

Ellen Matloff, MS, Understanding your Genetic Risk for Cancer September 6, 2009 Welcome to Yale Cancer Center Answers with Dr. Ed Chu and Francine Foss, 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. Foss is a Professor of Medical Oncology and Dermatology and she is an expert in the treatment of lymphomas. 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 1888-234-4YCC. This evening Francine welcomes Ellen Matloff, the Director of Cancer Genetics Counseling at Yale Cancer Center.

Foss What is genetic counseling? Matloff Genetic counseling is really a communication process. Some people hear the word counseling and they think therapy, and that's not what genetic counseling is. It's a communication process by which we have a family come in, we take their entire family history or their pedigree and we figure out if the cancers in their family look like they are hereditary, meaning caused by a single genetic change or mutation.

Foss Can you tell us what type of cancers you use genetic counseling for? Matloff We see almost every cancer, but certainly the most common are breast, ovarian, and colon, but also uterine, melanoma, medullary thyroid cancer, other forms of thyroid cancer, and rare cancer syndromes like retinoblastoma or Cowden syndrome and Gorlin syndrome. Approximately 5% to 10% of all cancer is known to be hereditary, meaning it is known to be caused by a single genetic change running through the family, but there are probably 20% to 30% of your patients that have some family history of cancer that would warrant genetic counseling.

Foss Can we backup for just a minute, and for the sake of our audience, could you explain what genes are and how you actually screen for genes? Matloff A gene is a single unit of heredity. If we think about our DNA, our DNA is in the nucleus of each cell in our body, and of course every part of our body is made up of cells. We have cells in our blood, cells in our skin, cells in our organs, and in the center of those cells is something called the nucleus and the DNA, or the genetic blue print for the body is in that nucleus, so that's what we are really talking about. We are talking about looking at the blue print for our body and seeing if within that blue print there is an instruction that would put someone at higher risk of developing cancer.

Foss How do you know which genes put you at higher risk? Matloff Good question, and we are learning more about that everyday. If you asked that question 2:55 into mp3 file <http://www.yalecancercenter.org/podcast/sept0609-genetic-risk-for-cancer.mp3> fifteen years ago when this program started, we really had very little genetic testing available for hereditary cancer. Everyday we are learning about new genes, and based on the family history we see patterns, patterns that remind us of certain genes, and probably ten years from now you and I will be having an entirely different conversation about this.

Foss We have heard a lot about all the money that's gone into this so called Human Genome Project trying to sequence every gene in the human body. Matloff Yes. Foss Has this really impacted genetic counseling yet, have we learned enough that we have learned something about new genes for instance? Matloff Even though the human genome has been mapped, we are still trying to figure out what every

place on the map means. Has it impacted genetic counseling? Certainly, there are more genes available for testing, but there is still a lot of potential for growth and development and figuring out the human genome.

Foss Can you talk a little bit about the situation with identical twins? I have had a number of patients where one twin has had a cancer and the other hasn't, if they are genetically identical, how do you explain that?

Matloff In review, an identical twin of course means that the egg and the sperm came together to form one fertilized egg and that that fertilized egg then divided into two, and each of those embryos became its own human being. So, the genetic material in each of those twins is identical. Does that mean that each of those twins is going to go on and have exactly the same diseases in life, the exact same personality, score the same on aptitude test? No. Again, it is nature versus nurture. Is it that the person developed let's say prostate cancer because they have a mutation that caused them to get prostate cancer, or did they develop prostate cancer because of lifestyle issues, dietary issues, luck, was it a sporadic event? That's really the question, and even within my clinic, I will see patients who are identical twins and they carry exactly the same mutation and one of them will develop cancer and one won't. It's most likely that they have that inherited mutation, and that then there are some acquired mutations along the way. Again, is it caused by diet, is it caused by exercise or lack of exercise, is it caused by an exposure in the environment to tobacco or chemicals? I think the truth of the matter is, we don't always know.

Foss I think that's a very important patient related question because often times people come in and say well, gee, you know, my grandmother had breast cancer and my sister had breast

5:48 into mp3 file <http://www.yalecancercenter.org/podcast/sept0609-genetic-risk-for-cancer.mp3> cancer, but my mother didn't have breast cancer what is my risk? People think about it linearly and I think we often times don't incorporate that other factor, which is what are you exposed to and how did you develop differently, say in a different environment than your other family members?

Matloff Absolutely, and quite frankly, we can't always answer the question. I have a set of identical twins in my practice, one of them was a vegetarian and practiced yoga and she was the one who had cancer, and so you would think that she would have been the one spared, and we don't know why she developed cancer.

Foss Basically, you are saying that if you have a gene, you have inherited a gene that's a so-called cancer gene, it isn't 100% that you are going to develop that cancer?

Matloff Absolutely correct, and the lifetime risk with very few hereditary cancer genes, and there are a few exceptions, there are some genes that cause medullary thyroid cancer and if you live long enough the risk is virtually 100%; however, with most of the genes the risk is high, but not 100%.

Foss Can we talk about some of the common cancers in the United States, breast cancer, colon cancer, lung cancer, and prostate cancer? For most patients with cancer, do they need to worry about a gene?

Matloff For most patients with cancer, no, they don't need to worry about a hereditary gene. I would say that people who really need to be thinking about this are people with early onset cancer or family histories of cancer, and also a family history with a combination of cancers.

Foss Are there specific family histories that worry you more? In

other words, is it brothers and sisters, is it parents, is it grandparents?Matloff Certainly we worry more about close relatives rather than distant relatives. So, if the patient reports that her sister had breast cancer at 30, that would concern us more than my great aunt had breast cancer at 75. What would worry us even more would be if she said my brother had breast cancer at 30, so close relatives, an unusual presentation of cancer, and early ages of onset are all things of concern.Foss Can we talk a little bit more about some of these specific genes? I am sure that people have heard of BRCA1 and BRCA2 for instance and there are other specific cancer associated genes. How frequent are those genes seen?8:16 into mp3 file <http://www.yalecancercenter.org/podcast/sept0609-genetic-risk-for-cancer.mp3>Matloff

BRCA1 and BRCA2 in the general population are thought to occur in about 1 in 500 men and women, but if you have a personal history of cancer, of breast or ovarian cancer, or a family history of those diseases, clearly the risk is higher. If the patient is of Jewish Ancestry; however, in the United States we know that 1 in 43 American Jews carry one of the mutations for BRCA1 and BRCA2. If they have a personal history of breast, or especially ovarian cancer, which includes fallopian tube cancer or a primary peritoneal carcinoma, their risk is quite a bit higher and pancreatic cancer also falls under that umbrella.Foss In my practice, and certainly in the practice of other medical oncologists, it is not common that we refer patients for genetic counseling, should we be doing that more often?Matloff Absolutely, particularly in the year 2009. I would also say that for every single patient that comes through the practice, it's really important for us to obtain ethnicity, and not only ethnicity, but to say to each patient, are you of Jewish Ancestry? Too often we rely on their hospital questionnaire, which says religion, and you can be of Jewish Ancestry and not practice that, you could be an atheist, you could have converted to Catholicism, and that's a very important piece of the puzzle here.Foss Is there a specific questionnaire, say that's administered on a national level now that would be a genetic screening questionnaire?Matloff I don't know about on a national level. We certainly have one for our clinic that we give out to oncology practices to use, and basically it incorporates the things we have talked about, early age of onset, family history of the cancer in question, but also very importantly, family history of other cancers known to be caused by that mutation. So for example, the BRCA1 and BRCA2 genes, the breast cancer genes, also increase the risk for ovarian cancer and cancer of the pancreas, so we need to look for patterns.Foss Genetic counseling and genetic testing is important not only for other family members, but also for the patient themselves.Matloff Definitely.Foss In terms of looking at other things down the road.Matloff And it can affect their treatment, whether or not they have a lumpectomy or a mastectomy or a bilateral mastectomy, whether they also need their ovaries removed, it affects their management, the management of their family members; it is really critical.10:51 into mp3 file <http://www.yalecancercenter.org/podcast/sept0609-genetic-risk-for-cancer.mp3>Foss

It sounds like this might be a scary thing for a lot of patients when you start talking about this, looking for these genes and other risks that might be out there for them. How do you handle that fear piece?Matloff That's where the counseling comes in. People come in,

often times we see people who are newly diagnosed or people who have seen family members develop cancer or die of cancer which can be very frightening, and so to have them come in before they have testing to figure out which test would be most accurate for their family and to talk about the ramifications, both positive and negative is critical. For most patients, I would say when they go through that process and make an informed decision before having testing and they understand what the different outcomes are, those are the patients who find it empowering instead of frightening.

Foss In terms of thinking about family, how many family members do you usually bring in for genetic counseling? Is it all the family members or do you do it piece by piece?

Matloff It really depends on the family. When we take the history, we take four generations. That would be their parents, their grandparents, aunts and uncles, cousins, and if they know the information on great aunts and uncles and first and second cousins. We also take siblings, children, grandchildren, and then depending on the family structure, who is living, who lives in the area, sometimes we will see a family and see 20 members of the same family usually all individually.

Foss Ellen this has been a very good discussion and I would like to talk a little bit more about the nuts and bolts of how you counsel these patients when we come back. You are listening to Yale Cancer Center Answers and we are here discussing cancer genetic counseling with Ellen Matloff.

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Foss Welcome back to Yale Cancer Center Answers. This is Dr. Francine Foss and I am joined by Ellen Matloff, an expert in cancer genetics here at Yale Cancer Center. Ellen, we talked a lot about genetic counseling and why this is important for patients, could you walk us through what happens when we identify a patient that needs genetic counseling, how do we get them to your office and then what resources are available to them?

Matloff When a patient is identified as being at increased risk, they call our office and make an appointment. We then send them a brochure ahead of time, unless it is an emergency consult, but this brochure outlines what information they should try to research before coming to our office. We certainly like, if they have had cancer, a copy of their pathology report and their medical records, but also a whole family history which many people have to collect because they don't know this information ahead of time. The most important elements of the family history would be who in the family has had cancer, what type of cancers specifically they have had, meaning where the cancer started, how old that person was when they developed cancer, and we want this not only on the patient, but on the patient's parents, siblings, grandparents, aunts and uncles, cousins, children, and grandchildren, and again not everyone knows this information. Some people come to our office and they are adopted. They have no family history information, so we take whatever we can get, but certainly the more information the better.

Foss And likewise, it's important to note that this is for brothers and sisters that are genetically related to you.

Matloff All of these relatives are genetically related. Sometimes people will bring in information about sister-in-laws and brother-in-laws, and we don't really need anything that is not blood related.

Foss What is the actual process of genetic testing?

Matloff

The process of genetic testing is perhaps simpler than people imagine. A lot of people think that you will need bone marrow to do genetic testing, when we really we need a simple blood sample, and that's usually our method of collection. It is one small tube of blood, which we draw right in our office.15:59 into mp3 file <http://www.yalecancercenter.org/podcast/sept0609-genetic-risk-for-cancer.mp3>Foss What if a family member doesn't live close enough by to come to the center, can you collect a sample somehow?Matloff We can and we do. Often times we will coordinate with that family member's health care provider or refer them to a genetic counselor in their area. We have done this certainly out of the city, out of state, and even out of country, we coordinate this.Foss Sometimes we use a cheek swab, or some saliva for genetic testing for other things that we are doing say in the laboratory, do you do that in the clinic as well?Matloff We do sometimes use a spit sample or a cheek brush sample. It is not our first choice in terms of method of collection, in terms of stability if you are mailing this through the mail, or even in terms of amount of DNA, but it is an alternative that we sometimes use.Foss Does this get covered by health insurance?Matloff Great question, and this is a big concern of patients. The majority of the time the patient actually needs a genetic test and we can get their health insurance to cover the cost of both testing and counseling.Foss And what if the patient doesn't have insurance?Matloff We do see some patients who are uninsured completely, and for very high-risk patients we tap in to some funds that we have to cover the cost of testing. We can only do that for patients at greatest risk.Foss When we talk about insurance companies, we also talk about divulging information to those companies. Could they get access to our records and find out who is carrying a bad gene? This is a concern for a lot of patients and may impact them in the future. Could you speak a little bit about the legal aspects of this?Matloff This is called genetic discrimination and certainly this has been a main area of concern within cancer genetics for the last decade. I can tell you that our concern about it as testing was rolled out were so great that a lot of laws were put into place, both locally and nationally, to protect patients. Luckily we have seen very few cases of health insurance discrimination along the way. I think what patients don't recognize is that if they have already had a cancer diagnosis, of course that's on their record and if they are going to be discriminated against by a health insurance company, most likely its going to be based on their cancer diagnosis. We18:30 into mp3 file <http://www.yalecancercenter.org/podcast/sept0609-genetic-risk-for-cancer.mp3> really haven't seen this play out the way we thought we would in the health insurance spectrum. Life insurance and disability insurance is a whole different cart of apples, and so we do talk to patients about securing life insurance, if they have never had cancer, securing that life insurance before they learn if there at high risks to develop cancer.Foss Is there a statute of limitations, in other words, can the life insurance companies go backwards six months and then cancel your policy?Matloff Well, if you think about it, its not that six months ago you developed a mutation, right. You would have carried that mutation since you were an embryo, and so I don't know if certain life insurance companies have policies about how recently you would learn the

information, but that wouldn't really make very good biologic sense. Foss I think this is an important time to just touch on protected health information for patients, once you find out that a patient has a gene, how do you protect that information? Matloff It's a very tricky question, because if I find out that someone has a mutation for hereditary cancer syndrome, we are going to recommend one of the three things. Either increased surveillance above and beyond what is offered to the general population, chemoprevention, meaning taking a medication to reduce their risk of getting cancer in the future, or even in some cases a preventative or prophylactic surgery. These things cost tens of thousands or even hundreds of thousands of dollars, and so clearly, we want their insurance company to cover those things, and to get their insurance companies to cover them, we share the information that they are at higher risk or the insurance company wouldn't pay for them. Of course, with the patient's permission, we usually do divulge this information and I have to tell you the insurance companies have been remarkably good about paying even for things like reconstructive surgery if a woman has her breast removed preventatively, which is very expensive, \$30,000 to \$40,000, and why are they paying for that? Well when you compare the cost of that surgery to the cost of a cancer diagnosis, when the patient develops cancer and has to have that surgery, has to have chemotherapy, radiation, tamoxifen for five years, and hospitalizations, it's much less expensive to go through genetic counseling, testing and to go through surveillance or prevention. Foss Health care is really a hot topic politically now. And not wanting to get on either side or the other, could you just comment on whether or not genetic testing and this kind of coverage that you are talking about is going to be a part of our health care planning in the future? Matloff No matter how you feel about the Obama administration and the health care plan, I think everyone can look at the approach, which is to have streamlined medicine that is more efficient and more effective become a part of the future, and moving forward, I think that would make sense to everyone. If we are going to have a more effective and efficient health care system, I think it's fairly clear that genetic counseling and testing has to be part of this plan, why? Well, right now for example, every woman is offered a mammogram at age 40 with an annual mammogram every year after. In reality, some women need their first mammogram at 25 and it's quite likely that other women need their first mammogram at 45; if you were able to look at their genetic information and see who is really at greatest risk. So, not only will genetic counseling and testing allow us to more accurately tailor a woman's risks and then her medical care, and men's risks, it would allow us to save money by avoiding procedures and surgeries that are not necessary, and screen patients at high risks and catching their cancers or even preventing their cancers from occurring in the first place. Foss It sounds like in this era of molecular medicine, and knowing all we know about these genes, perhaps it would be better to actually be screening people at the level of their primary doctor for instance before anybody develops a cancer. So, screening people when they are younger and identifying who is at risk and then perhaps making different recommendations to them as they

carry out their life. Matloff I think that makes a lot of sense and the question becomes who should be doing that genetic testing? Ten years ago, the person at the head of the Human Genome Project thought that this would fall into the primary care doctor's lab, but what we found is that in this era of 15 minutes per patient visit, the average physician or nurse is not able to, on top of their plate of a full physical exam, taking a family history, all of the things they have to do, also do genetic counseling and testing. When we have seen it done in that setting, we have seen a lot of mistakes, we have seen the wrong test ordered, tests misinterpreted, people believe it or not having prophylactic surgeries that they didn't need, and people being told they are at low risk who are actually at high risk. One thing adding to the complexity of this situation is that some of the genetic testing companies who are making pure profit off these tests are really pushing these physician's offices to do their own testing. Keep in mind that the liability falls to the physician, the profit goes to the company, and so what we really recommend is that the primary care physicians take a great family history and determine which of their patients need to be referred to genetic counseling and then outsource that. Foss Is there an easy link up between your center and the primary care physicians in Connecticut so that they know how to refer the patient in? Matloff Yes. In Connecticut, if someone is interested in referring a patient to Yale Cancer Genetic Counseling, they can either go to our website, and I would recommend just going to Google into mp3 file <http://www.yalecancercenter.org/podcast/sept0609-genetic-risk-for-cancer.mp3> and Googling Yale Cancer Genetic Counseling, or they can call us at 203-764-8400. Although, I would like to also mention that there is an excellent center at UCONN. We have outreach centers around the state including Danbury, Greenwich, and Norwalk, and there are providers in every state. Listeners who may be hearing this who want more information can go to the National Society of Genetic Counselor's website, which is nsgc.org and there is a little thing to the left that says find a counselor and you can find a certified genetic counselor in your area. Foss That touches on another question I was going to ask you, which is once the patient gets their genetic testing done, is it put into some kind of national database, and is it possible that a patient might gain from being part of such a study, so to speak, so that they might learn some additional facts about, say their genetic type, and does that ever get back to the patient? Matloff Great question. We don't have a national database, but I think what you will find if you see a certified genetic counselor you will get the kind of long-term care and follow-up that you are talking about. For example, we have a newsletter, a website, a facebook page, and a blog, all updating patients on the new information that's emerging every day. I think most certified genetic counselors also have some mechanism to report back the patient's new developments. Foss Just in closing Ellen, is there any new and exciting research that you would like to tell us about at Yale Cancer Center that's related to cancer genetics? Matloff There is a lot of exciting research, but I would say the big thing on the forefront at the moment is the use of something called PARP inhibitors, potentially in the treatment of women who carry BRCA1 or BRCA2 mutations and have breast or ovarian cancer. These are

specific inhibitors that seem to work particularly well in people carrying one of those mutations and this kind of personalized medicine that's personalized to the genetic makeup of the patient, I think, is the wave of the future and you can tell me if you agree. Foss Absolutely, and this has been a really exciting conversation tonight. You have been listening to Yale Cancer Center Answers and I would like to thank my guest Ellen Matloff for joining me. Until next time, I am Dr. Francine Foss from Yale Cancer Center wishing you a safe and healthy week. If you have questions 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.