

[MUSIC PLAYING]

**LISA KENNEDY** In my other life that still continues, I'm an oncology nurse practitioner. So I try to get in most Fridays-- not today--  
**SHELDON:** to be back in the infusion center to be working with patients and survivors.

And it came to me probably, well, probably about maybe nine, 10 years ago-- I've been in the same center for 20 years-- that at Huddle, I was hearing about patients coming back again with another cancer.

And it was just kind of extraordinary to me, because we have that process-- maybe you do in your center-- where when people finish a treatment plan we have them ring the bell or we take a picture and maybe give them a certificate, and they're done with their treatment and we kind of move them into the realm of what we now know as survivorship, something that we've developed and are continuing to develop now.

And I started reading more and more about why were people having second new cancers, or third. I even had a patient with four primary cancers. It seemed extraordinary to me.

So this has been something I've been talking about and people have had to listen to me about for a while, so thank you for inviting me to talk about it. And what we're finding is now there's more literature to help guide us understanding what it means to be a cancer survivor, and what it means to take care of cancer survivors and make sure they get the surveillance and the education that they need so that they can take better care of themselves.

So today we're going to talk about cancer prevention and survivorship, something sort of an oxymoron. When I first started talking about it people would say, well, they already had cancer. So let's kind of talk about what does cancer survivorship look like in the United States. And these are probably some numbers you know already.

We have many, many and a growing number of cancer survivors, thank goodness. We're doing a better job. We're screening. We're finding cancers earlier. We're treating cancer more successfully. And our survivors are aging.

So the vast majority of those 15.5 million survivors in the United States are over the age of 40. So when you look at these numbers, you'll look down and you'll say, gee, 60% of them are over the age of 65. So we have a large and growing population of aging cancer survivors who often have other issues associated with co-morbid conditions, risk exposure for many years that can be contributing to the incidence of a second cancer.

Luckily, as you see at the bottom, only 1% of our survivors are in the 0 to 19-year-old age bracket. That's because only about 1% of cancers are diagnosed in that age group, thank goodness.

So you're going to hear Deb Mayer talk later today about the tsunami of cancer survivors. But I'd like to focus on the tsunami of aging cancer survivors.

As you may know, age is the number one risk factor for cancer-- not a thing we can do about it. Every day we wake up, we're one day older. But thank goodness we're here.

If you look at this aqua purple green and then red and you see what's happening here, that group-- not the blue-- that group is that over-50s who will be having a cancer diagnosis. Look at that proportion of all cancer diagnoses. So it's really in that older age group where we're seeing a first cancer diagnosis.

The dotted horizontal line that you see is actually the year at which the first baby boomers hit 65 years old. So you can see, we're just kind of growing and growing as a group. But we're also seeing-- and I can say that, because I'm a baby boomer-- but you can also see why the majority of our cancer is occurring in an older-age population.

By 2040, it's estimated we'll have over 26 million survivors in the United States after a cancer diagnosis. Fantastic, right? We're doing all the right things. We're finding cancer earlier. We're treating it. We're treating pre-cancers now, right? We're finding cervical changes or colon polyps during routine screening and colonoscopy.

So we're actually, hopefully, preventing many of these from becoming cancers. But we'll have this growing number of cancer survivors in the United States. And Deb Mayer will talk more about what it means to care for them.

The other good news is that the five-year survival rates have increased for three decades now, even more so in blacks than in whites. So we're seeing an overall increase in survival. In the United States last year there were about 1.7 million new cases, and here in Pennsylvania about 77,000.

What happens if lightning strikes twice? No cancer survivor ever expects they're going to get another primary cancer, right? I've had some of my patients say to me, well, I already had cancer. It already happened. And they ring the bell and they feel like that's the end. And goodness, don't we all wish that that was the truth?

I wish I were here to tell you that for some of our survivors that that's not going to be the truth, and that they will have a second cancer. And it can be as high as 25% depending upon the age and type of cancer will have a new second, third, or fourth malignancy.

And the first study that was done using SEER data from 1973 to 2000, they thought the incidence was about 7% of cancer survivors would have a new cancer diagnosis. But they started to see some patterns, even by looking at that data, where young women who had mantellar radiation for Hodgkin's lymphoma, about a third of those women developed breast cancer by the age of 50 because of the radiation in the field.

In a recent paper that came out just last fall, the SEER data was looked at again for five years between 2009 and 2013. And they found 765,000-plus incident or sentinel primary cancer-- so the first cancer. But they also found in that group that they'd had another 141,000 where this was a second or higher-order cancer-- so a new cancer diagnosis.

The majority of these cancers, as you can see here, 25%-plus, were in the 65-year and older group. And I'm not just talking about right breast cancer and then a left breast cancer. We're talking about other cancers. Let's look at what those were.

In that SEER dataset, what they found the most common first cancer, sentinel cancer, associated with a new cancer diagnosis were the leukemias-- so the myeloid and the monocytic leukemias. Cancers of the anus, anal canal, and rectum followed by the cervix, vagina, and vulva, and then the lung and other respiratory cancers.

So you can just see by seeing these what were the biggest risk factors-- prior cancer treatment in the case of cytotoxic drugs for leukemias; viral infections, particularly HPV and anal and cervical cancers; and of course, tobacco exposure.

In the over-65 age group, the most prior cancers were actually in another site. And we'll talk about why that might be happening.

OK, we're all getting older. I already talked about that. Not much we can do about that one. What are some of the other underlying risk factors? Hereditary risk, and even viral infection like HPV, or other viruses that we'll discuss; treatment late effects from chemotherapy and radiation therapy; and then preventable causes of cancer that may be related more to health behaviors, like tobacco exposure, obesity and weight, sun exposure and UV light exposure, exercise and physical activity, alcohol, and environmental exposures.

So what do we know about heredity? I won't even talk about age, because luckily if we're here, we've got another day. So there's nothing much we can do about age, but we can identify that as a population.

What we do know is heredity counts for about 10% of all cancers. And as you can see here and you know from a lot of discussion in our world and publicly about BRCA mutations, as you can see in this pedigree, this is where we have been learning a lot about hereditary cancers. And here's one with a BRCA1 mutation in the family.

But we are also gaining more clues about when should we have a flag go up about increased hereditary risk for our patients. Currently these are the sort of clues that we should be looking for when we're deciding whether or not to be doing a full genetic testing with a whole panel or particular targeted panels. So a cancer in two or more close relatives on the same side of the family, early age at diagnosis-- so those under 50. And as you know, that's not common, from that colorful rainbow chart I showed you before, that the under-50 cancers, thank goodness, are uncommon.

But it should put a flag up for us as clinicians and people who care for survivors that there's something we need to be watching. Bilateral or multiple cancers. Triple negative breast cancers. Multiple primary tumors in a cell for the immediate family.

A constellation of tumors that could be consistent with a hereditary syndrome like breast and ovarian cancer with a BRCA1, BRCA2, or the colon and endometrium with the Lynch composite of genes. Rare or unusual cancers, like male breast cancer. More than 20 colon polyps-- so that would be something that's found incidentally on a routine colonoscopy. Or there could be a family history of-- I always say it wrong, right? Because it's too long. Huh?

**SPEAKER 2:** Lynch syndrome.

**LISA KENNEDY** Lynch syndrome. Let's do that. That's much easier than saying that big long one, isn't it? Thank you, Jim. Specific  
**SHELDON:** ethnicity-- I think the Ashkenazi Jewish ancestry is one we're all aware of. But I think we have to start thinking also about other ancestry.

And evidence of autosomal dominant transmission-- so that's that equal transmission between men and women that then it skips a generation, and every child has a 50/50 chance of getting it.

So we know from the genome sequencing that we have 30,000 genes in the human genome. And I have here in this blue table some of the genes that we know where mutations take place so that they're high-penetrant genes where there's an increased susceptibility to cancer.

But having been at the FDA just last month and heard them talking about whole genome sequencing, there are many, many-- more than 70,000 variants on these whole genome panels-- where we don't know what they mean yet, what they nicely call VUS, or variants of unknown significance.

My sense is we're probably going to learn more and more as we do more genetic testing about where these hereditary patterns occur and what these mutations, these variants mean for hereditary risk.

In addition, sometimes we have multiple genes that can cause increased risk for a single cancer. And certainly, breast cancer is a good example of that, where you can have all these different genes that you see in the gray petals around the breast cancer that can influence breast cancer risk.

On the other hand, we also have multiple cancers that can be associated with a mutation on a single gene, like the TP53, where numerous cancers can be associated with one genetic mutation.

For people who are identified as having inheritable cancer syndromes, their lifetime risk is often greatly elevated above the normal population who do not have these mutations. So for example, in the pink here on the top box you see that if there is a mutation in breast and ovarian cancer genes like BRCA1 and BRCA2, they have up to an 87% lifetime risk of having breast cancer. Or in the blue bar, for those with a Lynch syndrome-- the MLH1, MSH2, and so on-- up to 99% lifetime risk of having a colon cancer in their lifetime, and other cancers.

So how are we going to go about capturing this group of people, probably a growing group of people where we can actually identify the genetic mutations that put them at higher risk? Well, we have to be using those clues I showed you so that we're starting to look for those people with their first cancer and saying, these are some of the risk factors that they have, and do they need genetic testing and counseling?

So we need a risk assessment process to identify them. And that has to happen beginning in the clinical situation. It doesn't happen at the genetic counselor, because not all people see the genetic counselor. So we need to learn about that so that we can identify our patients.

At that point we'll be able, either through ourselves or through trained genetic counselors or advanced practice nurses who are doing genetic counseling, to collect a family pedigree and decide if genetic testing is warranted. This would include, of course, if they should have pre- and post-test counseling, which is always essential whenever we're doing genetic testing.

Because we have that 70,000 variants of unknown significance, many patients will come back with these VUSes on their test results, and it can be very alarming and anxiety-producing for not only patients, but their families. So we have to have expertise in genetic counseling and have those people available.

Of course, the star here is the need for regular updating of family history. This should be occurring across cancer survivorship so that we understand the family history and what's going on so we can better help our patients. These are just a couple of resources at the bottom too that you can look at for assessment.

So what happens in survivorship that isn't related to hereditary syndrome, that other 90% of patients? Well, as we age we collect somatic mutations. We continue to have exposures across our lifetime, carry on with our normal behaviors, and we start to gather more and more mutations of our genetic material.

We have more exposure to risk factors in our environment. And if we're survivors, we may well have had chemotherapy or radiation therapy. So we need to be very careful when we're assessing our patients in survivorship so that we're actually tailoring their survivorship to make sure that we're not only surveilling and following them with screening tests but we're also making sure that we're helping them do the best job.

Our patients who come back in-- well actually, even with the first diagnosis one of the first things they say is, what did I do to get this cancer? What can I do differently? And even for some patients, it's their families who say, I don't want to have this happen to my family. What can we do as a family?

So it's really not just about a patient, is it? It's not just about a survivor who's had a cancer diagnosis. It's about helping families as well.

So we need to be looking. So what are those characteristics, such as age at diagnosis-- which we've said is the younger is something where we have a clue that maybe something else is going on. What they've had for previous cancer treatment, and thinking about long-term effects. And by the way, we probably have not much of any idea what the long-term effects are for immunotherapies yet. We're just barely into that world, and so we're not seeing what the long-term effects are going to be. But we're going to have to watch that as well.

So we do have some information about long-term effects of cytotoxic chemotherapies and radiotherapy, but we really don't know yet what's going to happen with immunotherapies.

But there are certain risk factors and co-morbidities that may be associated with increased risk for a second or subsequent cancer, and behavioral and lifestyle factors that may actually be in the control of patients to take charge of. We're going to talk about those.

We need those survivorship plans that incorporate the surveillance recommendations, and more communication plans. You can call them treatment summaries, survivorship care plans-- whatever you want to call it, we really need to work on that communication between the oncology team and the primary care team to make that more seamless transition, and also improve the care for our patients. And finally, as I said, a hereditary risk assessment.

So what are these continuing risk factors that could be setting patients up for another cancer? Well, guess what the green is, right? Tobacco. Tobacco, obesity, and pathogen exposure. Just like we saw that next SEER dataset, the most recent one, is that these are the ongoing issues, some of which patients can change and some of which they can't.

These lifestyle factors may be associated with up to a half of all cancers. So tobacco, obesity, lack of exercise, sun exposure, and alcohol intake-- so things we don't often want to talk about or kind of own. And certainly, it's often hard to get patients to change. Anybody who's worked in research and tried to get people to change their behaviors, it's very difficult. But we need to talk about it. We can't give up on this.

Number one, we can't give up on tobacco. I know, I know. We've been talking about it for 40 years, but we can never give up on it. A third of all primary cancers are caused by tobacco use. And 62% of all cancer survivors have been exposed to tobacco. So it's not just about the person who has had a cancer. It's also about the family nearby who may also be affected by tobacco exposure.

So what do we want to do? What are our goals? Well obviously, helping our patients avoid all tobacco products would be front and center. I saw today a study came out. And there's this sort of trend I see among my patients-- we have a lot of lung cancer patients, tobacco exposure-- and they're saying, well, if I vape, maybe I can quit. What they found today is that actually, vaping made it even harder for smokers to quit.

So that was a study that just came out this week. So we have a lot of work to do there. We want to encourage the smoking cessation.

We want to be scanning our patients. We have new guidelines for chest CT for patients at high risk. But in a study published in 2012-- and I wish I had a more up-to-date version of this-- only 2% to 4% of eligible Americans that actually had a chest CT to scan to see if they had, hopefully, a smaller, earlier stage lung cancer that's more treatable.

We are seeing trends towards more long-term survivorship, thank goodness, due to earlier detection. But I think we can do better here and get our patients who are smokers and have a 30-pack year history into our screening programs.

Obesity-- definitely one when I brought this up at home, nobody wanted to talk about this one. Could it be that 20% of all cancers are associated with obesity? Is that possible? But frankly, BMI is not just a strong indicator of things like heart disease and diabetes, it's also a strong predictor of certain cancers, particularly those that are related to hormones and those that are related to inflammation.

Obesity is associated with an increased risk of esophageal post-menopausal breast cancer, gall bladder cancer, kidney and colorectal cancers, and pancreatic and endometrial cancers. There is a group called the American Institute for Cancer Research in Washington. They're very actively involved in talking about a healthy cancer diet. I know that's on your agenda for speakers today, and I think it's a very timely topic.

So what can we do? We can reduce inactivity and control weight by limiting sugary foods and beverages, restricting portion size, avoiding processed meats, eating less red meat-- which I think is so sad, because I think they actually put bacon in there somewhere between red meat and processed meats.

You always take this personally, right? It would be very hard for me to give up bacon. Avoiding grilling meats-- gee, what a shame, right? Who doesn't use a barbecue in the summer? And increasing vegetables to two and a half cups a day, not including white potatoes, is the AICR recommendation, and adding whole grain foods.

In addition to this kind of overlapping are the poor dietary habits where there's too little fiber and too much of these other foods that we just talked about, including salt-preserved food, that actually put us at increased risk for certain cancers. And so again, it's that same healthy diet that you're going to be hearing more about today.

OK, this is the one that always gets everybody going. There was an ASCO policy statement came out in December that has gotten quite a bit of press and was probably one of the most difficult papers for ASCO to put out. And that's about alcohol intake. Both the International Association of Research in Cancer and the World Health Organization classify alcohol as a group 1 carcinogen. It's the same grouping as tobacco.

That's extraordinary, I think. I think when you hear that you go, wow, how is it possible that we're not talking more about alcohol? Right now they're saying about 5% of cancers are associated with excessive alcohol intake. And as you know, often that's confused or sort of co-varies with tobacco intake in our patients.

So what could that be? Tobacco may be associated with excessive alcohol intake. It could be esophageal, pancreatic, oral pharynx. Occasionally lung cancers too, but these three were the most strongly associated.

And for these patients, particularly those with esophageal, head and neck, kidney, and liver cancers-- they should probably never drink alcohol, that it actually is going to increase their risk of a second cancer. So we want to make sure that we're telling our survivors that.

For people who don't have cancer-- since it's Friday night, I don't want to alarm anybody-- they're saying to limit alcohol intake to one drink per day for women and two glasses per day for men. So whether you calculate that on a weekly basis or you do it on the weekend only, I don't know. But everybody always wants to know, well, how much can I drink? Those are the current recommendations.

Pathogens-- that was one we talked about earlier was our number three for secondary cancers. And probably 60% of all cancers are associated with pathogen exposure.

Now of course, we want to reduce exposure and treat infections. But we also want to make sure we're keeping a primary prevention focus here and thinking about vaccination programs and the public health policies associated with vaccination programs, particularly for HPV.

So treating and preventing infection with pathogens-- well, some things we can prevent and some things we can't. H. pylori infections actually account for about a third of all stomach cancers. But we can treat H. pylori infections. And so we should be treating our patients with proton pump inhibitors and antibiotics to decrease their risk of stomach cancers.

For hepatitis and hepatitis B and C, which account for about 80% of primary liver cancers, we want to be treating hep B with antiviral drugs for control. And you know throughout the commercials during the evening news that we have treatment for hepatitis C for cure.

HPV vaccinations-- boy, if we could get boys and girls vaccinated for HPV, we could prevent 70% of cervical cancers and probably 30% of anal, oral, and vulvar cancers. Wouldn't that be something?

And of course HIV-- we want to make sure that we're treating our patients with anti-retrovirals and promoting safe sex practices to decrease their risk of cancer as well.

Insufficient physical activity-- is this when we all get up and stretch? I get the standing desk today. This is actually a risk factor. So it contributes to adiposity-- so obesity. It may be associated with alcohol intake and poor nutrition.

It's associated with a decreased risk-- increased physical activity is associated with a decreased risk of postmenopausal breast cancer, colorectal cancer, and endometrial cancers. And regular exercise can help control weight and reduce cancer-related fatigue.

So the current goals in the latest NCCN guidelines are 150 minutes a week of moderate activity-- and I know you'll be talking about this during your cancer rehabilitation talk later on today-- or 75 minutes of vigorous exercise. And they may have some other recommendations, as well. So avoiding prolonged sitting is right there, and adding in strength training two times a week.

Sunlight and ultraviolet light exposure-- we know this accounts for 90% of all non-melanoma skin cancers. We have to be working and doing better with this. The latest publications that have come out this year are showing a decrease in non-melanomative skin cancer.

And I think it's related to these sort of slip, slap, slop, right? Slip on the clothes, slap on the SPF. And avoiding, of course-- those public health campaigns where we're getting young people particularly out of tanning booths and ultraviolet light exposure-- very important. We can't give up on that.

And for those people with more than 50 moles, getting regular skin checks. It doesn't have to be monthly. But for those who have had skin cancer, it can be that often.

So what can we do to increase our screening and improve our cancer prevention in cancer survivorship? Well, for those with tobacco use, we want to be encouraging, of course, cessation. But for the screening activities, we can promote chest CT, spiral CT for lung cancer screening in our at-risk patients. And work with hygienists and dentists to be doing oral exams, particularly for patients at risk.

If they have an HPV infection, we know that we can use pap smear. It works very well for detecting very early cervical changes that can be pre-cancerous. And routine physical exams as well as, again, oral exams. So working with our partners in oral health and dental care.

Previous chemotherapy-- people who've been exposed to anthracyclines and monoclonal antibodies like trastuzumab may be at greater risk for cardiac toxicity. So we can be monitoring them for cardiac problems with ultrasound or MUGA scans.

And for those who have had cytotoxic chemotherapy, particularly those who have had leukemias and cytotoxic chemotherapy, we want to make sure that we're doing routine blood counts.

For those with previous skin cancer, we want to be looking at screening exams and the frequency of screening exams based on the type of skin cancer, whether it's a melanoma or a non-melanomative skin cancer.

For those with potential hereditary risk, we want to pursue genetic counseling, increase screening as indicated by their mutations, and update their family history regularly.

To treat that risk factor of obesity is that ongoing work with nutritionists and promotion of a healthy balance between intake and energy output, and encouraging patients to have a BMI of less than 30.

So targeted surveillance based on our risk assessments can help direct our screening and our testing and follow-up during survivorship. We can identify patients who might be at a higher risk for a recurrence of their first cancer or a new cancer. Older patients are at a higher risk due to their lifetime exposure and their infections, such as HPV or of course, tobacco and alcohol use.

New cases of CML who have had prior treatment with cytotoxic chemotherapy are at high risk for recurrence--not for recurrence, excuse me. For newer cancers, we want to keep a closer eye on them.

And overweight or inactive adults are at a greater risk for second cancers due to cancers related to hormones that are hormone-sensitive, particularly breast cancer. And we want to be sure that we're encouraging them to have a healthy lifestyle, and building in programs that have a healthy diet, have cancer rehab, have exercise programs.

Many clinical trials do not include older patients or people who have previously had cancer. It's going to be very difficult to see the effectiveness of our interventions unless we include older patients and cancer survivors in our clinical trials.

And finally, cancer survivorship is a teachable moment for people with cancer and their families. As you can see here, I picked the clearance rack for cancer survivor. I would like to not see our patients come back. I would like to see them ring the bell and get their certificate, and take a picture with their nurses and have that be the last time that they have a new cancer diagnosis.

We can target our risk assessment and our surveillance during survivorship so that if we're going to find these new cancers, we're going to find them earlier. And that we can be not only educators, but coaches for our patients for healthy behaviors like healthy eating, like physical activity.

We can encourage vaccination and screening programs so that we don't see those cancer cases related to HPV in the future. And we can collaborate more with primary care providers so that we're understanding what they're seeing in their practice and what we've seen in our practice so that we're starting to work together on survivorship care and taking better care of people who've survived one cancer so they don't have to survive a second cancer.

And those are just some references for you, and some other resources are on your slides as well.