

Genetics and Cancer
Webcast
October 16, 2007
Banu Arun, M.D.

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Andrew:

Hello and thanks for joining us once again. Broadcasting from Seattle, I'm Andrew Schorr. It's a pleasure to do this every two weeks. I learn so much, and we connect with leading experts at M. D. Anderson in so many different areas that affect us when we're concerned about cancer. Take a look at our whole library of programs we've been doing. And then always I meet people who are inspiring to me, people who've dealt with cancer themselves or in their family.

And when we talk about dealing with cancer in your family you say, Is there a genetic connection? So if mom or dad or your sister or brother had cancer or even your child you say, Could it run in our family? Now, most of the time, at least with what we know now about science, it doesn't. But in some cancers there is the chance, five to 10 percent of all cancers may be hereditary. So then you say, well, Could that be us? And if so what do we do about it?

So, not surprisingly, they are expert at that at M. D. Anderson, and they have a clinical cancer genetics program. We're going to hear a lot more about that, but first let's meet somebody who's been affected by this. So Jan lives on the north side of Houston. She's 44.

Jan, let's learn how cancer and a genetic connection intervened in your family. Tell me about your sister Gail from Minnesota.

Jan:

Well, when my sister was 42 she was diagnosed with breast cancer, and at the time we both lived in Minnesota, and she came to M. D. Anderson for treatment and had chemotherapy, a lumpectomy and radiation because her cancer had progressed through her lymph system. It was very aggressive.

Andrew:

So she went through that treatment. Now, where did the question come up could there be a genetic connection? What happened there?

Jan:

Well, in our growing up our grandmother had breast cancer twice and eventually died of cancer. And all of her four sisters had breast cancer as well, and so we knew in our family that we had a family history. And it was kind of a black cloud

that hung over all of us wondering if any of us were at risk for breast cancer. So in the course of my sister's treatment we started gathering information and consulted with a physician through the genetics counseling department at M. D. Anderson. And because it came from my father's side of the family, the history, he was the first member of our family to be tested for BRCA 1 and 2. And after he was tested positive both my sister and I tested, and we were both tested positive as well.

Andrew:

What did you do about it?

Jan:

Well, when we got our results back my sister was still in treatment. We got our results back in March of 2001, and she finished treatment in April. And what we decided to do was have prophylactic surgery to have a bilateral mastectomy, a hysterectomy and an oophorectomy which would remove my ovaries because the kind of mutation that we have put us at great risk for ovarian cancer as well. And my sister had the same surgery because her risk of getting cancer again was not diminished by the fact that she had already had cancer. Her cancer risk was still very high because she had the mutation in her genes.

Andrew:

And the ovarian cancer, too.

Jan:

Yes.

Andrew:

That's a big decision. And for you, who had not been diagnosed for cancer, had not been treated for cancer, no sign of cancer, to have your breasts removed then of course go through reconstruction, have your ovaries removed, that's a big deal.

Jan:

It was a big decision, but for me it really wasn't as difficult as you would think. I had seen my sister go through a year of treatment, which was grueling. And at that point we were both so thankful to have the knowledge that we had this gene because I really believe that knowledge is power and because we had hard facts that we had this gene and we had good information about what our risk was, to me it was a very simple decision. I had six weeks from the time we tested to the time we got our results back, and in that six-week period of time my husband and I really talked it through and made the decision that if I were positive we would proceed with the surgery.

I was 38 at the time, and every woman in my family had been diagnosed between the ages of 38 and 42. And because I'm the mother of two daughters I didn't feel that I could take the risk myself of developing cancer when I had something I could do that would reduce my risk from about 80 to 85 percent for breast cancer to

about three percent

Andrew:

Well, you mentioned something we need to follow up on, and that is you have two daughters, one who's 18 and one who is 14. So have you talked about this, and have either of them been tested to date?

Jan:

We have talked about it. They walked through this whole process with my sister when her treatment happened 2000 and 2001. And I was living in Minnesota when I had my surgery, so I was away from home for six weeks to have surgery, so they watched through my recovery as well. And my older daughter turned 18 last July, and she informed me yesterday that she has scheduled an appointment for January 3rd with the genetics counselor at M. D. Anderson, and she's going to be tested in January. They really like to wait until kids are older, from the information I have, until they're legal adults because, as you know, it's a lot of information and you are required then to process that information, and they want to make sure you have the maturity to be able to do that.

Andrew:

Well, you must be proud of her, though, that she's thought about it and is going to get more information. It's so important for her health, too.

Jan:

It's very important, and I'm very proud of her. And I have three cousins who tested negative, and for them that anxiety that they had about their increased risk was alleviated. So we have a 50/50 chance.

Andrew:

One other question for you, Jan, you're talking about it. Now, a lot of people would get this information and kind of bury it. They might take action themselves but they wouldn't be on the internet or on the radio talking about it. They'd be very concerned, whether it's for insurance or all sorts of things. Why are you speaking out?

Jan:

The first day my sister had chemotherapy she met someone who became one of her best friends who was terminal when she met her. She was 36 years old. She had genetic breast cancer in her family. She did not have the opportunity that I have to do the testing before she was diagnosed, and her cancer was so progressed that she didn't survive. And she was an inspiration to me and my sister to talk to women, any opportunity we get, about breast cancer, about getting mammograms and preventive care but also not to be afraid, that if you have one of these genes that there are things that you can do and that knowledge is very powerful.

And whatever decision you make as a woman, because some people don't make the

same decision I made, at least if you have the information and the facts at hand you can make an informed decision, and I think that creates a much less stressful scenario than always wondering if you're going to be hit by a diagnosis of breast cancer.

Andrew:

Well, you are inspiring, and, Jan, we're going to be back to you in a minute.

But let's meet a physician at M. D. Anderson who specializes in this, and that's Dr. Banu Arun. Now, Dr. Arun is a breast medical oncologist, but also she's co-director of the clinical cancer genetics program. Dr. Arun, so I talked about five to 10 percent of the cancers being hereditary, and Jan brought up about BRCA1 and 2. So help us understand. These are genes that have been identified where there can be a much higher risk of breast or ovarian cancer. Is that right?

Dr. Arun:

Yes, that's right, Andrew. And thank you for giving me the opportunity to join you tonight. So, luckily, only up to 10 percent of the breast cancers are hereditary or genetic. So this means 90 percent of the breast cancers happen because of some other reasons not related to mutations in these known genes. So 10 percent of these breast cancers which are hereditary, most of them are related to mutations in the BRCA1 or BRCA2 genes, so that takes about 85 percent of them. And then the rest are really some other gene such as p53 or p10, which are seen very, very rare. So I will be mainly concentrating on the BRCA1 and 2.

So these genes or, rather, mutations in these genes can be found by sequencing the genes from a simple blood draw. If an individual has a mutation in one of these genes breast cancer risk, life-long breast cancer risk is up to 80 percent and life-long ovarian cancer risk is up to 50 percent in individuals. There is also a risk of developing second new breast cancers. For example, if we test an affected woman and she is cured from her breast cancer she still has a risk of developing a new one in the opposite because of this mutation, which is about six times higher than the average population.

Andrew:

Right. And that's what Jan was talking about with her sister who'd already been treated for breast cancer in one breast in her case deciding to have the other removed because she was at higher, much higher risk of having breast cancer there.

Dr. Arun:

Exactly. And this is why we actually have found that doing the genetic risk assessment in our care centers is really very, very helpful, because ideally when there is a strong family history we don't want to start with an unaffected woman. We want to start with the woman who has breast cancer because the likelihood in finding the problem or the mutation is the highest in that person. Plus the results

may have immediate effect on the treatment choice.

Unfortunately, for example, we have patients coming in after ten years of diagnosis, most probably because these genes were new at that time and nobody was really doing clinical testing, and they've had let's say a mastectomy and radiation therapy, and then they find out that they have a BRCA mutation and then they have to undergo another surgery so that's a little bit more difficult.

But if we do the assessment up front during the diagnosis not only we establish a mutation in the family which can help the unaffected individuals we can also - these results can also help planning further management for the affected - for our affected patient. Again, double mastectomies, maybe doing the oophorectomy sooner than later which might help us with some hormonal treatment for breast cancer. Maybe we want to avoid radiation therapy. Instead of doing a segmental mastectomy we would do a total mastectomy. So having this information besides everything helps us with the immediate treatment decisions also.

Andrew:

Okay. Now, let me ask you about this, now, on one end of the scale would be to have your breast removed prophylactically, like Jan did, her sister had the - both ended up both breasts removed and of course the reconstruction, the oophorectomy. But let's back up. So if there's a suspicion or there's a question, a woman just wants to know, first you sit down with a genetics counselor, right? You don't do not pass go, go to the blood test, have surgery. Tell us how it starts. Take us through the process.

Dr. Arun:

You are exactly right, of course. We initially when a patient comes in with a suspected family history our patients meet with our genetic counselors first. That is a, I think, very helpful consultation which can last anywhere from one to one and a half sometimes even two hours. What is discussed there, they take a very detailed family history which includes the maternal as well as the paternal side. And we try to document all cancer cases, not only breast but ovarian and any other cancers in the family including the age onset, which is very important. After that information is all gathered - and sometimes our patients might not have the details and they have to get some information from their mothers or sisters or some other family relatives, and they then call us back with some additional information.

So once we have all of the information together, hopefully during the initial session, our genetic counselor then starts discussing the likelihood of finding a mutation in our patient. So we don't immediately recommend genetic testing, but she takes the family history and then we all meet. She comes out and she meets with me, and we go over the family pedigree. Then we all come back inside again, and then we discuss what, if you will, the red flags are in the family which would make us think that there might be a mutation. And if the probability of carrying a mutation is high enough then we discuss maybe you would benefit from genetic testing.

One important thing is also we always try to ask our patients, Why do you think this information will be helpful? For example, if we have a patient who already had bilateral mastectomy for breast cancer ten years ago who also had her ovaries removed and does not have first degree female relatives living who would benefit from this information, this patient might not opt to do genetic testing even though it's medically indicated because she would not use that information for anything.

So we basically discuss everything from A to Z. What is your risk? What is the likelihood of finding it? And if you find it how can we use this information, and are you comfortable with receiving positive results or negative results. Are you also comfortable with some type of result which will not exactly tell you what the risk is. And that discussion takes more than an hour, and we usually do not proceed unless we are all on the same page and know what we are doing.

Andrew:

Okay. Thank you for taking us through that. There's a lot more to talk about as we continue our program. It's fascinating topic, an important topic if someone in your family has been affected by cancer or you have. And then we're going to talk about what do you do with the information, and that's what Dr. Arun was just getting at. Even if it's positive, how do you handle that? How do you process it? What steps do you take? Do you have surgery? Do you have a lot of surveillance, checkups, etc.?

We welcome your calls at 1-877-711-5611. You can also send us any mail as some people already have at patientpower@mdanderson.org. You're listening live to our webcast on cancer and genetics. Patient Power sponsored by M. D. Anderson Cancer Center. We'll be right back.

Break

Andrew:

Welcome back to Patient Power. Andrew Schorr here live on mdanderson.org with one of our every two-week webcasts. Patient Power, this is where we connect you with leading experts from M. D. Anderson inspiring family members and patients. We're talking today about genetics and cancer.

We have with us Jan from the north side, the Woodlands area outside Houston. And maybe you heard if you heard the beginning of the program how her sister was diagnosed with breast cancer in her 40s, and then Jan still in her 30s found out both of them and their dad tested positive for the BRCA1 gene for breast cancer and ovarian cancer. And both sisters decided to have bilateral mastectomies and then reconstruction. It was prophylactic, if you will, with Jan because she had not been diagnosed with any cancer, and they had their ovaries removed too. So big deal. And then Jan has an 18-year-old daughter who's scheduled to see the doctor too to see what's up with her.

Also with us, of course, is Dr. Banu Arun who is with the clinical cancer genetics program. She's actually co-director. Dr. Arun, you were explaining that you have genetics counselors there and people meet with them and you kind of plot out what's going on. Also in discussion with you, you decide with the patient, Well, what would you do with the information, if it's negative, if it's positive, if it's indeterminate, etc.

So let's talk about what you do short of surgery. Let's say it's positive. The woman maybe has been treated for breast cancer. Ovarian cancer is certainly a scary diagnosis. How do you keep checking on a woman if she may be at higher risk? What do you do there?

Dr. Arun:

Right. Well, let's start discussing the unaffected high-risk woman first.

Andrew:

Sure.

Dr. Arun:

So let's say we have a 33-year-old young woman who tested positive for the BRCA1 mutation and does not have a diagnosis of cancer and otherwise doing well. Obviously, we give the results to our patients during their second visit. The initial visit is the workup I had mentioned and the blood draw. It takes about three to four weeks to get the results from that specific laboratory. So we schedule a second visit. And we do not like to give results out over the phone because, as you will see in a minute, it has really significant implications. And we rather like to discuss it face to face, make sure that our patients ask us any questions they want, and we want to make sure that our patients understand all the risks and preventive measures we're going to discuss.

So the patient presents again for a second visit when we have the result and we accumulate the results. And if it is a positive result we mention again, so that we can help our patient making the best decision, what it means in terms of developing breast cancer and ovarian. And again we quote that there is an up to 80 percent risk of developing breast cancer. That's life-long, though. It doesn't mean it's going to happen the next day. And also the up to 50 percent risk of ovarian cancer. And we usually wait a minute and see what these numbers mean to patients because it can mean different things to different people.

Then we start discussing since now we have this information what we would like to do, and we start discussing the options. The options, as you have heard, range from screening to aggressive measures such as removing the breast and the ovaries. In terms of screening the guidelines we recommend is that obviously patients do their monthly self breast exam. We see our patients every six months. I see my patients every six months in the high risk breast clinic for clinical breast

exams. And we then also do yearly mammograms and yearly MRI screening of both breasts.

I don't know if everybody knows but the American Cancer Society guidelines were just reviewed a couple of months ago and they are now including MRI screening in BRCA mutation carriers. We have been actually doing this over the last three years, but I'm very pleased to see that it has become now standard of care, and hopefully many other institutions are going to adopt this as well. So again self breast exams, clinical breast exams and screening with yearly mammogram and MRI is discussed.

We also discuss a drug which is called tamoxifen, which can reduce the incidence of breast cancers by about 50 percent. But as I'm saying, it's only 50 percent so when we discuss it with one of our patients we really don't know if she would be falling into the 50 percent who will benefit or the 50 percent who will not. So it's very difficult to predict if a certain patient will benefit from that.

The other little caveat about tamoxifen is that tamoxifen can induce some unpleasant side effects. It can increase the risk of blood clots and maybe uterine cancer. The other issue which is currently being studied is that tamoxifen might not be very effective in BRCA1 related prevention but more in BRCA2 related prevention. So for a BRCA1 patient we discuss the tamoxifen but it might not be the best option.

And then the third option obviously or risk management option would be the bilateral mastectomies. Again, that is the most aggressive approach, however it is the most effective because it reduces breast cancer risk by more than 95 percent. We like to discuss things in detail, and we do not directly tell our patients you have to do this, you have to do that. However, we try to give the facts so that the best decision can be made.

One thing which comes up and my patients ask me, So what do you think, Dr. Arun, is MRI better than surgery? I don't think we can compare because MRI is screening and the surgery is preventing it. When you do surgery then the tissue is removed and you have a very effective way of preventing it. MRI is only screening, so even if you do MRIs every other month if cancer develops it will develop, so we cannot prevent it from happening. With MRI, hopefully we can pick it up a little bit earlier where it is easier treatable.

Andrew:

Okay. I've got a few questions for you. First of all, related to ovarian cancer, so there do you do regular ultrasounds? Because so often ovarian cancer is found later, and that can be devastating. So what do you do if someone doesn't have their ovaries removed to be looking for that early?

Dr. Arun:

Right. So with ovarian cancer, again, our group does every six months follow ups and pelvic examinations. They also include a blood test where they are looking at CA-125 levels every six months and following the levels. And in terms of drug prevention there's really not much out there for ovarian prevention, so if the our patients do not want to proceed with the screening then the other option really remains to remove the ovaries. And again it's the same case scenario as it is in breast, it is the more aggressive but the most effective option because it reduces ovarian cancer risk by more than 95 percent.

Andrew:

Dr. Arun, I know you're a breast medical oncologist but I know there can be a connection related to HNPCC, related to ovarian and colon cancer, and FAP, with all these polyps somebody might develop in their family. Can you speak about that at all.

Dr. Arun:

Right. So HNPCC is a syndrome where ovarian and colon cancer cases are seen in the family, and there are again certain mutations which can be identified with the blood tests such we are doing it in the BRCA case scenario. With HNPCC in terms of screening, it's the same thing. Again, either very, very careful screening for colon cancer and ovarian cancer or, again, the more effective way would be doing a colectomy, for example, and again the oophorectomy. One of our gastrointestinal physicians is devoted to this area, and he is following our HNPCC patients and doing the colon cancer screening for our patients.

Andrew:

Okay. Let me see if I get the acronym right. So it's hereditary nonpolyposis colon cancer, or HNPCC.

Dr. Arun:

Exactly.

Andrew:

And then this other one FAP or familial ad - you better say it for me.

Dr. Arun:

Yeah. Familial adenomatous polyposis.

Andrew:

Right. And that's where you have just a bazillion polyps, hundreds of polyps.

Dr. Arun:

Yes. And in those families and cases who have the mutation the likelihood of developing of these little, tiny little, hundreds of adenomas turning into cancer at age 40 or 50 is so high that again a preventive surgery is most probably the most

appropriate approach because it is very difficult to keep doing colonoscopies and following these hundreds of little polyps and wait and see if one of them or several of them will turn into cancer because one has to keep biopsying every single of these polyps, which is obviously very difficult.

Andrew:

Right. I understand. And I know there can be children where this happens and might need that surgery at an earlier age, but it's better than, of course, the devastating effects of colon cancer that advances.

We're going to take a break, and when we come back we're going to address ourselves to email questions we've been receiving from all of you. And also you're welcome to give us a call as we discuss genetics and cancer. Our phone number again is 1-877-711-5611. You can also send us an email at patientpower@mdanderson.org. We'll be back with our experts when we continue Patient Power sponsored by M. D. Anderson Cancer Center.

Break

Andrew:

Back live on the M. D. Anderson website with this edition of Patient Power on genetics and cancer. Okay. We're going to put Dr. Arun on the spot now, but she knows a lot about genetics and cancer. We've been getting her email questions so, Dr. Arun, you're all set? You're ready to go?

Dr. Arun:

Yes, I am.

Andrew:

All right. This one came in from Carrie from Kingwood, Texas. And you've described this a little bit, maybe you can just sort of rattle through it really quick. "What's the process for genetic testing? Is it a scan or a blood draw or will I just be filling out forms?"

Dr. Arun:

Okay. So the technical part is very easy. It's just the blood draw and it goes out to an outside lab. There is only one single lab in the US doing it. So it's a trip there. Of course, there is some paperwork involved. One is obviously us determining the medical necessity of this, and then the second part is the request forms which is very easy to do, and the third part would be then the insurance authorization.

Andrew:

Okay. And just recap for Laurie here. Laurie writes in from Katy, Texas. She says, "I have a range of cancer history in my family and extended family. Can you list the top hereditary cancers? I'm curious about my own risk."

Dr. Arun:

So I think that's a good question. So if there are multiple female members with early onset breast cancer in their 30s, 40s, and ovarian cancer, if there's male breast cancer, then we could be concerned about what we just talked about, the BRCA1 or the BRCA2 mutations. If there are multiple cases of leukemias, young breast cancer, sarcoma, which is a type of bone cancer, lung cancers, so if there are multiple different cancers and especially two or different type of cancers in one person, then we are concerned about the syndrome which is called Li-Fraumeni or the mutation is in a gene called p53 or p-5-3. As I mentioned at the very beginning, though, that is a very small, very small subgroup of genetic problems in relation to breast cancer.

Then there are rarer syndromes, one we just discussed, the HNPCC, where there are a number of colon cancers and ovarian cancers in the family. And finally there's a syndrome called Cowden's syndrome, which is a mutation in the p10 gene, and in those cases we see a lot of uterine, thyroid and breast cancers in the family. There most probably might be some other or overlapping syndromes, but at this point we don't know the genes for these diseases.

Andrew:

You know, when someone looks at their family history - now, people are now learning was there breast cancer, was it early age, was it a first-degree relative, even a man in the family as well. But sometimes people just say there's a lot of cancer in my family. And Jamie writes in from Houston and she says, "I don't have a family history of breast cancer although I do have cancer in my family, lymphoma, sarcoma and lung. Would it be beneficial for me to undergo genetic testing?"

Dr. Arun:

That is a very good question too. I want to make clear that whenever we want to identify a mutation it would be the best if an affected individual who has the cancer actually presents with genetic counseling and testing. Sometimes that's not possible, then we sometimes end up testing the unaffected people. However, it is best if the affected individuals come and see us.

Andrew:

Okay. So here's the \$64,000 question people ask, Janice writes in from the Woodlands there in Houston, "Should I tell my insurance company I'm getting genetic testing? I fear they will drop me if I have the gene." Any advice there? And I'm going to ask Jan about that, too.

Dr. Arun:

That, of course, question is asked everywhere and every time. In fact our genetic consultation session, one part of it is devoted to the subject. One thing is that if a patient comes in for genetic risk assessment obviously that's in the medical records because it's a standard process and whatever is happening in physician's offices is

documented. So the insurance company will know about the risk assessment and if blood is sent in for genetic testing.

Now, our patients have the choice to self pay and not charge the insurance, and they will not be interfering with the testing and the requisitions coming in to them, but the out-of-pocket pay is about \$3,000 or so for the genetic testing. Almost, almost all of our patients go through insurance, and the coverage depends obviously on the insurance companies, but it's pretty good. We have an up to 90 percent coverage, anywhere between 80 to 90 percent coverage of the testing, so the out-of-pocket or the co-pay is not that much.

There are state and federal laws preventing discrimination, either job-wise or insurance-wise or anything. So there are laws. However, obviously, we as physicians cannot guarantee that nothing will happen, but there are laws preventing from discrimination. I have personally not seen any of my patients dropping out from insurance or so because of the genetic risk assessment and testing.

Andrew:

Jan, I want you to weigh in on this. You thought about this and you've spoken out about it, and I'm sure people have said to you, Oh, boy I don't know if I could do that, or if it's positive, Boy, if someone found out. What do people tell you, and what do you tell others? You know, this decision of having the testing and if it's positive the fear that it would be misused somehow.

Jan:

You know, I believe that knowledge is power, so for me having the information was more important than being concerned about the insurance risk. Because of my family history my insurance company identified me as having breast ovarian syndrome, meaning I had enough people in my family that had breast cancer that put me in a high-risk category, and that was enough for them to approve my surgery. Everyone's insurance is obviously different. But from their perspective before I ever had the genetic testing done I was high enough risk to make it worth it for them to treat me prophylactically.

Andrew:

Here's some more questions that have come in. Dr. Arun, we have a question from John in Houston. He writes, "I'm 23 and have irritable bowel syndrome and a history of colorectal cancer. What age should I begin screening, and should I have genetic testing?"

Dr. Arun:

So, obviously, if John already has colorectal cancer then he should be under surveillance all the time by his oncologist. The genetic testing depends on his family history. If there are other first-degree relatives at least in two generations having had colorectal cancer also, then he certainly should discuss it with his

oncologist who is following him up and then consider testing.

Andrew:

Okay. And does the history of IBS weigh in at all?

Dr. Arun:

So the history of the irritable bowel syndrome can increase the risk of colorectal cancer. So his colorectal cancer could be purely because of that and not because of family background. But not knowing it, what I would say is to look into his family history and if it is significant do the testing or consider genetic testing. If there's no family history most probably it's not genetically related but rather because of the irritable bowel syndrome.

Andrew:

Okay. Here's a question from Sylvia in Houston. And she says, "My husband's father passed away from breast cancer. Does that make our son or daughter more likely to get it or are they both predisposed."

Dr. Arun:

So that is a very good question. So we try to test males who have breast cancer for the mutation, and if they are positive then of course their daughters and sons are tested also for the mutation. Now, because her husband's father passed away, it is very difficult to judge at this point if he had a mutation or not. Because if he had a mutation, yes, I think her husband and his kids are at definitely higher risk. If the father didn't have the mutation then the risk is very low. So the only thing we can say now is that the risk might range from very low to very high, and to better assess this her husband could maybe consider genetic counseling.

However, the family history, the rest of the family history is important as well, so if there are other females in the family with breast cancer and if they had it at young age and if there's ovarian cancer, that definitely supports the fact that they should consider genetic counseling. But if he was the only one and there were many other females who didn't have any problems, that really is a more relieving factor, I think.

Andrew:

Okay. Now, as we said at the outset and we've repeated a couple of times, approximately five to ten percent of the cancers are hereditary, and so we are learning where genetic counseling and testing comes in. But most cancers today, we're saying, are not. But it's kind of a moving target, and I want to understand this, Dr. Arun. Is it likely that other genes or mutations that we're not aware of today will be identified and that percentage will change and increase over time?

Dr. Arun:

I don't think so. I don't think so because the BRCA1 and 2 covers most of the hereditary cancers. When we talk about other genes we talk about the rest of the

15 percent of the cases where the family history is very strong, a number of young females had breast cancer but the gene is negative and we don't know what's contributing to that. So in those cases we think there are some other genes or gene/gene interactions going on which might have predisposed them to cancer.

So I think the percentage will not change, but we'll have something to work with. So when we have a negative test result in the very significant family then we don't know what to tell our patients. But if we identify that gene then we can test to for that gene and we know what the reason is they are having all of these cases and we can make better recommendations.

Andrew:

Yes. So where are we with research? M. D. Anderson is a leading research institution. What are some of the areas you're looking into now when it comes to cancer genetics? What's sort of around the corner, if you will?

Dr. Arun:

There are several aspects. One area is early diagnosis. So let's say one of our patients has a BRCA mutation. First of all, not everyone who has a BRCA mutation will develop cancer, and the second question is, which a lot of our patients ask, when should I do the mastectomies? When should I do this? When do you think I will get the cancer? We don't know because what we are quoting as a risk is a life-long risk.

So we are looking at some other factors which might contribute to earlier onset or later onset in these mutation carriers. We, for example, don't know if smoking adds to the risk, if hormone replacement adds to the risk. We really don't know if getting pregnant with the mutation is bad or good. There are some studies saying it's protective, some studies saying it's not. In fact we just did a study, which is not published yet but will be published, that pregnancy is protective also in BRCA patients as it is in the general population, so that is one very interesting area.

We are also at this point trying to understand are these genes acting different in different ethnic backgrounds. We have studies going on with our Hispanic patients, with our African-American patients. So that's a very important area of research. We are doing some screening studies with MRI. And we are also trying to develop agents because there are patients who don't want to commit right away to mastectomies and want to continue with screening but tamoxifen is not the best drug for prevention, so we are working on some other prevention drugs with some vitamins analogs, with celecoxib or with some other, newer agents.

So I think because these genes were only cloned 10 to 15 years ago we are at the very beginning of this. And I think it's very exciting because we came this far within the last ten years, and I can only imagine how much more we will be learning and achieving within the next ten years and hopefully doing more and more early diagnoses. One other recent advancement is that the treatment, the

chemotherapy of breast cancer might also change in patients with BRCA1 mutations, and that is a very, very new area, so we are doing some research studies in that area, as well.

Andrew:

Okay. That gave us a lot that you're working on.

We're going to take a short break. When we come back we have more questions for you, Dr. Arun. And we want to get some wrap-up comments from you as we draw to the end of the hour and also from Jan, who has thought about this a lot. We'll be back with more Patient Power and genetics and cancer brought to you by M. D. Anderson Cancer Center.

Break

Andrew:

We cover a lot of ground in these webcasts and, you know, you can't find this anywhere else. So this is what we do. We cover a lot of ground every two weeks. Remember, you can go back over it with our replays, transcripts. And please tell others about Patient Power because I think it makes a big difference for people.

Dr. Banu Arun, clinical expert in genetics and cancer, we have a couple more questions for you. One is just a practical one. People listen all over the world and in many other states besides Texas, if a patient lives out of state can they still get genetic testing through M. D. Anderson without too much travelling?

Dr. Arun:

So as I tried to explain, it will be a little bit difficult to cover everything without face-to-face contact. Theoretically, it's possible because it's just a blood draw and the blood can be drawn anywhere and can be sent out to the lab. However, if we get requests we tend to refer patients to their closest genetic counselors because there is a list, a network of genetic counselors who basically do the same at their institutions working with their physicians. So we try to guide them to their closest centers to undergo this discussion, understand what it's about and then have the blood drawn and then discuss the results.

Andrew:

Okay. Let's say somebody chooses to come to M. D. Anderson and there may be some ongoing discussion, can their local primary care practitioner be involved as well?

Dr. Arun:

Yes. There are different ways to do that. We either can take the calls of their physicians or we can do teleconferences. Sometimes we even do three-way conferences over the phone when the patients is there with us and then their treating physician. So we keep the communication definitely open.

Andrew:

Okay. Here's another question for you. So we talked about these blood tests for like BRCA1 and 2. "Are these genetic tests always conclusive or could it come back as a maybe?"

Dr. Arun:

Yeah. That is a very good question and that is a topic which we discuss in detail with our patients. When we get results we can either get a result saying that there is definitely a deleterious mutation, or we can get a result saying no there is no mutation. Then we can get some result saying that there is a mutation in the gene but it's of unknown clinical significance. So what this means, the gene is not normal, but we don't know yet if that abnormality can cause the cancer or not because there are not enough cases. These cases are called VUS cases. If we get these results then, unfortunately, we do not know more than we knew at the beginning. And before the testing we discuss this scenario with our patients.

Andrew:

Okay. One area I wanted to cover and real briefly and that is, Who do you tell? So you all come up with the test result, let's say it's positive. How do you counsel people whether they should then tell a sister who lives in another state, discuss it with their daughters. I'd love to know what you tell people, how it gets handled.

Dr. Arun:

So once we have the results then we go back to the pedigree and basically track back. So we tell the patients this is you, you have the mutation so your sister here, and we try to draw it on the pedigree and show it, has a 50 percent chance or risk rather of carrying the mutation. Your kids have a 50 percent risk of having it or your mother or your father, depending on from where it comes. And then we tell them that they should discuss the result with their family members and tell them that we would recommend they would be tested as well.

Now, because the family members are not M. D. Anderson patients we cannot say anything more than that. However, we try to convey the message to our patients that whatever our patient went through their first-degree relatives should undergo as well wherever they live. If they are obviously close to here or they want to travel to M. D. Anderson, we always welcome them in our clinic, and the testing is a little bit easier because now we know which gene and where the mutation is. So the family members are just tested for that specific mutation and will not undergo the whole gene sequencing. That makes a difference in terms of the cost and the insurance

Andrew:

I see. So, Jan, just a word from you. And that is, so here your daughter's aware of all this and she wants to get tested. Now, I know you had - your sister was tested, your dad was tested, your sister, you. There were some other family members who were tested and it was negative, right?

Jan:

Correct. Yes.

Andrew:

So it's not always, and there's this 50 percent chance in first-degree relatives. So what would you say to people if they are tested positive on communicating with other family members to say, Look, here's what happened with me, I would urge you to look into this for your own benefit. How would you coach them on that?

Jan:

I would say it's critical. My dad has a cousin who had breast cancer and didn't tell anybody she had breast cancer, and we were unaware that someone else in his generation presented with the cancer, and that would have been very helpful information on the front end to know what our cancer risk was when we had our initial genetic assessment, our risk assessment. So I think it's really important that you share your genetic profile when you have concerns with your family members who could also be affected. Because it will change perhaps the course of their decision making in terms of getting genetic counseling themselves.

Andrew:

Yeah, I'm a big believer in that too. One other question for you, Jan. At the time of your sister's diagnosis you were all living in Minnesota, and you later moved to Houston. Why did you come to M. D. Anderson?

Jan:

This one woman that we met who was in chemotherapy who was terminal, my sister asked her what she would have done differently. She lived in Nevada at the time of her initial diagnosis, and she said she would have gone to M. D. Anderson for a second opinion. And so my sister made the decision to go to M. D. Anderson for a second opinion, and they found that her cancer was more progressed than had originally been diagnosed in Minnesota. So it changed her treatment protocol considerably. And that's why she decided that the best care she would get and be most comfortable with was at M. D. Anderson. And she moved here for a year, and my mom and I tag-teamed coming down to take care of her. And we had great care here.

Andrew:

And things have worked out for your sister, too.

Jan:

They have, yes. She's cancer-free.

Andrew:

Yeah, that's so neat. Well, what would you say then, Jan, as we wrap up, to people about pursuing the genetic question if they have a family like you where, as you find out, there are a lot of people with cancer and with breast cancer or maybe it's ovarian cancer too, what would you say to them as far as, let's say, pursuing it with the genetics program at M. D. Anderson?

Jan:

You have nothing to lose by gaining information. The genetic counseling program is so thorough and it will give us so much information. Nobody will pressure you to make any kind of decision. You'll have the information, you'll have the facts, and then you're prepared to make the decisions that are best for your own health. Some people may proceed to get genetic testing, some people may not. But even if you proceed with the genetic testing you have a 50 percent chance possibly of getting a negative result, which my cousins did. I had three female cousins who tested negative, and all this anxiety this underlying anxiety they had about getting breast cancer was alleviated. So you have everything to gain by getting the information.

Andrew:

Well said. Well, we wish you all the best and certainly for your daughter too, right?

Jan:

Absolutely. Absolutely.

Andrew:

May well be negative and that would be good news.

Jan:

That would be good news.

Andrew:

Very good information. Yeah. There you go. Thank you, Jan.

And, Dr. Banu Arun, I'll give the final word to you. It must be very satisfying that you have your group at M. D. Anderson, the clinical cancer genetics program, where you can work together with people who have this concern and get them as much information as available so they can make sound decisions.

Dr. Arun:

Yeah. It's indeed very fulfilling for me to have a lovely group of clinic nurses and genetic counselors and our surgical colleagues, and especially our patients who come and want to learn. And, as Jan mentioned, it's really a no-pressure

environment. We love to share the facts and information and help our patients making the best decision, the best - what is best for them.

The message I want to convey is that if there are young individuals in the family affected with cancer that they should share this with their healthcare provider. It can be a gynecologist, it can be a primary care physician or internist. And it really doesn't matter if it's the maternal or paternal side. Paternal side is as important. And then maybe consider genetic counseling if their physician or healthcare provider thinks it's appropriate.

Andrew:

Okay. Great information. We've gone a couple of minutes over, but it's been time well spent. I want to thank Dr. Banu Arun who is with us who is the co-director of the clinical cancer genetics program at M. D. Anderson and a breast medical oncologist, and Jan, who's talked about her family history very openly to help all of us.

In two weeks, November 6, we'll be back with another program. This one will be on advances in the treatment of myeloma. And there have been advances. And remember we've got this vast library of programs with leading cancer experts and people who are very inspirational, as Jan is.

Thank you so much for being with us. I'm Andrew Schorr. Remember, knowledge can be the best medicine of all. You've been listening to Patient Power brought to you by M. D. Anderson Cancer Center.

Please remember the opinions expressed on Patient Power are not necessarily the views of M. D. Anderson Cancer Center, its medical staff or Patient Power. Our discussions are not a substitute for seeking medical advice or care from your own doctor. That's how you'll get care that's most appropriate for you.