



The Genetic Link

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Guests: Karina Brierley and Claire Healy,
Certified Genetic Counselors, Smilow Cancer
Genetics & Prevention Program

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Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about genetic links to cancer with certified genetic counselors Karina Brierley and Claire Healy. Dr. Chagpar is an Associate Professor of Surgery and the Assistant Director for Global Oncology at Yale Comprehensive Cancer Center.

Chagpar First of all, why don't you each tell me a little bit about your background and what exactly genetic counselor is?

Brierley I am the Chief Genetic Counselor for the Cancer Genetics and Prevention Program here, and I have been a genetic counselor working specifically in cancer genetics for over 15 years. For genetic counselors, there is a wide range, and we happen to work in cancer genetics, but there are genetic counselors that work in cardiac genetics, prenatal, pediatrics, so a lot of different things and genetic counselors like myself have a master's degree in genetic counseling.

Chagpar Terrific. Claire, tell me about yourself.

Healy I have been a genetic counselor for almost 10 years. I am the outreach coordinator for the program here. My goal is to help bring genetic counseling to the community, not just here in New Haven but to the care centers around the state to have increased access to genetic counselors, for people who may not want to travel and I see our role as genetic counselors to help patients navigate through the process of genetic testing, understanding the implications of genetic testing and really helping patients navigate through what can be a difficult and scary time.

Chagpar Karina, let us take a step back for a minute and talk about cancer genetics. What exactly is that? Are all cancers related to some sort of underlying genetic mutation? What exactly is cancer genetics?

Brierley When we talk to the patients, one of the things that people are often surprised to learn is that most cancers are not due to a genetic change, or at least an inherited genetic change, so most cancers are in fact just chance or sporadic occurrence, and it is only about, on average about 10% that are hereditary, and so what we are looking at is patterns in families or individual histories that might give us clues as to which might be hereditary and then offer options in terms of testing that might answer those questions for the patients.

Chagpar When you talk about looking at your family and so on, there are now a variety of tests, you turn on the TV and you see commercials that say, get your mother a Mother's Day present of

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this genetic test. Is that the same? Why do people need to come to you when they can order a test off the TV?

Healy That is a really great question. Those tests that you see advertised on TV are oftentimes geared towards ancestry testing, so helping you try to further confirm where your family came from prior to the United States and sometimes they do include some medical information as well, but it is oftentimes not as comprehensive as the genetic test that a provider can order, either a doctor or a genetic counselor. If you have a family history of heart disease or cancer in your family and you are really concerned about what your risk for that disease might be, that type of testing is really not going to give you as comprehensive an answer as a genetic test that a provider can order.

Chagpar Let's talk about the difference between genetic counseling and genetic testing. Ordering a test is one thing and you get back an answer, black, white, mutation, no mutation, yes, no, but why do people need to come and see you as genetic counselors, that seems to be a pretty easy answer, right?

Brierley I think for a lot of people, that is what they are expecting, that genetic testing is going to give you a black and white answer, but unfortunately, it is not; there is black, white and gray. There are genetic changes that we do not always know if they are just a normal variation or if they are something important. That is one reason. The other is that it also is in the context of your history. We have to look at the answer and say does that answer make sense in the context of your history? If we do not find anything, but your family history is still very concerning, that probably means we just missed something and we do not have the answer today. And so, for genetic counseling, it is helping people navigate what is the right test that is going to give us the best answers and also then putting it in context and interpreting it based on family history, talking about what choices make sense for a patient based on their test results and their family history taken together, and also who else in the family should be tested or who might be a better person to test in the family to answer the question as to whether it is hereditary or not. So, it is kind of putting all of that in context, and also these tests can be pretty emotional for people sometimes and so helping them make good decisions and helping them have the support to make the decision that is right for them as well.

Chagpar It sounds like genetic counseling is really the key to all of this, right? Am I ordering the right test, am I interpreting it right, who else needs to be tested and so on and so forth. But all of that starts with people being referred to you. Now, both of you talked about if you have a family history, what exactly does that mean? Like, if my paternal great, great, great grandfather had prostate cancer when he was 87, does that count?

Healy Usually when you are thinking about a family history and you are thinking about meeting with a genetic counselor, thinking about doing genetic testing, you are really thinking more of

either a family history as something that is occurring at an unusually young age, like breast cancer before 50 or multiple people who have all had the same type of condition in a family, like multiple people who died from heart attacks at early ages or in the context of hereditary cancer, multiple people who have all had the same type of cancer. With your example I would say, no a great, great grandfather with prostate cancer at a later age is probably not something that would qualify you for really needing to meet with a genetic counselor or really needing any genetic testing.

Chagpar What if you are adopted, what if you do not know your family history and you are diagnosed with cancer? Should you be seeing a genetic counselor?

Brierley Sometimes just personal history alone is enough, so we see patients that are adopted that have, as Claire mentioned, cancer at a particularly young age, and since we often think of cancer as a disease of the ageing process, if we see people with an early age of diagnosis, for most adult-onset cancers that means under 50, so if they have had breast cancer or colon cancer under 50 and then we have that they are adopted so that they have limited information about their family history, sometimes that is enough, or a cancer that is rare or a tumor that is rare enough that is oftentimes caused by a genetic mutation, so there are certain rare tumors, so those kinds of things alone can qualify someone for testing.

Chagpar And you mentioned Claire, about cancers of the similar type. One of the most common examples of hereditary cancers that I think everybody has heard about in the news is BRCA and everybody has heard Angelina Jolie's story. But in her case, for example, her aunt had ovarian cancer, but somebody else in her family had breast cancer and so those are not in the same organ, they are not the same cancer.

Healey That is a very good point. It is not just multiple people who have had the same type of cancer, but if there are related cancers in the family. So, if you have the combination of breast or ovarian cancer, that can be a red flag, the combination of colon and uterine cancer in the same family or breast and pancreatic cancer can be a red flag as well. And so, it is really not necessarily up to the patient to know all of that but to make sure that they are giving their provider at their annual physical as comprehensive information about their family history as possible, so that their provider can help them decide whether or not it is appropriate to see a genetic counselor.

Chagpar Okay, that makes sense. So, let us suppose they go to their primary care provider and the primary care provider says, "hmm, well, I'm not really sure here, but it might be something that is genetic as an underlying issue." Remember most cancers as you said, Karina, are sporadic. They are bum bad luck, it is just the luck of the draw, and then they come and see you. What exactly happens at genetic counseling, what does that entail?

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- Brierley Ours usually starts on the phone with our intake people that schedule the appointment and they take a little bit of information about the reason why someone is concerned or being seen in terms of their family history. We also, at our center and many centers now, use on-line tools, so we send people a link to a family history questionnaire where they answer some questions about their personal medical history and family history. If they do not have e-mail or they do not get a chance to fill that out ahead of time, the start of the visit will be taking that information about their own personal medical history, their family history, we just sketch out everyone in the family – how many brothers and sisters, aunts and uncles who have had cancer at what ages, and then we talk more about some of those risk factors that we have been talking about. These are the things we see in your family, these are the things that we do not see in your family. Based on that information, we think that you do meet criteria to consider genetic testing or we do think there is a reasonable chance that there is something hereditary, and based on that, here are some of the testing options, here is what it might tell you and help people make decisions about what they would like to do. Whether they want to do testing, how extensive the testing they want to do, what they might decide if we found something.
- Chagpar How much does that visit with the genetic counselors cost? Is it covered by insurance? I can imagine that patients are kind of thinking about do they want to do this or not knowing that most cancers are sporadic but the information that you provide is really valuable, but they do not want a huge bill because their other doctors have already sent them huge bills. Help us to understand that. Is this something that their insurance is going to cover?
- Healy Most insurance companies will cover the cost of genetic counseling, and if you are concerned about that, we can often put you in touch with our billing department that can help sort out whether or not your insurance does have coverage for genetic counseling, and for the most part, most patients do not pay more than a co-pay for the cost of the visit.
- Chagpar Perfect. And after you have sat down with the patient and you have gone through all of these options, and let us say, you see some pattern, you have drawn out this huge pedigree, that concerns you. Are you thinking about certain particular mutations that you want to test for or is it that there are a panel of tests that you want to do all at the same time? How do you decide on what test to order?
- Brierley As a practice, we have panel-based testing now which did not use to be an option, and that really came along in the last few years, and oftentimes what we will talk about depends on the family history, so sometimes it looks really specific for a very specific thing and sometimes it really does not, so now beyond the example of BRCA-1 and 2, those are the most common genes for hereditary breast and ovarian cancer, but they are not the only genes, they account for the biggest percentage, but we now know that there are some other more modest-risk

genes or moderate-risk genes that account for some other cases. So, oftentimes what we offer patients is panel-based testing or the choice of more targeted testing versus panel-based testing and help them decide.

Chagpar Excellent information. We are going to take a short break for a medical minute, and then after the break, we will learn more about genetic testing and what to expect.

Medical Minute

Support comes from AstraZeneca, providing important treatment options for patients with different types of lung, bladder, ovarian, breast and blood cancers. More information at astrazeneca-us.com.

This is a medical minute about breast cancer, the most common cancer in women. In Connecticut alone, approximately 3000 women will be diagnosed with breast cancer this year, but thanks to earlier detection, noninvasive treatments and novel therapies, there are more options for patients to fight breast cancer than ever before. Women should schedule a baseline mammogram beginning at age 40 or earlier if they have risk factors associated with breast cancer. Digital breast tomosynthesis or 3D mammography is transforming breast screening by significantly reducing unnecessary procedures while picking up more cancers and eliminating some of the fear and anxiety many women experience. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.

Chagpar This is Dr. Anees Chagpar and I am joined tonight by my guests, Karina Brierley and Claire Healy. We started talking before the break about who should get genetic counseling and what exactly that visit entails, and we got to the point of figuring out whether you should get a test for a single mutation or a set of mutations, which is a test that tests for multiple mutations using a single sample. Now, one question I have for you Claire is, are these all blood based or do people give you a saliva sample or what kind of test is it exactly?

Healy Most of the time, it is blood. But you can get DNA from multiple different sources. Sometimes, we do use saliva, but I think a lot of people imagine that is a cheek swab like you see on CSI, when in reality, it is a spit sample, so it is actually about a teaspoon of saliva that we collect. I always tell my patients that it takes about 5 minutes so do not get discouraged when it does not fill up right away and multiple people have said to me I would rather do blood. And sometimes, we can also get DNA from skin if it is necessary, but usually it is blood or saliva based.

Chagpar So you take this blood sample and you send it off for this test. How long does it take to get the results back, Karina?

Brierley It depends on the test. Most of the tests that we do, most of those panel-based tests, usually take a few weeks to get the test results back. If it is urgent for treatment decision making, we

can often expedite testing, so some of our patients that are newly diagnosed with breast cancer for example need that information quickly and oftentimes the lab can get that back to us in about a week or so. But mostly, people should expect a few weeks turnaround.

Chagpar Claire, you told us before the break that most insurance companies cover genetic counseling and that most patients only pay a co-pay. What about the test itself?

Healy Your genetic counselor is going to be your best help in navigating the insurance process in terms of coverage for genetic testing, and it is not easy to say that patients will have coverage for genetic testing as it is for genetic counseling, so we do have to take into account whether or not the patient meets national guidelines for genetic testing, whether they meet their insurance company's criteria, what labs are in network versus out of network and the genetic counselors are available to help the patients navigate that process. So, we will try and match up as much as possible to make sure that the patient has coverage, and then if they do not, we will talk to them about out-of-pocket payment options, which have luckily significantly reduced in price over the last several years.

Chagpar I can remember a time when the cost of genetic testing was in the 1000s of dollars, which might give patients a little bit of the heebie jeebies when thinking about whether or not to go through this. So, when you say that prices have dropped, how significantly have they dropped, is this actually something that a real human can afford?

Healy The price has dropped from 1000s of dollars out of pocket to usually a couple hundred dollars out of pocket. The laboratories that we use oftentimes have financial assistance programs for patients and we can help navigate the process of applying for coverage through those as well if necessary.

Chagpar So, talk to your genetic counselor? Alright, so the patient has seen you, has gotten their pedigree, you have decided on a panel of tests, you have taken this blood sample, you have sent it off, they did not get a huge bill, they are very grateful, 2-3 weeks later - the tests comes back, what are the possibilities of what that tests could be, Karina, and what happens then?

Brierley Again, that is kind of where the genetic counselor comes in and our team comes in. We review everything as a team and then we talk to the patients about their results, either on the phone or in person or both and basically there are typically 3 different test results we can find. They scan through all the genes that they are looking at and it is completely normal, negative results. They scan through the genes and they find a mutation that they know is associated with risk, and the third is the variant of uncertain significance which is that kind of gray area test result where it is a genetic change that the lab cannot completely interpret at this point; it could be that it is just the normal variation, which most of those end up being normal variation, but it could be something important.

- Chagpar Let's talk about each of those 3 scenarios. First scenario, you have this family history that was concerning, you go and you get your test, test comes back negative. What does that mean? Does that mean I am free and clear, hallelujah! This was just sporadic, I can celebrate, no mutation, I am baseline risk.
- Brierley No. So, even if we do genetic testing, we look at a panel of genes that we think covers the majority of risk that could be explaining the family history and everything is negative, really what that means is perhaps there is a genetic risk in the family that the patient has not inherited which would be good news or perhaps we do not know what gene is explaining the family history at this point in time because we still do not know what number of genes in the body are responsible for it, and so in that case, we might recommend genetic testing to other people in the family to try and help clarify that situation and we might still recommend increased screening or even sometimes prevention to those families even when they are negative.
- Chagpar So, a family history still counts even if you are negative for a panel of genes, but it is nice to be negative better than being positive, so let us suppose you are positive, Karina, let us suppose you test for a genetic mutation and lo and behold you have that genetic mutation, okay so now you have this information, what does that mean and how do you process that?
- Brierley It is going to depend on what gene it is in and the rest of your family history and your own history, so again we are advocating here for genetic counseling, that is kind of where that comes in and talk about okay now that we have this mutation, what are the risks that are associated, how high are they? Which cancers are we concerned about? How high are the risks, and does that mean that we just have to add some additional screening and start younger than we would in the general population or is the risk high enough that we might consider prevention through taking a medication or even a preventative surgery, so we talk about all of that. We talk about what it means for the family as well. Who else in the family might be at risk and might need testing, so we go over all of those things, and sometimes, for young patients especially, they may not do everything that would be mapped out as options immediately, it might be taking things one step at a time and what makes sense for this in 5 years and the next 5 years. And our knowledge is going to evolve over time for some of these genes that are newer as well. So, it is oftentimes just looking at everything again in a context of personal preferences, family history, how high the risks are, all of those things together.
- Chagpar So, if you have a genetic mutation, the first thing is, you can get some advice on preventing cancers, it means you are at higher risk, but maybe you can do something about that. It also puts your family at increased risk, right? So, what is the process then? I mean, do you have to tell your family about this mutation that you have because they also may be at risk or can you keep that a secret, what are the rules, Claire?

Healy There is no hard and fast rule, but we would really prefer you not keep that information a secret. Your family members, your first-degree relatives, second-degree relatives, third-degree relatives, even farther back if you are in contact with them should really be notified of that information because they are all at risk to have the same mutation. We share genes in common with our family members which is what makes us related and so those relatives should have the chance to know that information so they can make informed decisions about whether they want testing to determine whether they need increased screening or prevention as well.

Chagpar And so, the other aspect to all of this, I would assume is, when you are sitting down Karina, you are talking to these patients and you are going through okay, you have this mutation and these are recommendations either for increased screening or for prophylactic surgery or whatever, I can imagine that that is an unbelievably emotional discussion, and how do you counsel patients just in terms of that whole concept of oh my god, am I going to give an increased risk to my children, you know, I caused my cancer, all of that emotional baggage that comes with this.

Brierley That is part of our training and part of our job, and oftentimes when I talk to patients I try to normalize it, but really from our training in genetics, we know like all of us carry certain mutations, we all have a handful of mutations, I think people are aware of that so people do not really think about it that way. I try to tell people all of us have these mutations, we all have a handful, we did not control either we inherited them or passed them down, but in this case at least we know, and now we know that mutation would have been doing whatever it was doing anyway, but at least we know and we can take action and hopefully prevent and sometimes people actually find it reassuring to know and be able to take action and be able to be proactive and really have an explanation for why they got cancer, it gives them some control sometimes, so there is kind of a mix of emotions and it is hard to predict for one person what is going to feel like or what things are going to be concerned about, but I think we are just there to kind of listen and support and help use that information in positive ways.

Chagpar I think knowledge is power for many patients, and so, as you say, you would have had this mutation whether we would have told you about it or not, but now that you know, potentially there are things you can do about it. Claire, the other issue is, if you know about this genetic mutation and you know that that genetic mutation does XYZ, it increases your risk for various malignancies or whatever, what are the implications that that has in terms of getting life insurance, keeping a job, etc., etc., I think patients might be really fearful about getting genetic testing because gosh if those results are in your medical record and you are asked about it on a form, could you be denied coverage later?

Healy That is probably one of the most common questions we get asked as genetic counselors. So, there are two separate types of insurance to think about, there is health insurance and then there is life insurance, disability insurance, long-term care insurance, and in terms of

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health insurance and even employment to your point, there are laws that prohibit the results of your genetic testing being used against you as a preexisting condition. So, your health insurance company, your employer cannot use that information to charge you a higher premium, deny you coverage, and those laws have been in place for a long time now. In terms of the life insurance, disability insurance, long-term care insurance, there unfortunately are not laws that prohibit those companies from using this information as a preexisting condition, so as part of my counseling process, I talk to the patients about that ahead of time before they go forward with testing and a lot of times for our young patients who have not had a cancer diagnosis, we might say it sounds like you are really interested in testing, hear the concerns about those types of insurances, would you prefer to wait and get those policies in place before you have testing because once you have a policy in place, they cannot use that information retroactively.

Chagpar As follow-up to that, could somebody for example get one of these off the TV tests that you give some medical information, although you mentioned that it was not as robust and not as good as official genetic testing, I mean certainly we cannot use 23andMe, for example, and that is just one company, for medical decision making, we require an actual test from a bonafide company to make any kind of medical decisions. Could they get that, keep the results to themselves as a secret, then if it tests are positive, go get really good insurance and then come to you?

Healy The life insurance companies are getting savvy and they are asking patients on those 100-page questionnaires you have to fill out when you purchase life insurance if you have had genetic testing and if so, what the results were, and so you are obligated to answer that honestly. You have had 23andMe testing, I do not know that I will classify that as sort of the gold standard of genetic testing, but I think there are some concerns about how that information could be used against you by those companies.

Claire Healy and Karina Brierley are Certified Genetic Counselors. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. I am Bruce Barber reminding you to tune in each week to learn more about the fight against cancer here on Connecticut Public Radio.