

Welcome to Yale Cancer Center Answers with your hosts doctors Francine Foss, Anees Chagpar and Steven Gore. Dr. Foss is a Professor of Medicine in the Section of Medical Oncology at Yale Cancer Center. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital and Dr. Gore is Director of Hematological Malignancies at Smilow. Yale Cancer Center Answers features weekly conversations about the research diagnosis and treatment of cancer and if you would like to join the conversation, you could submit questions and comments to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. This week it is a conversation about Pediatric Malignancies with Dr. Alyssa Le. Dr. Le is a Pediatric Hematology Oncology Fellow at Yale School of Medicine. Here is Dr. Anees Chagpar.

Chagpar Alyssa, why don't you start by telling me a little bit about yourself and what it is exactly that you do?

Le I am a local native, born and raised in Connecticut, and basically what I do is work with and enjoy taking care of my patients. As you said, I am a Pediatric Hematology/Oncology Fellow and what that consists of is taking care of patients in our clinic as well as on our floor who get admitted for any sort of reasons, whether it is for treatment or fever, and then I also on the side participate in some research programs and I am doing some clinical work with some mentors over at Yale, so my time is pretty full.

Chagpar That is great, tell me a little bit more about what exactly pediatric hematology/oncology is? I understand that it is working with kids, but what kinds of cancers do these kids present with?

Le Pediatric hematology/oncology actually encompasses a lot of different illnesses and diagnoses, so in terms of hematology, that is related to blood, so we see patients with anything from anemia to problems with their platelets, whether they have problems with bleeding or bruising and then oncology is what we deal with quite a bit and that is cancer. The most common cancer that we see is something called acute lymphoblastic leukemia, ALL, so in terms of presenting, patients can present with what looks like the common cold, a fever and some fatigue. They could have body aches and it is acute in onset, unfortunately, because a lot of times when patients come in parents will say, could we have caught this earlier, but unfortunately, as I said, it is acute, so it comes on pretty suddenly. Patients might be pale, some patients might have bleeding problems and that is one of the biggest diagnoses we see. We see a whole range of other diagnoses from other sorts of leukemias and what leukemias are is cancers of the blood, but then we also see more what we call solid tumors which are what people think of as masses and these can range anywhere from a pediatric diagnosis such as neuroblastoma, that is something common in the younger patients, to cancers that you see in adults similarly, stuff like sarcomas, brain tumors, so we see a whole number of diagnoses.

Chagpar Let's talk a little bit about that, one thing that struck me as you were

describing the most common kind of pediatric cancer, ALL, is that it can present with symptoms that seem like the common cold, a cough, a fever, looking pale. I can imagine if I was listening to this show and

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thinking, well it is snowing outside, my kid has got a cold, but is it a cold or is it ALL? That is going to freak a lot of people out. How can you tell the difference if you are a parent listening to this show, should everybody be worried about their kid having ALL?

Le Definitely not, most kids when they get sick are going to have a cold. These kids sometimes can start out looking like they have the cold but then they get sick much faster. What leukemia is, is a cancer of the white blood cells and when that happens, one of the white blood cells decides that it is not going to die. All of our blood cells have some sort of mechanism that tells them when to die. These cancer cells decide not to die and they start dividing and as they divide, they fill up your blood factory called your bone marrow, and when that happens, it pushes out regular cells, so patients start not making enough red blood cells, which are the cells that carry oxygen throughout your body or platelets which are the cells that help you clot, so patients that have leukemia, they look more pale. They might have abnormal bleeding, sometimes from their nose, from their gums, and have bruises as well, but if a child has a cough, runny nose, that is going to be a cold. These are patients typically presenting with very high fevers as well and they just look very pale, very run down, but if a parent is ever concerned then they should definitely call their doctor, and bring their child in to see their pediatrician.

Chagpar So if a cold is not acting just like a cold, if it is worse, if it is a high fever, if your kid starts getting bloody noses, that is a signal that you need to worry.

Le And looking pale and just not feeling right, but as I said, common things being common, it is going to be a cold. Pediatric cancers really are not that common, so the majority of the kids who are going to get sick, it is not going to be anything to worry about, like leukemia.

Chagpar How common are pediatric cancers? How many children will end up getting a cancer?

Le I do not have exact numbers for you on that.

Chagpar But certainly it is not as common as many of the cancers that we think about, like breast cancer or lung cancer.

Le Right.

Chagpar Pediatric cancers must be far less common than those.

Le They are much less common. Unfortunately breast cancer, prostate cancer,

they are pretty common in the general adult population, whereas pediatric cancers really are not. You can go to some schools out in the community and they will never have a kid who is seen by us or one of the neighboring hospitals whereas I think all of us know somebody who has had breast cancer, who has had colon cancer. I am lucky to say growing up, I did not know anybody with a pediatric cancer and I think a lot of people can actually say that, but I find that when kids do have cancer, it

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does impact a lot of people. It impacts communities, so unfortunately when families or communities find out about a kid having cancer in the community, they get a little more stressed and worried about their own kid, but as I said, luckily, it is not incredibly common. But if a parent believes or is concerned that there is something wrong with their child, they need to bring their child to their pediatrician and discuss it, definitely.

Chagpar It sure does make a difference when a kid has cancer and you know that kid. I have talked on this show before about a very, very close friend of mine whose child ended up with leukemia and amazingly did relatively well, but it still was heartbreaking to think about this kid with cancer, so let us talk about that. When you think about pediatric cancers, I think everyone would agree that it is absolutely one of the most devastating things that we hear about because no child should get cancer and even though it is rare, some do, how do they do with that diagnosis, is the prognosis really dismal?

Le It depends, for instance, standard-risk acute lymphoblastic leukemia, which is the most common, we have cure rates that are 90 to 95%, so obviously a diagnosis of any sort of cancer is going to be devastating to the family, to the child, even to us as doctors, it is always so hard to go in because you are going to change their life by just telling them the diagnosis regardless of the outcome because it is going to be something that they are going to live with. There are other cancers where their prognosis is not as good. Some more solid tumors that have metastasized throughout your body, which means spreading throughout your body, sometimes their prognoses is 35%. There are some brain tumors where prognoses are in the 10s and 20s, so it really depends, but I think that the general theme is, it is absolutely devastating when patients and families hear this diagnosis because it does throw a wrench in everything and your plans and your kids schooling and work and just everything, but for the majority of patients and families they completely rise above it. I always find it so amazing with the really little kids, even if they have very aggressive therapy, sometimes you cannot even tell, they are just being kids, they do not know that they are sick and I feel like that is always a huge comfort for the families.

Chagpar Yeah.

Le Many people they just rise above it and it is devastating at first, but then you do what you have to do to get through it and be there for your kid.

Chagpar Yeah, I keep thinking back to this one pediatric patient that I know personally who is running around and he is playing sports and he has no hair, but he is being a kid. What are the long-term effects? It is great especially in ALL so let's just focus on that for the moment because it is the most common and it is such a blessing that it has such high cure rates.

Le For standard risk, sometimes for higher risk, it might be a little lower, but yeah for standard risks, that is right.

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Chagpar And that is really due to chemotherapy in large part right?

Le Yes.

Chagpar What is the impact of kids getting chemotherapy long term? We have all heard about chemo brain, does this affect cognitive function in adulthood? Do these kids go on to live long healthy, happy, productive lives? Do they go to college? Do they do well in school? Tell us a little bit more about the ramifications of the treatment on their long-term health and long-term prognosis.

Le That is a great question because our treatments are great, but unfortunately, everything that has a positive also has a negative, so the chemotherapy that we use affects some good cells too and can cause some long-term problems. You talked about cognitive, sometimes patients can have a little bit of a decrease in their IQ. Unfortunately with leukemia, it can spread to your spinal fluid, so we have to do spinal taps in which you take some of the spinal fluid to make sure that there are no cancer cells in there and then we also give chemotherapy and it is thought that that could potentially effect some cognition, but not huge amounts. At Yale and throughout the country we have clinics, survivorship clinics, and the one that we have at Yale is the HEROS Clinic, and when patients are done with their therapy, they still follow-up with their primary oncologist but then they also follow up with the HEROS Clinic about once a year and monitor any sort of long-term effects that patients can have. Some of the medications that we give can sometimes cause neuropathy, some numbness and tingling in the toes, some problems walking, and if we are able to pick that up, patients can go for physical therapy. We have a neuropsychologist that works in our clinic and is able to do some screening and if there are any problems that are picked up, we are able to get people the appropriate care that they need. Overall, patients end up having productive lives. I have a wonderful patient who is applying for college soon and she wants to be a pediatric oncologist and I do not think there is going to be anything that stops her. I think she is an intelligent girl, she is doing well in school and that is a great thing for us that we are helping beat this disease and then these kids do go on and lead productive lives.

Chagpar That is awesome Alyssa. We are going to pick up on this conversation and talk more about solid tumors after we take a short break for a medical minute. Please stay tuned to learn more information about pediatric cancers

with Dr. Alyssa Le.

Medical Minute This year over 200,000 Americans will be diagnosed with lung cancer. More than 85% of lung cancer diagnoses are related to smoking and quitting, even after decades of use, can significantly reduce your risk of developing lung cancer. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital at Yale-New Haven to test innovative new treatments for lung cancer. Advances are being made by utilizing targeted therapies and immunotherapies. The BATTLE-2 trial at Yale aims to learn if a drug or a combination of drugs based on personal biomarkers can help to control non-small cell lung cancer. This has been a medical minute brought to you as a public service by

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Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. More information is available at yalecancercenter.org. You are listening to WNPR, Connecticut's Public Media Source for news and ideas.

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined today by my guest Dr. Alyssa Le. We are talking about pediatric malignancies, one of those devastating diagnoses when kids get cancer. We talked before the break about ALL, which is the most frequently diagnosed pediatric cancer, where the prognosis and the treatments are really effective, 95%, that is awesome, but Alyssa, let us talk a little bit more about solid cancers, where I understand the prognosis is a little bit more grim. What is the most common solid cancer for kids?

Le It ranges with age, the most common solid cancer that anybody can think of is possibly a brain tumor. There are so many different types of brain tumors; however, some are benign, some are malignant, so it is hard to say which is the most common. In terms of other solid tumors, age ranges are pretty important when thinking about that, with younger children, one common cancer that we see is something called a Wilms' tumor and with the Wilms' tumor you will commonly hear a mom or grandma or somebody bathing their child and actually feeling a mass in their child's belly. The children look pretty good but the parent feels something abnormal and what Wilms' tumor is, is a tumor that arises from the kidney. We have very good treatments for Wilms' tumor as well if it is not metastatic or if it is just a primary tumor, we actually are able to treat our patients in the outpatient setting and they do very well. I have patients who have completed therapy and are back in school and really enjoying, playing and back to being kids.

Chagpar The Wilms' tumor, is that treated again with chemotherapy or because it arises from a kidney, like a solid organ, does that involve surgery, radiation, how does that work? Are there multiple disciplines treating that tumor?

Le With solid tumors, there normally are multiple disciplines. For Wilms' tumor,

if it is just one at a primary site, surgery is a big component of it, so after a biopsy in order to figure out what the tumor is, if they are able to remove the tumor, then the surgeons will do that and that sometimes comes at a cost of the child losing one kidney but it is okay because people can live with one functioning kidney and then they do get chemotherapy, depending on the type of tumor and how it spread, some tumors, we use radiotherapy for. One of the more common tumors in adolescence is soft tissue sarcoma, so some sarcomas are treated with radiation and that is targeted at where the primary site is. Sometimes, if we cannot get the whole tumor out, radiation is a component of therapy along with chemotherapy, so it really is a multidisciplinary way of treating these patients and we work together very closely with our surgeons with our radiation therapists and oncologists, making sure that we are treating the patient appropriately. We actually meet once a week and do a Tumor Board and discuss any new cases that we have and discuss any cases that we might have questions on, so it is a good way of getting everybody together, and coming up with the most appropriate management for that patient.

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Chagpar Just to clarify, because we were talking about Wilms' tumor and then we also talked a little bit about sarcomas, those are two different entities, right?

Le Yes.

Chagpar Tell us a little bit about how they are different and about their prognosis, does one have a better prognosis than the other? How do they compare to ALL, for example, which is very treatable?

Le We do have good treatments for all sorts of tumors. It is hard to say which one is more treatable than the other because you also have to think about stages, so any disease that has not metastasized is more treatable than something that has, so a stage I non-metastatic Wilms', we have good survival rates, into the 80's and same with sarcomas as well. Unfortunately when cancer spreads it is harder to deal with and harder to manage, but we still do have good outcomes for all of our diagnoses, some unfortunately are worse than others such as when there is metastases, that is when the outcome starts to drop off a little but the hopeful thing is we are part of clinical trials and looking at the best new treatments coming up for patients.

Chagpar A lot of people I treat, in the adult population, sometimes still think of clinical trials as human experimentation and particularly for kids because many parents are very protective of their children. Do you find that they are more hesitant to participate in clinical trials because they do not want their child to be a "guinea pig" or do you find that parents are actually very enthusiastic about clinical trials because one, there are not very many children who get these diagnosis and so this is the only way to advance the field and two, this is a potential option for their child to get tomorrow's therapies today.

Le As we keep saying pediatric cancers are rare, so we at Yale are part of something called The Children's Oncology Group, which is an international consortium of many different hospitals and their patients, and what we do is we follow the children's oncology group protocols. When there is an open study, meaning a study using the backbone of what is the standard care, but looking at a new medication or different dose modifications that has passed through phase I and phase II clinical trials, then we are able to say, we know there is some safety behind it, but we invite our patients to enroll in these studies, for instance, there is one study that was opened recently for rhabdomyosarcoma and it used an antibody therapy, so it was using the same exact background of the medications that the patient would get if they were diagnosed with rhabdomyosarcoma, but then they were given this extra medication to see if outcomes change. I think when you talk to parents about this, some parents are very excited about it, and think wow, maybe this is really going to change the outcome because we know what the outcomes are with the backbone but we are hoping that through the trials, and sometimes they are based on adult trials, and we know that there has been some efficacy with that, there is some promise that our outcomes are going to get better. There are some parents that do not want to be a part of that, but I would say the majority of the parents, if we offer them to be part of one of these open studies, they jump at the opportunity because this is something that can potentially help with the outcome that much more and then also,

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as I said, since we are doing better with our treatments and outcomes there are other studies that we are doing to try to limit some of the long-term outcomes that some of our patients are at risk for, but overall, as I said, we have had really good response rates. If there is a patient that has a tumor that is not responding, sometimes we will also send the patients out to other places that have more phase I and phase II trials, but the majority of our patients that are offered the Children's Oncology Group trials will actually agree to it.

Chagpar I think the nice thing about these cooperative group trials like the Children's Oncology Group is that you are really looking at a national and international consortium, so this is the world's greatest scientists and physicians who are putting their bet on the next great therapy.

Le Right.

Chagpar Can you tell us some recent studies that have transformed the way that you treat pediatric cancers that have risen from clinical trials? How have clinical trials impacted on how you treat patients?

Le With each clinical trial that we use, they see if the new medication that has been used or the new decrease in medication, if that has any change in the outcomes, then if that does, that ends up getting changed as the standard of care. As I said, with rhabdomyosarcoma, they are looking at an antibody therapy, for neuroblastoma which is another cancer that younger children get, there was a

study looking at antibody therapy and now kids are routinely getting antibody therapy because it was showed to be efficacious, so the clinical trials really are helping with moving pediatric oncology even further ahead and I think that is why survival rates have improved dramatically over the past 20-30 years.

Chagpar It is the same thing in breast cancer which I treat where we are finding that clinical trials are giving people what is going to become standard of care tomorrow, giving it to them sooner because we have found that we have moved the field so much further down the pike with clinical trials that then become standard of care and so you keep incrementally bettering therapy. Tell me a little bit more about some of clinical trials that look at limiting toxicity because we talked before the break about the concerns that I think many patients, and certainly many parents may have, certainly if I ever had a child who had cancer, who had to get chemotherapy or any kind of therapy, I would be very concerned about long-term outcomes and I was thrilled to hear the story of the patient of yours who wants to be a pediatric oncologist, so tell me a little bit more about some of those studies, studies that might be looking at neuro protection, protecting their heart and so on so that they can live long and healthy productive lives.

Le To go back in time, if you had leukemia in your spinal fluid or if it was high risk, it was treated with cranial spinal radiation and that proved to really effect people neurocognitively and we have since backed away from that, we now use intrathecal chemotherapy which is a chemotherapy into the spinal fluid, so I think the whole thing behind some of these clinical trials is as you said, to decrease long-term effects, whether it is decreasing doses or getting rid of certain medications. For

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instance, there is one medication that can cause some heart toxicity, so some studies can decrease the amount and dose that we are giving with that. Hodgkin's lymphoma which is the most common lymphoma that we see in pediatrics, it arises in your chest and your mediastinum, and a while back a lot of young women were getting radiation to their chest and this was leading to a huge number of people ending up getting breast cancer later on in life and now they have studies looking at how effective is our chemotherapy and if it is effective enough after a few cycles of chemotherapy we are eliminating radiation from these patients and eliminating that increased risk for breast cancer because the late effects can be traumatic, but unfortunately, one of the late effects of getting chemotherapy is getting a secondary cancer in the future, so that is also one of the things that people have been looking at as well to try to get these patients cured and to have them live productive lifestyles.

Chagpar When you talk about long-term effects in second cancers, I go back to thinking about the HEROs Clinic that you were mentioning, the survivorship clinic for pediatric patients at Yale and just in our last minute, can you tell

us, do those pediatric patients who have been cancer survivors need additional screening for cancer?

Le Depending on what sort of therapy they get, they get different sorts of screening, sometimes one of the chemotherapies can cause problems or cancers in your bladder, so we check their urine. Sometimes there are increased risks for breast cancer, so we do mammograms and MRIs but it is definitely looking at the patient and depending on who the patient is it is very tailored to them.

Dr. Alyssa Le is a Pediatric Hematology/Oncology Fellow at Yale School of Medicine. We invite you to share your questions and comments, you can send them to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC and as an additional resource, archived programs are available in both audio and written format at yalecancercenter.org. I am Bruce Barber hoping you will join us again next Sunday evening at 6:00 for another edition of Yale Cancer Center Answers here on WNPR, Connecticut's Public Media Source for news and ideas.