

Welcome to Yale Cancer Center Answers with Dr. Ed Chu and Dr. Ken Miller, I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and he is an internationally recognized expert on colorectal cancer. Dr. Miller is the Director of the Connecticut Challenge Survivorship Program and he is also the author of "Choices in Breast Cancer Treatment." If you would like to join the discussion you can contact the doctors directly at canceranswers@yale.edu or 1-888-234-4YCC. This evening Ken welcomes Ellen Matloff, the Director of Cancer Genetic Counseling at Yale Cancer Center.

Miller Let us start out with a very basic question, what is genetic counseling?

Matloff Genetic counseling is really a communication process, we take a detailed family tree, which we call a pedigree, and we try to figure out if the disease or cancer is running through the family.

Miller Historically, when did this field come into being?

Matloff That is a good question. I believe that genetic counseling first came on the scene in about 1970 as its own independent field. If you think about it, it's interesting because that is really before we had genetic testing.

Miller Can you say a little bit more about what created the interest and what the field was like before all the testing started?

Matloff People knew that something was running in their family, and they would come in and a pedigree would be drawn, and just by looking at the pedigree they would make a risk assessment saying it looks like this is running in your family, or your chance of carrying this genetic change or mutation is about 50% or 25% based on the family tree, and here is what we think you should do about it. None of it was based on genetic testing data for that individual, it was all based on guesstimates and family history, so things have really changed.

Miller I want to ask you for your prediction, we are going to talk in a couple of minutes about the tests that are available and the genes that have been identified, but if we were to look ahead 50 years, do you think we have identified half of what is out there, or two-thirds, or ten percent, do you have any guesses?

Matloff I would say that we have only just stuck our toe in the water, and that probably in the next 50 years we are going to dive in. This is because of a couple of reasons, the technology, even in the last 10 years, has improved so vastly and it is difficult to predict what will be

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available 10 years for now, and we are also finding so many different ways to use the information. You well know from your field that we may find that genetic testing is really the underlying key to things. We might be able to say, okay this is a patient with breast cancer, would she do best on this chemotherapy or on this chemotherapy, would she be a good candidate for tamoxifen, or based on her genetic mutations would she not respond to tamoxifen? We are going to find that genetic testing and interpreting that data really helps us to make good decisions. We may be even able to say, well this patient is at increased risk for blood clots, so let us not put her on tamoxifen, let us put her on this drug, and that is really going to affect her treatment decisions.

Miller That says that it is more than just looking at risk and why cancer happens, but also the treatment options.

Matloff You have got it.

Miller Which opens up a whole new world of possibilities.

Matloff It is really huge, and some of the testing that is now available, and I think the listeners should be aware that, some of it is a little shady in my opinion. Now on the internet, through a couple of websites, you can have genetic testing for a variety of different genetic mutations and variances, and something called SNPs. People get reports back that, believe it or not, are sometimes 75 pages long and include silly things like can you taste Brussel sprouts, or do they taste bitter to you? So all of you out there whose mothers made you eat Brussel sprouts and told you that they tasted good, some of you may have a mutation that actually made them taste bitter. Interesting, I made sure to tell my mother of that. But there are also things like are you at increased risk for heart disease, are you at increased risk for certain genetic diseases, and I have to say that some of these tests have reached the market place before we really understand the utility of the testing or how accurate it is. Genetic counseling is going to take on a whole new meaning, people are going to be flooded with all this and we are not going to know how to interpret them. I would dare say that even their physicians will have no idea how to interpret the data.

Miller Let us go back to a topic we have discussed here on the show before, which is physician involvement. In community practice and elsewhere, at one's doctor's office, they are able to just order a test for the breast cancer gene, the BRCA gene. What is so bad about that? What is your opinion?

Matloff Well, my opinion of course is biased, because I work in this field, but what I see happening is that the company that has a patent on the testing therefore wants to makes a lot of money

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from this testing and is pushing, pushing, pushing all of these physicians and nurses, and believe it or not, even some office managers are ordering this testing thinking that they are doing their patients a service, but what we are finding, and what national studies are finding, is that they are misinterpreting the test results and giving patients the wrong information. This not only bleeds out to that patient, but their family members, their grandchildren, it affects generations of people. The liability for that falls directly onto the physician and what they do not realize is that for every test they order, their sales rep gets a commission. There is really a conflict of interest here, and I would say for a test that costs \$3000 that has this kind of clinical importance not only for the patient but also for family members, you better make sure that the right test is ordered and that it is interpreted correctly.

- Miller I'll throw in my own two cents here, but it is almost the same as people who would send themselves for a screening CAT scan. I have seen a number of patients who had findings that were of cysts in the liver or the kidneys, and these were things that were not cancer, but created tremendous amounts of anxiety.
- Matloff Absolutely, and one thing we have also seen is that BRCA1 and 2 are only two of the genes involved with hereditary breast cancer. We know of many others, and believe me, there are many to come, so people order that test and think they ordered the right test for the patient, it is not hereditary, and then I see the pedigree with wide eyes and think, oh my gosh they completely missed the syndrome here, they ordered the wrong test.
- Miller I think our audience has probably been reading about genetic testing. What diseases, what cancers, do you hear in someone's history where you say, Gee, there could be a genetic link here?
- Matloff There are many. When it comes to breast cancer, in addition to BRCA1 and 2, there is a gene called P10, which can include risk for breast cancer and thyroid cancer and several skin findings. There are genes that include not only breast cancer but a variety of malignancies; sarcoma, leukemias, and lymphomas. Some of these are quite rare, but we certainly do see them in our clinic. There are other genes that include not only breast cancer but unusual colon polyps and GI findings, and then of course there are completely separate genes that include ovarian cancer, but colon and uterine cancer, those are a whole different range of genes. There are dozens and dozens of genes that we know about so far and certainly many more that we are exploring.
- Miller Let me give you a scenario; a woman who has got a strong family history of breast cancer

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is tested and does have one of the BRCA genes that you told us about, what can a woman do with that information?

Matloff If someone learns that they carry a mutation in BRCA1 or 2, we actually can do a lot for them. First of all, their surveillance would not begin at age 40 as it would for the average woman; it would begin at age 25, or 10 years before the first breast cancer in her family. It would include not only a mammogram, as the average woman would be offered, but also breast MRI, which has its pros and cons so we would not want to offer this to every single woman. It is so highly sensitive that at least 10% of woman who have an MRI have a finding that often requires biopsy, but for our population of high risk patients this is more sensitive. We can also offer this population medication like tamoxifen or Evista, which they can take before they ever get breast cancer to reduce the risk of getting it in the future. Some women choose to have their breast removed preventively, which I am sure sounds like a very drastic option, but if you could see some of the histories in these families, for some of these women it is the best choice for them personally. This also has an impact on the risk for ovarian cancer, something that some families are not even looking for. So again, we can offer them surveillance, although I should mention that the surveillance options today are limited and we are working on new surveillance options. We can also talk about birth control pills, which reduce the risk of developing ovarian cancer, as well as removing ovaries and fallopian tubes at some point in time, usually by age 40, to reduce their risk of ever developing ovarian cancer.

Miller Sitting here and listening, and for the audience too, we are talking about some women having bilateral mastectomy and potentially having their ovaries removed, some say, my goodness that sounds awfully drastic, but for women who choose that, you are working directly with them. What is your thinking, and what is that process like for them? How do they feel afterwards?

Matloff First of all, let me acknowledge that it is drastic; there is no doubt about that. I have a patient right now who is in her mid 30s and who is having this procedure this week and believe me it's a tough, tough thing to get through. However, she found out about a year ago that she carries a BRCA1 mutation, and in that period of time she has had both mammograms and MRIs that have shown little spots and we did a biopsy. Then we had to wait for the pathology, and now it is a week later, or 10 days later and you are not sleeping at night and her husband is not sleeping. This kind of anxiety over a lifetime, particularly for people who have already survived a cancer or who have watched close family members or friends die of cancer, is very difficult to live with, and what happened with this particular woman is that they found a spot that they believed was cancerous and when they

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investigated it more closely with ultrasound, they found that it was not cancerous, but behind it was a spot that was cancerous that they came close to missing. She has a small cancer that hopefully has not spread anywhere else, but for her, she just came to the point where she knew her risks were high, and it wasn't worth it.

Miller I have to say my own experience has been the same. As you know, probably each year, I have one or two women choose bilateral mastectomy, and I think it's pretty essentially, each one has said they are glad they did it. What is your observation over a long period of time?

Matloff My observation is that when the women are the ones driving the decision, when it is their decision made with the support of a spouse, a parent, a sibling, or a friend or a family member, and they have had genetic counseling, had the testing, and they made an informed decision over time and they owned the decision, they feel good about the outcome. For people who are coerced into having the surgery before they are ready, they often feel that maybe it was not a decision they would have made. I cannot say enough about informed consent.

Miller Which is something that we value in other parts of medicine, and it sounds like it is also very important in this process as well.

Matloff Absolutely.

Miller We are going to take a short break for a medical minute and then we are going to come back and talk some more about cancer genetic counseling with Ellen Matloff from Yale Cancer Center.

Medical Minute

Here in Connecticut the American Cancer Society estimates that almost 1000 people will be diagnosed with colorectal cancer every month. The good news is that when you are detected early, colorectal cancer is easily treated and highly curable, that means that if you are over the age of 50 you should have regular colonoscopies to screen for this disease. In the case of patients that develop colorectal cancer, there are more options than ever before, thanks to increased access to advanced therapies and specialized care. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for colorectal cancer. Patients enrolled in these trials are given access to medicines not yet approved by the Food and Drug Administration. This has been a medical minute and you will find more information at

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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 joined by Ellen Matloff who is an expert in cancer genetics and genetic counseling at Yale Cancer Center.

Miller Ellen, we talked a little bit about the BRCA gene in breast cancer, but you have been telling us that there are other diseases linked to our genes as well. Can you give an example say of a family where a colon cancer is related to a genetic risk?

Matloff Absolutely. There are many different types of hereditary colon cancer, but I will give you an example of two of the more common types. For example, within the last year I saw a teenage boy who had been having some blood in his stool, and thank goodness, he told his mom about it and got checked out. He learned that he had literally hundreds of polyps in his colon. The unfortunate thing about this story is that his dad had died of a colon cancer in his early 40s, and when I went back and read his medical records he too had hundreds of colon polyps. Also of interest, this young man's sister, during a routine eye exam, had been noted to have a finding called CHRPE, or congenital hypertrophy of the retinal pigmented epithelium, which kind of looks like bear tracks on the retina. Although it did not affect her vision, when we see that very unusual finding it gives us a heads up that there may be this syndrome, which is familial polyposis, or FAP in the family. So that is one syndrome, its rare, its caused by a mutation in a gene called the APC gene and we see hundreds or thousands of colon polyps in members of the family at very young ages, teens and 20s, and most of these people, if left untreated, will develop a colon cancer by the age of 40.

Miller What can you do about it?

Matloff It is a tough syndrome because when someone presents with this many colon polyps, at this stage, the colon is carpeted with polyps, meaning there are so many polyps that you can't even see when you do a colonoscopy; they cannot all be removed. So, in this particular circumstance, we had to remove this young man's colon. Now, that is the bad news, that we had to remove his colon, the good news is that he didn't have a colon cancer yet so he can hopefully avoid the fate of his dad dying of a colon cancer in his early 40s. If we know sooner, as we will with his sister who is younger than he is, we can begin colonoscopies right away and hopefully remove colon polyps before they become carpeted. Sometimes we can keep up with that for a little bit longer before having to remove the colon.

Miller Let me ask you about melanoma, which is a big interest here at Yale Cancer Center. What

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family history related to that would raise your eyebrows and say there is something going on?

Matloff With melanoma it is when we see people diagnosed with a melanoma at a young age, which we would consider before the age of 50, particularly if they have multiple primary melanomas. Sometimes we see people who say, "I have had two separate melanomas, or three or four." That is certainly a red flag. Also, when there are other family members who have had melanoma in several generations, and particularly when we see melanoma and a cancer of the pancreas in the same family, it makes us wonder about an underlying genetic predisposition

Miller In that scenario, when someone does have a genetic predisposition, what is the strategy for them, how do they use the information?

Matloff That is interesting. When we see someone with melanoma in the family, of course there are certain things we advise everyone; avoid blistering sunburns, wear sunscreen at all times, and to take advantage of some of the clothing lines out there, which I am sure you know about, that actually act as a barrier to the sun. Some people think that if they are wearing a hat or a T-shirt that is a barrier to the sun, but its not, and there are special lines of clothing that completely block sun exposure. If we know that someone is at high risk to develop a melanoma, clearly we would take these extra-added steps to reduce their exposure. We would also want them to be seen by a dermatologist at least twice a year for a full-body check. When we say a full-body check, it is a full-body check, this means looking at the skin under your hair, looking between your toes; it's a really detailed exam, and that would be the first step.

Miller I will ask you more about this process because you are in a sense working with the patient before you find something, when you do find something, and after. What is the process like? How long does the patient spend with you? What are some of the questions that they ask?

Matloff It really depends on the patient and on the case, but when someone learns they carry a mutation, one of the things I say to the patient is that this is not the end of our relationship, its the beginning, I am going to follow them from here on out and tell them as clinical trials open up that they are candidates for, or as we have new information. Which I have to tell you, we change our recommendations certainly on a yearly basis because the information is evolving so quickly. We re-contact these patients, they are part of our mailing list, they get e-mails and newsletters with updates, and in some of the families where we have not identified a gene, we follow them particularly closely, because new genes come out, we

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need to contact them and say there is a new study, we are looking for new genes, do you want to be a part of it?

Miller An interesting thought is that even if we may not be able to do anything about it now in terms of prevention, perhaps there will be some new strategies.

Matloff You better believe it, that is what we are counting on. For example, some topical medications are being investigated for certain types of hereditary cancers, that if you have a very early onset skin finding, perhaps a cream could be put on that finding and it could reduce the risks that it ever develops into a basal cell carcinoma or other types of skin findings.

Miller Let me pose you another scenario, which I bet happens sometimes. Say there is a family with a known abnormality, let us say in BRCA or APC that you were telling us about, but one of the family member says I do not want to be tested, how do you counsel them?

Matloff Going back to the family I was discussing with the APC mutation, this was the answer I got from the 15-year-old daughter. She did not want any part of it, and was not interested in a colonoscopy. I mean, can you blame a 15-year-old for saying that? So we did some negotiating, and the kind of negotiating we did was talk to her and say, "Listen, this is not fun, I get it, but getting colon cancer is even less fun than this and if we do this genetic testing and you do not carry the mutation in the family, you wont have to get this intervention, if you do, you are going to need this intervention." One of the things we do is try to look at this scenario and say, "Listen, this stinks, I wish you did not have to go for whatever this procedure is, but it is so much better than a diagnosis of cancer."

Miller Did she understand it as a 15-year-old?

Matloff Yes, she still was not too hot on it, but we were able to negotiate a deal and you know she did it; she is a reasonable person.

Miller Hearing all aspects of your work, there is some science, there is some counseling, and there is psychology, typically, what is the background and the training for a genetic counselor?

Matloff Most genetic counselors have a strong background in science, most of us have pre-med or biology type majors in undergrad and many of us also have a background in psychology. Then our graduate education is exactly the same, so very strong in genetics but also strong in psychology and even in sociology because you are dealing with families here.

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Communication is a really critical part of genetic counseling and something that we are all still working on as we continue our work in the field.

Miller Some practical issues; does health insurance cover genetic testing?

Matloff I am happy to say that yes, most of the time it does cover genetic counseling and testing for patients who need it. And this is only getting better as time goes on, which I am really happy to report.

Miller Another practical question, if someone is tested and found to have an abnormality, what impact does that have in terms of life insurance, health insurance?

Matloff Genetic discrimination is the phenomenon you are describing, and we do know that, particularly for people who want to get life insurance or disability insurance, everything counts and some people do not know this about life insurance. Let us say that you have really high cholesterol and you are trying to get life insurance, your medical records are reviewed and that counts. Let us say that they find out you are a heavy smoker, that counts, if you are obese, that counts, if you have genetic testing, unfortunately that counts as well. One thing I ask people to do is if they want to get life insurance they should consider this before we do genetic testing. If they have already had a diagnosis of cancer, which many of our patients have had, then probably that is the biggest black mark on their record and genetic testing will probably not increase the risk much more than a past diagnosis of cancer.

Miller Thank you because that is really important information. Let me ask you, do people need a referral from a primary care doctor to come for genetic testing?

Matloff It depends on their insurance. We would certainly take them without a referral, they are self-referred, but sometimes their insurance requires a referral.

Miller I know you spend a lot of your time with patients and with their families, but let me also ask you about some of the research initiatives that you are involved with in your group.

Matloff We are doing several things. One of the areas we are interested in has to do with sexuality in cancer survivors, particularly BRCA1 and 2 carriers, and people with a hereditary colon cancer syndrome called HNPCC. These women often remove their breasts or their ovaries in order to reduce their risks of getting cancer. We now know that it is very effective in reducing their risk of getting cancer, but what does it do to their body image? What does it do to their sexuality? Those are some issues we are exploring. We are also involved in

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several research studies looking at families who have a strong family history of breast cancer but do not carry a BRCA1 or 2 mutation; do they carry a certain SNP or single nucleotide polymorphism, basically a tiny genetic change in their DNA that might be increasing their risks of some cancers? So, we are looking at that and we are involved also in some trials looking at certain subsets of patients with breast or ovarian cancer, and whether or not certain medications are helpful in those populations.

Miller Let us go back to the first study on sexuality, is that an interview study? How are you conducting that?

Matloff It is an exploratory kind of first round study where we have interviewed patients from all decades of life, so women in their 20s, 30s, 40s, 50s, 60s, and 70s who have tested BRCA1 or 2 positive. Some have had surgery, some have not, and we see what it does to them growing up knowing that they are at increased risk to develop breast cancer, how does that make them feel about their breasts as they going through puberty, and it is very interesting.

Miller It sounds like a really great study to do that really may have an impact on how we counsel people.

Matloff I think so.

Miller It looks at that whole time period at risk, which is different. Now, let me ask you a couple of things as we are coming to the end, what are some national resources for people that want to learn more about genetic risk for cancer?

Matloff There are several. You can go to cancer.gov where there are lots of resources about cancer genetics. You can also go to FORCE or, Facing Our Risk of Cancer Empowered, by just typing it into Google and it will come up. That will give you a lot of information about BRCA1 and 2. There is also a new organization called BeBrightPink, which is for young women who are either at risk for hereditary breast and ovarian cancer or who carry a BRCA1 or 2 mutation, and we are really excited about the energy behind this new group.

Miller If someone wants to contact your office and your program, how do they do that?

Matloff They can do a couple of things. They can Google, Cancer Genetic Counseling at Yale, and our website will come up, or they can call our program at 203-764-8400.

Miller I want to thank you.

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Matloff Thank you Ken, my pleasure.

Miller It has been great having you. Again, this is Dr. Ken Miller from Yale Cancer Center and Yale Cancer Center Answers wishing all of you a safe and healthy week.

If you have questions for the doctors, or would like to share your comments, go to yalecancercenter.org, where you can also subscribe to our podcast and find written transcripts of past programs. I am Bruce Barber and you are listening to the WNPR Health Forum from Connecticut Public Radio.