in life.
- Miller: There is a large audience out there of women and families of women who have had breast cancer. When you see a new patient with breast cancer who, let us say, has had a lumpectomy and been found to have breast cancer, what are the factors that you look at in terms of her risk of recurrence? Then as a follow-up, what to do about that risk, how do you assess it?
- Michael: Historically our best predictors of determining someone's prognosis, meaning what are their odds of relapsing in the future even though they appear to be cancer free after their surgery, were based on how many lymph nodes in the armpit had contained cancer because that is the first place that the cancer spreads to generally. The second most important feature is the size of the tumor. These are very crude ways of looking at a cancer, determining how big it is and how many lymph nodes has it spread to, although, as more research is done we are getting a little bit smarter and it is more the biology of each individual tumor. We are just learning now how to look more at the biology than simply measuring the size, which is a very crude way to look at things.
- Chu Typically, once surgery has been performed, what are the general recommendations for follow-up therapy?
- Michael: Let me emphasize that the cure rate for breast cancer has been increasing, and has been increasing for two reasons. One is what we talked about earlier, which is early detection; the earlier that it is detected, the less likelihood that it will ever relapse, therefore, the higher the cure rate. The other reason why the cure rate is going up is more and more effective adjuvant therapies. Let me say a little bit about adjuvant therapy.  
Adjuvant therapy is the treatment that a woman might receive after the surgeon has completely removed the tumor and she appears to be cancer free. The concept is that there is always some chance that some cancer could be left behind in the body, some microscopic little bits of cancer from the tumor could have gotten into the blood stream and travelled throughout the body. They could be hiding in other places in the body even though they are completely undetectable at the time of the

diagnosis and the surgery. Because they are not causing symptoms, you cannot find them when you examine the patient and they are too small even to show up on our most sophisticated types of scans. So we take our best guess at judging what the odds are that there might be some cancer left behind, using things like I said, the lymph nodes status and the size of the tumor, and then we decide if we should give adjuvant treatment which is medical treatment after the surgery in an attempt to eradicate any of these tiny little microscopic pieces of the cancer that could be hiding anywhere else in the body to prevent a woman from ever relapsing for the rest of her life. That is critically important because if a relapse occurs in other parts of the body, that defines stage IV breast cancer. That is the definition of metastases. Metastasis is a tumor growing in some other part of the body because it spread from its original place. Almost always stage IV, or metastatic breast cancer, like many other cancers, is incurable. The best goal for cure is to prevent it with adjuvant treatments after the surgery.

Chu: One of the main concerns expressed by women with breast cancer facing the possibility of receiving adjuvant therapy, are the potential side effects associated with the treatments. Can you talk about that?

Michael: In the case of breast cancer, there are three potential types of medicines used for this adjuvant therapy to prevent relapses. For those women who have tumors that contain estrogen, we know that estrogen is very important for feeding the cancers, so therefore, the most effective therapy is the antiestrogen pills like tamoxifen or some other newer ones that postmenopausal women can take. For estrogen positive tumors, antiestrogens are the main stay of treatment. For those tumors that we talked about that are HER2 expressing tumors, the HER2 positive tumors, Herceptin is very effective at reducing the risk of breast cancer. For all other types of cancers and sometimes in addition to these treatments, we use what is considered conventional chemotherapy. It is the kind of chemotherapy that can be used to treat any other type of cancer. Chemotherapy is usually associated with more side effects than the antiestrogen treatments or Herceptin treatment, and many people who have experienced friends or family members going through cancer treatment with chemotherapy are familiar with some of these side effects such as hair loss, nausea and low blood counts, but we have other medicines that can effectively counter balance these side effects. For example, we have excellent anti-nausea medications so that is not an issue like it was 15 or 20 years ago. We have medications that can prevent the blood counts from getting too low. We have ways to counteract some of these side effects, but chemotherapy obviously is the more difficult treatment to go through compared to the others.

- Chu            You have raised a very important point Mike, and that is that over the last five to ten years, we have developed much greater supportive measures to be able to support our patients through their chemotherapy treatments.
- Michael:        Exactly, and this is what we call as you said, supportive care. Care in preventing the side effects of treatment and helping them get through treatment. Sometimes we need to adjust the dose of the chemotherapy, or sometimes we need to delay a treatment to give an extra week to recuperate from any possible side effects from the prior treatment before that. One of the true advances in treating cancer, which is not so obvious because it does not hit the front page of the newspaper, is how much better we have gotten at supportive care and helping people get through their chemotherapy treatments as gently as possible.
- Miller            When people picture someone receiving chemotherapy, they picture a person being very sick. I wanted to ask you, on a day to day basis, when women come in and are getting adjuvant therapy, preventive therapy, what is the feeling like in the clinic for them with the nurses, is it a somber event, what is that like?
- Michael:        Let me preface the answer by saying that there are different types of chemotherapy and even within one type of cancer such as breast cancer, there are different chemotherapy programs that we choose depending on the specifics of the individual case and different people may be susceptible to different side effects even when they are treated with the identical chemotherapy. However, for the most part, people are able to go on with their daily business and do everything that they normally do. Most of my patients who are getting adjuvant chemotherapy continue to work fulltime if they want to during all of their chemotherapy treatments. My favorite story that I like to tell my patients when they are just beginning is the woman that I had who was in her early 40s and was an athlete. She was on a very competitive volleyball team and throughout her entire course of chemotherapy she never missed a game.
- Chu:            Which is a great testimonial to people's resilience, to the supportive care and to a good doctor. When a patient comes to a center like Yale, or to another breast center, what does multidisciplinary care mean?
- Michael:        For many cancers we are realizing that the optimal way to treat it involves different types of specialists. At a minimum, for something like breast cancer, it would involve a surgeon and a medical oncologist such as myself who gives any adjuvant treatments and also becomes sort of the quarterback of the team. In many cases radiation treatments supplement the treatment. The most common reason for this in breast cancer is women

who do not have a mastectomy but are able to have a lumpectomy. They keep their breast and need radiation to the breast to ensure that the cancer that was in the breast will not come back. More and more we are working together in teams of different specialists, and this is what we refer to as multidisciplinary care for cancer. In addition, I have described how we give the adjuvant medical treatments after the surgery. We are now sometimes giving the adjuvant medical treatments before the surgery to shrink the tumor first before the surgeon goes to remove it to optimize the surgery. Obviously that requires very close coordination between the different doctors who are involved in the care; this is what we mean by the multidisciplinary approach to treating cancer.

Chu I might actually include two other members of that team who also play very critical roles, the radiologist and the pathologist.

Michael Right. These are the behind the scenes people. The radiologist reads the mammograms, the MRI or the ultrasounds and informs us exactly what the extent of the tumor is and which surgery we might need to do. The pathologist tells us what type of cancer it is and does all the tests on it finds out which receptors are present. Genetics doctors are sometimes involved when it seems to be a genetically inherited cancer. The results of the genetics tests sometimes come into the decision making as to what type of treatment the patient is going to have or going to choose.

Chu Also, here at the Yale Cancer Center, we pride ourselves in having social workers who also play a very active and integral role.

Michael: Social workers, chemotherapy nurses, nurse practitioners and research nurses are very important as well.

Chu It is really a big village.

Miller The Yale Cancer Survivorship Clinic is important in terms of followup care as well. Mike, I want to thank you for joining us on Yale Cancer Center Answers.

Michael It is my pleasure to be here.

Chu This has been a terrific session as always, and we look forward to having you on a future show to hear more about all the great things that are going on in the breast cancer world. Until next week, this is Dr. Ed Chu and Dr. Ken Miller from the Yale Cancer Center wishing you a safe and healthy week.

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