

Yale CANCER CENTER *answers*

WNPR Connecticut Public Radio



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The New Frontier of Genetic Counseling

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Yale Cancer Center Answers

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Welcome to Yale Cancer Center Answers with doctors Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC. This week, you will hear a conversation about genetic counseling with Danielle Bonadies. Danielle is Assistant Director of Cancer Genetic Counseling at Yale School of Medicine and here is Francine Foss.

Foss Danielle, could you start by telling us a little bit about yourself, about your background and how you came to Yale?

Bonadies I actually got interested in genetics many, many years ago back in a high school biology class and from there I pursued many of the sciences in my studies and in college I really spent most of my time focusing on not only biology, but I also got interested in psychology and so when I learned about the field of genetic counseling it really was a profession that blended both the science aspect as well as some of the patient contact and my background in psychology and so it really felt like a good fit for me.

Foss Can you talk about how one trains to be a genetic counselor?

Bonadies Genetic counselors all have master's degrees in genetic counseling or human genetics. So it is an advanced graduate training. It often includes many field rotations and learning about the many different aspects of genetic counseling which can include prenatal, pediatrics, adult as well as cancer genetics, which is the field that I have specialized in.

Foss Can you talk about exactly what genetic counseling is? Our audience has heard of genetic testing, and lots of stories about the human genome on our show, but the issue of genetic counseling is a little bit different than that. Can you talk about exactly what this field this?

Bonadies Genetic counseling can really be summarized as a communication process and in my case, in my field, it is about hereditary cancers. It is a communication process between a patient and his or her genetic counselor about the personal and family history and so there are multiple aspects to this. The first part of genetic counseling includes an individual getting ready for their appointment or may be even just considering genetic counseling and so often they talk with their primary care physician may be their gynecologist or other health care providers and one of the things that is really helpful in preparing for genetic counseling is researching a person's family history so if they can go back and interview family members, learn about the cancers that have been in their families, what types of cancers and at what ages those relatives were diagnosed that can really help the genetic counseling process be very smooth once they do have a meeting, but at their genetic counseling appointment it is their family history that mapped out and we try to get at least three to four generations of family history and that information will help their genetic counselor determine, which genetic tests might be best in that family.

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- Foss Can you identify which patients should be coming to a genetic counselor?
- Bonadies Sure, there are several risk factors that we consider when we try to determine who might be a candidate for genetic counseling. So an individual that has been diagnosed with cancer at an early age, for example breast cancer or colon cancer under the age of 50, or maybe a woman who has had more than one breast cancer, any person who has been diagnosed with ovarian cancer is a great candidate, individuals who have had rare cancers such as a man who has had breast cancer. There are also certain ethnic backgrounds such as individuals who have Jewish ancestry who have higher risks for certain and specific genetic syndromes and so all of those individuals are good candidates for genetic counseling and possible testing.
- Foss A woman out there, as you mentioned, under the age of 50 who has breast cancer should present to a genetic counselor for advice?
- Bonadies Yes, and even that risk factor alone without any other family history is enough to warrant genetic counseling.
- Foss Sometimes women say, you know I do not have any daughters, should I worry about this?
- Bonadies That is also an excellent question. The information that can be gleaned from genetic counseling and testing can be helpful for that individual as well, so it can help us learn what their cancers risks might be in the future. For example, for women diagnosed with breast cancer at 48, maybe they have chosen to have breast conserving therapy, maybe a lumpectomy, radiation, hormonal therapy, but if she learns that she carries a genetic predisposition to breast and ovarian cancer, we then know that she is at risk of a second breast cancer as well as ovarian cancer and so we can help tailor her medical management and either screen or possibly prevent those cancers in the future.
- Foss So there are two real interests here one interest is the patient, him or herself, and then the other interest is other family members that may carry those genes.
- Bonadies Certainly genetic counseling and testing provides information not only for the individual, but also their entire extended family, so not only their children, their siblings, and their parents but also aunts, uncles and cousins and so as part of that, when we meet with an individual for genetic counseling we really talk about the family as a whole because sometimes a person sitting in front of us is not the best person in the family for testing. Rather it is their mother who had an early onset breast cancer, so as part of their evaluation we also help determine who in the family might be the best to have testing first.
- Foss Two questions about the appointment with you, first of all how does the patient actually get referred to you? And then second of all, do patients actually need to bring copies of medical records from their family members?

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- Bonadies** They can get referred in multiple ways. They can get referred through one of their providers or they can self refer, the part that really hinges on that is what their insurance requires, so if their insurance requires a referral to a specialist, then they need to get that from one of their physicians. In terms of medical records, that can be extremely helpful to have for genetic counseling because it can change the type of testing that might be appropriate for that person or for their family, so a careful review, particularly of pathology reports not only to confirm the cancer is in the family, but also to determine what type of a breast cancer or what type of an ovarian cancer, can be extremely helpful as well.
- Foss** One of the obstacles that I hear in my practice about this is that women and men likewise are fearful of going to a genetic counselor because they are fearful that they might hear some news that they do not know what to do with. Can you address that issue?
- Bonadies** I think that is a common concern, what do I do with this information once I get it back? And I always try to talk with patients about how we are doing this process to provide them another piece of information so that they can make the best medical decision about their own care and so that also their family members can have that information to help guide their medical management and we do have many options available to individuals who find out that they have a hereditary cancer syndrome. We have screening options. We have medications to help reduce risk, and in some cases we also have surgical options, and it is all tailored to the individual based on their age, where they are in their life stage and their personal preferences, so it is really again a communication process about what the best choices might be for them.
- Foss** Can you talk a little bit about what exactly is tested? Is this a blood test or does one need to actually get the tumor cells and test the tumor cells?
- Bonadies** That is a great question because of course tumor testing is also a very hot topic right now to help tailor treatment, but our area is more of hereditary mutations. So these are mutations that have passed down in the generations and to do that testing we do take a blood sample or sometimes a saliva sample to look for very specific genes. We now have about 30 hereditary cancer syndromes and so choosing which test might be most appropriate for that patient or their family member is also a part of that process.
- Foss** When a patient comes in for testing, there is say one generic test that you do looking for all of these possibilities you are tailoring it for their individual history?
- Bonadies** Exactly, we take a very detailed personal and family history and that helps determine which test might be best for them and again, in which family member we should be doing that testing. So, it is not just a simple blood draw. It really is tailored to the history that is in the family.

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- Foss And again, just clarifying for the audience, these particular genes are genes that are in all of your body's cells. They are genes that you were born with and they are not genes that say mutated and caused a cancer specifically.
- Bonadies Yes, that is correct. So the genes that we are looking at present in all of the cells of our body and if someone has mutation, they were born with that mutation. They inherited it likely from one of their parents and it impacts their cancer risks. So these genes normally work to provide protection. They are very good genes for all of us to have and when we find a mutation within these genes it reduces the amount of protection that that individual has.
- Foss If there is a family say with three or four children, is it likely that they all inherited the same pattern of genes or is there a frequency among those three or four children for that gene to be found?
- Bonadies It really is dependent on which hereditary cancer syndrome we are talking about in terms of the exact risks, but in general, most of the hereditary cancer syndromes are inherited in what we call an autosomal dominant fashion, and so this means that if a parent carries a mutation each of their children has an independent 50% chance that they have also inherited that mutation or a 50% chance that they do not carry that mutation, and again it is independent for each child.
- Foss Are there instances where say both parents may carry a recessive gene that is not expressed and then when the two parents get together and produce children, there is a gene that appears that was not there in either parent?
- Bonadies There is one hereditary cancer syndrome that includes colon cancer and colon polyps that is inherited in a recessive pattern, as you said where both parents have to be carriers and that disease only gets expressed when a children inherits a mutation from mom and from dad, but that is only one of the many hereditary cancer syndromes that we know of.
- Foss When a patient then comes in and you do a very careful history, the next step is to get the blood sample. Do you do all that in your office at the time of the visit or is that done at a separate time?
- Bonadies We coordinate everything at our office, so genetic counseling, and genetic testing, and this is actually a really great and important question and timely because several major insurance companies have actually now mandated that genetic testing be ordered by a provider who has advanced training in genetics and so we are able to coordinate this entire process for them. We believe that these insurance companies have put these polices into place to help reduce some of the errors in ordering of those testing and also in the interpretation of those tests from providers who may not have advanced training in genetics.

Foss So the other providers that would be ordering those genetic tests would be other physicians?

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Bonadies Exactly, there is data now to show that even other providers, oncologists, gynecologists who ordered the test often either order the wrong test or maybe too much testing and then those results sometimes do not get interpreted in the proper manner and insurance companies have seen this as well and so they are now mandating that many patients have genetic counseling as well as the testing.

Foss We are going to have to take a quick break now for a medical minute. Please stay tuned to learn more about genetic testing with Danielle Bonadies.

*Medical
Minute*

Breast cancer is the most common cancer in women. In Connecticut alone approximately 3,000 women will be diagnosed with breast cancer this year. But there is new hope, earlier detection, noninvasive treatments, and novel therapies provide more options for patients to fight breast cancer. Women should schedule a baseline mammogram beginning at age 40 or earlier if they have risk factors associated with the disease. With screening, early detection, and a healthy lifestyle breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center to make innovative new treatments available to patients. A potential breakthrough in treating chemotherapy resistant breast cancer is now being studied at Yale combining BSI-101 a PARP inhibitor with the chemotherapy drug irinotecan. This has been a medical minute brought to as a public service by the Yale Cancer Center. More information is available at yalecancercenter.org. You are listening to the WNPR, Connecticut's Public Radio Station.

Foss Welcome back to Yale Cancer Center Answers. This is Dr. Francine Foss and I am joined tonight by my guest, Danielle Bonadies. We are here tonight talking about genetic counseling and genetic testing. Danielle, we talked a little bit about the process of genetic testing and the reasons why we do it in the first part of the show. I wondered if we could touch on some other topics this part of the show, namely some of the controversies that are going on in genetic testing and I will just mention a couple of them and I am sure you can give us details. One of them is the whole issue of genetic testing. In the news we have Angelina Jolie and her disclosure about her family cancer syndrome and the other is the Supreme Court decision on gene patents. Can you enlighten us about these?

Bonadies Cancer genetics has really been thrust into the national spotlight with some of the news coverage of these topics this year. It was in May 2013 that Angelina Jolie wrote a New York Times editorial where she disclosed that she had had a prophylactic bilateral mastectomy, or surgery to remove all of her breast tissue, and she did that because she carries a hereditary mutation in the BRCA1 gene and we know that individuals who have mutations in that gene are at increased risk

for not only breast, but also for ovarian and several other cancers, but those are the two main ones and her disclosure has really thrust cancer genetics into the spotlight. Our center as well as centers across the country saw an increase in volume by 400% in our calls and interest in genetic counseling, and this has started a discussion about prophylactic surgery, but also raised

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awareness about hereditary cancers, and then the second topic that you brought up was the Supreme Court. The Supreme Court did hear arguments about patents on two genes, BRCA1 and BRCA2, which as I just mentioned are related to hereditary breast and ovarian cancer and in June 2014, they ruled that patents on these genes were invalid. So the monopoly that one laboratory had had on these genes for many years was now over and other labs could begin offering this testing, and they did that in a matter of hours. Testing became much more widely available and the cost of that tests also plummeted by 50%. So this has really opened the door in terms of access to this testing. It is being done by other laboratories at much less cost and so many more patients are being able to have this testing.

Foss Are there other genes that will follow suit that companies had tried to patent?

Bonadies There are many, many patents on different hereditary cancer genes as well as many other genes, but these two were unique in that one laboratory had enforced their patents on these genes, which was really not done on other genes. Often, if a gene is patented, it is licensed to a variety of laboratories and so testing is available. So this was really a unique situation.

Foss So did Angelina Jolie's story prompt lots of women with breast cancer to come in and want to have testing for BRCA1 and BRCA2?

Bonadies It did, it really has raised awareness particularly about BRCA1 and BRCA2, and as I mentioned in our first segment, that is a very common test that we discuss with patients and also order, but there are many other tests, particularly for hereditary breast cancer, and so evaluating that person's history as well as their family to determine which tests would be best for them is also a part of the process.

Foss Can you tell us the frequency of expression of BRCA1 and BRCA2? Out of all women out there with breast cancer, what percentage of them actually has this gene?

Bonadies That is a really hard question to answer because much of it depends on the age that they were diagnosed, but in general we believe that about 10% of breast cancers are hereditary.

Foss For most women out there with breast cancer, if they come in, will you find anything specific in the majority of women?

Bonadies No, for the majority of women, we will get a negative test result, but that is not always reassuring. It has to be interpreted based on their family history. So for example, if we have a family where

there are multiple generations of individuals who had breast cancer or ovarian cancer, maybe some at early ages, and we get a negative test result, we are not reassured by that because we still have this striking family history that we need to pay attention to and so we interpret those test results in light of a family history and offer that individual options going forward in terms of their management.

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- Foss So the negative test result just means that looking at the genes that we know about, we have not found a mutation, but it does not mean that there are not ones that we do not know about yet.
- Bonadies Exactly, we can only offer testing of course for what we have available today, which I will say is pretty good. We have a lot to offer, but we just do not know everything yet.
- Foss What about the situation of ovarian cancer, another one that is associated with these genes, what frequency do you find these genes in ovarian cancer and what percentage of women with ovarian cancer have a genetic predisposition?
- Bonadies It is actually fairly similar, so in general, a woman who has ovarian cancer, about 10% of the time it will be hereditary, and again, that is going to be influenced by their family history and if there are other significant cancers in their family such as if that woman happens to be Jewish, then the risk will be higher than that.
- Foss You talked about ethnic groups being at higher risk and you mentioned Jewish Ancestry. Are there other ethnic groups that need to be concerned about family cancer syndromes?
- Bonadies When we talk about hereditary cancers it is actually the Ashkenazi Jewish population that we're focused on in terms of their cancer risks or particular mutations within the BRCA genes that are most important for us to look at.
- Foss Is there any data looking at specific populations such as African Americans where we know that there are disparities in healthcare access and also we know that for some diseases like prostate cancer the disease is worse in African American men than in Caucasian man. I am just wondering if there any disparities in gene expression that have been noted in specific populations?
- Bonadies There are some differences between ethnic groups. For example, there are specific mutations or types of mutations that can be more commonly found in certain ethnic groups and that has also taken into account in terms of the type of laboratory technology that we might offer that individual.
- Foss Thinking about the whole issue of genetic testing that we talked about, and some of the controversies with the Supreme Court, there are some other things going on with respect to direct consumer genetic testing and you mentioned 23andMe, which is kind of a catchy topic. Can you tell us what is 23andMe is and how does that impact on genetic testing?

Bonadies Sure, so direct to consumer genetics companies are companies that offer information about ancestry, physical traits and often some health conditions such as Alzheimer's, diabetes and breast cancer risk, and these are companies that offer individuals usually an online forum to provide the company with their health information to answer a questionnaire and then that company will send them a kit in the mail and they can do a cheek swab or a saliva sample and send it to that company

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and then they get some information back about their risks. However, the FDA has recently caught up with some of these companies because they have not been regulated and there has not been any quality control about some of the testing that they are doing and it has not been validated. So the FDA recently ordered one of the main companies, 23andMe, to stop sales of their products that contain health-related information and so that has now stopped.

Foss Does that mean that they can't do the genetic testing or just that they can't give information about the results?

Bonadies It means that they should not be providing individuals with those types of test results and so they are still able to offer their ancestry and that type of information to individuals, but not information about disease specific risks.

Foss Do we know how much these tests were costing consumers?

Bonadies The tests were being marketed at a fairly reasonable cost. Some of the companies charge approximately \$100, but these tests are not being interpreted. I have seen some of the tests myself. They are actually very confusing, for example, we have several patients who have been seen through our program and we know that they carry a BRCA mutation but when they have their tests through 23andMe because maybe they are interested in ancestry information, 23andMe tests very specific mutations within the BRCA genes but it does not pick up theirs and so they are confused why one test might be positive and one test might be negative and it is because that laboratory is using very different technology and so without going through those test results line by line and having a discussion with a genetics provider, those results can be very confusing and often misinterpreted by a patient.

Foss So these consumer tests could still be used to trace back your ancestry but not specifically to look at any medical conditions?

Bonadies That is the current state, yes.

Foss Are there any direct to consumer tests out there that you feel really can provide accurate medical information at this point in time?

Bonadies Not that I know of.

- Foss So you recommend then if a patient is interested in looking at these genes that they come to a genetic counselor?
- Bonadies Yes, because within each test there are various types of technology and again we need to make sure that that person is getting the appropriate genetic test. For example, if they go ahead and have

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- genetic testing through a direct to consumer company and all of their testing comes back negative, they may be falsely reassured that their risks are low, but it is because they have not had the right test based on their personal and family history, so I do suggest that they have a conversation with a genetics professional to really tease that out, make sure they had the appropriate test and that that test gets interpreted correctly.
- Foss Can you talk with us about some of the less common cancers that you do genetic testing on? We have talked about ovarian and breast, which are the big cancers. What about one of the rare cancers?
- Bonadies Some of the other common cancers that we do genetic testing for include colon, uterine, thyroid, melanoma, pancreas, and kidney so the list is quite extensive and what I would suggest is that if someone is potentially concerned that their cancer might be hereditary or want to investigate this more they should start a conversation with their health professional and they can also look at some resources online and then even just call a genetics department and have a conversation by phone for scheduling an appointment to see if they might be a good candidate or not. We can always do an initial evaluation over the phone.
- Foss Over the last five to ten years, is this list of cancers growing?
- Bonadies The cancers that we are able to do genetic testing for, yes, it certainly is growing and there is much more genetic testing available now than there was 10 years ago and so the patient's that are coming in today are really getting quite extensive genetic testing and we are able to revisit the patients that we have seen 10, 15 or 20 years ago and offer them updates to the initial testing that they have had. We try to keep in touch with those patients through newsletters, through our blog, we even have a Facebook page now, so lots of ways to keep in contact with patients.
- Foss Basically, what you are saying is that these tests are advancing over the last couple of years as there are new advances and new ways of doing these tests to pick-up additional mutations.
- Bonadies Exactly, the technology is always evolving. So the patient who had BRCA testing five years ago, today there are likely updates to that test that we could offer that individual.

Foss I do not think we ever touched on the turn around for these tests, the patient gets a blood sample or the saliva sample done, and when do they actually know the results?

Bonadies It really depends on the test that is most appropriate for them, but for most tests the results are available in between 3 and 4 weeks. And the longer turnaround time might be closer to 12 weeks, but again it depends on the test.

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Foss Then when they get the results back you have the discussion about how to intervene, so can you talk a little bit about some of the things that might happen as a result of say identifying BRCA1 or BRCA2 mutation, how does that impact the patient?

Bonadies And this is the conversation that we start with those individuals even before they decide whether they want to have testing or not, we talk a little bit about what those test results might mean and what their options would be if we do identify a mutation but their options get categorized into three categories of either increasing their surveillance, so for example for breast cancer we can offer them not only mammograms but also a yearly MRI. We can also start their screening at younger ages. In terms of options to reduce their risk we can also talk with them about medications that might be appropriate and for some individuals surgery might also be appropriate. So we begin that conversation and then refer them back to their providers to continue those discussions.

Danielle Bonadies is Assistant Director of Cancer Genetic Counseling at the Yale School of Medicines. If you have questions or comments, we invite you to visit yalecancercenter.org where you can also get the podcast and find written transcripts of past programs. You are listening to the WNPR Connecticut's Public Media Source for news and ideas.