Welcome to Yale Cancer Answers with your host doctor Anees Chagpar. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it’s a conversation about sickle cell disease and cancer in pediatric patients with doctor Farzana Pashankar. Dr Pashankar is an associate professor of Pediatrics in hematology oncology at the Yale School of Medicine, where Doctor Chagpar is a professor of surgical oncology.

Maybe we can start off by you telling us a little bit about yourself and how you got involved in doing what you do and what exactly do you do?

Essentially I had a really long, circuitous career journey, but I got involved in doing pediatric oncology when I was training in England, after which I did a pediatric hematology oncology fellowship in Canada. And after fellowship, the two areas that I really loved and wanted to focus my career
were sickle cell disease and solid tumors and development of clinical trials and improving care for children with sickle cell disease and cancer, particularly solid tumors. So those are the two areas that I have focused on in my career for the last 17 to 20 years and my passion primarily has been to focus on development of clinical trials for children for certain rare types of solid tumors, and also in bringing new and innovative therapies for sickle cell disease to our patient population. So maybe we can start with that. Is there much overlap between sickle cell disease and pediatric cancers? I mean, do children get sickle cell disease? Does sickle cell kind of lead to cancer or are these just two separate passions of yours that happen to coincide in the same individual? These are two separate passions, and because in Pediatrics we train in both hematology and oncology, these are two passions which developed during my training, but it is not connected in any way in terms
of children with sickle cell disease being more prone to getting cancer or children with cancer more prone to having any issues with sickle cell.

Let’s talk about each of the two in turn and let’s start maybe with talking about pediatric cancers. Any time we hear about children getting cancer, the uniform emotion that people feel is heartbreak. So tell us a little bit more about how you get involved. I know so many medical students come up to me and they say, how can you possibly dedicate your career to doing something that is so heartbreaking, but honestly after doing this for over 20 years this is such a rewarding journey. It is the time that a lot of families are going through probably the most intense and difficult time of their life and to be able to be a part of it and to help them navigate and think about the treatment decisions for their child and to be able to treat their child effectively, honestly, I don’t think there’s a substitute for that. I think it’s so emotionally rewarding. It is also heartbreaking at times. I mean, we do have children who could
have a recurrence and it is a lot of intense time thinking about not only the management but also supporting these families through that. But the relationships I've built with even the children that we've lost, the relationships built with those parents is just unbelievable. And after losing the child, they still think of us as being part of their family. And I think that bond is so valuable and precious. So yes, it can be heartbreaking at times, but it’s also extremely rewarding. And today I would say that we cure about 85% of children with cancer very successfully. So clearly we have done a really good job at trying to make advances and improve the life of these children diagnosed with cancer. And I think that’s such a key point is that whereas many people will think of cancer as a death sentence, now more and more what we’re finding out in a variety of cancers is that really we’re beginning to discover that many of these cancers are treatable and with good outcomes,
but you’re interested in solid tumors, so tell us more about the solid tumors that occur in Pediatrics and what kind of treatments we have to offer these kids. What the prognosis is, and the other thing that I’m always curious about on this show, we spend so much time talking about personalized medicine. The fact that now we’ve begun to really unlock the genomic abnormalities that occur in cancers we’re able to better target these abnormalities. Can we do the same thing in kids and is that resulting in higher cure rates? Great question and a lot to unpack. In terms of solid tumors, they really change across the age spectrum, so the solid tumors that we see in the much younger child are much more embryonal based tumors, such as neuroblastoma, Wilms tumors, retinoblastoma so much more embryonal based tumors, and then as you gradually advance and you’re coming to the prepubertal young adolescence, we start seeing more tumors such as the sarcomas, so the osteosarcoma, the soft tissue sarcomas which have an overlap.
with the adult population as well, and in addition, we see, besides these sarcomas, of course we see Rhabdomyosarcoma which occurs across the age spectrum from childhood onto the adolescent young adult population. So in terms of solid tumors, really the main areas or the main types of solid tumors we see would be the embryonal tumors. As I already mentioned and then sort of the sarcomas and the bone sarcomas. Those are the two big groups of solid tumors that we see. We also see interestingly a lot of rare tumors and one of my particular area of interest has been in rare tumors, and I’ve been very involved in developing clinical trials for these children with rare tumors through the Children’s oncology group, so the rare tumors that we see are things like nasopharyngeal carcinoma, adrenocortical carcinoma, thyroid cancer, which of course can occur in adults but also starts in young adolescence. So we see several of those patients, and now we’ve started seeing some of the tumors that are adult tumors.
earlier in Pediatrics,
such as even colorectal carcinoma. So that’s sort of the spectrum of
tumors we see in pediatric solid tumors.
I’ve not included brain tumors because
we almost separate brain tumors,
just like we do leukemia and lymphomas.
And I don’t treat brain tumors.
I focus on the extracranial solid tumors,
so those are the ones I’ve just mentioned
with regards to the treatment and
the role of personalized medicine or
immunotherapy in treating these cancers.
Again, the role of personalized medicine
is very well known in the adult oncologic world.
In Pediatrics we still do profile
most of our patients with solid tumors,
and there have been tumors
which have happened recently and
there’s a lot of excitement on
tumors where there’s a specific
targeted drug that is available,
and one classic example of this is the
TRK fusion cancers
where there is a specific drug
that has been developed with
excellent outstanding results.
So TRK fusion cancers can occur
from infants where you
have infantile fibrosarcoma’s that occur in
the first year of life,
and then TRK Fusion sarcomas are also seen in older adolescents and young adults, so in specific situations we do also use what the adults use much more frequently, which is a very targeted therapy based on tumor profiling.

How does prognosis vary amongst the pediatric cancers? Because you’ve kind of mentioned this whole spectrum, we have the leukemia lymphoma as one separate group and brain tumors as another separate group. But even within the non cranial solid tumors in pediatric populations we’re looking at everything from eye tumors, retinoblastoma’s to kidney tumors like Wilms tumor to sarcomas. So how do these vary in terms of prognosis, and have we seen a shift in terms of moving towards being able to treat these children better with new therapies? Yeah, so it is a whole spectrum. As you’ve already mentioned, I think we’ve done really well in some of these tumors. For example, in patients with retinoblastoma you have an excellent outcome,
particularly now with intra arterial chemotherapy delivering very focused chemotherapy.

We’ve also reduced the issue with long term side effects giving systemic therapy.

Treatment has evolved significantly over the last maybe 10-15 years with the development of an antibody called dinutuximab which focuses on the GD2 which is expressed by neuroblastoma cells.

So now we have this multi modality therapy that we do in addition to chemotherapy, surgery, and radiation.

We also have this immunotherapy that is done particularly for those who have high risk neuroblastoma in Wilms tumor, our outcomes have always been excellent, and we’re continuing to improve those outcomes.

And similarly I didn’t mention germ cell tumors, which honestly, is a really strong interest of mine, so we do very well in germ cell tumors.

And in all these four categories, I would say we have excellent outcomes.

In sarcomas, I think we still have challenges.

And the challenge really depends on...
the time of presentation, what the staging is, and for patients who present with metastatic sarcomas, be it Rhabdomyosarcoma or osteosarcoma, we still are challenged in terms of long term outcomes at times, and we have numerous clinical trials looking at different options which this is where we are looking to improve our outcomes by newer therapies. And as you mentioned, personalized therapies are so important to really try to get people involved in clinical trials to really move those therapies forward, it’s really great to hear that we’re moving in the right direction, at least for the majority of solid tumors in kids. We’re going to take a short break for medical minute and then learn more not only about pediatric cancer, but also delve into your interest in sickle cell disease right after this break. Please stay tuned for more with my guest Doctor Farzana Pashankar. Funding for Yale Cancer Answers comes from AstraZeneca, working to eliminate cancer as a cause of death. Learn more at astrazeneca-us.com. Genetic testing can be useful for
people with certain types of cancer that seem to run in their families.

Genetic counseling is a process that includes collecting a detailed personal and family history or risk assessment and a discussion of genetic testing options.

Only about 5 to 10% of all cancers are inherited, and genetic testing is not recommended for everyone.

Individuals who have a personal and or family history that includes cancer at unusually early ages, multiple relatives on the same side of the family with the same cancer, more than one diagnosis of cancer in the same individual, rare cancers or family history of a known altered cancer predisposing gene could be candidates for genetic testing.

Resources for genetic counseling and testing are available at federally designated comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital. More information is available at yalecancercenter.org. You’re listening to Connecticut Public Radio.

Welcome back to Yale Cancer Answers. This is doctor Anees Chagpar.
and I’m joined tonight by my guest Doctor Farzana Pashankar. We’re talking about sickle cell disease and cancer in pediatric patients. Before the break for any of you who missed it, there is no connection between sickle cell disease and pediatric cancers, except that our guest happens to be an expert in both.

Right before the break we were talking about pediatric cancers and the fact that some kids get solid tumors. This must not be very common, right? How common are pediatric cancers? Especially the non hematologic cancers? I think of course each one of those cancers is overall pretty rare and even leukemias, which are the most common pediatric cancer we say happens one in a million. So the solid tumors are much rarer and each one has a different frequency, so it’s hard to give a number for all of them combined. This is very interesting because as you may know, there’s a lot of interest in rare cancers, and the NIH was looking at developing a rare Cancer Institute in order to try and improve the outcomes in these rare cancers.
And when we were looking at defining what rare cancers is, it's very clear up front that every pediatric cancer is rare in that sense, but the solid tumors, particularly, many of the tumors we discussed are even much rarer than leukemia, which is already pretty uncommon. And I'm sure that every parent out there thinks that their child is one in a million, but really wouldn't want their child to be one in a million in this particular circumstance. And one of the questions that comes up and you mentioned that you had an interest in clinical trials, especially in rare tumors, is that so much of the data that we get that leads to best practice dictates how we treat cancer comes from clinical trials. And when you have these tumors that are so rare that are one in a million, how on Earth do we get the data to actually know what’s best practice to treat our children, and for every parent going through this,
I mean that is their deepest anxiety. That's a very good point and I think what I must say is that in pediatric oncology we have honestly and I am not taking all the any credit for this, but we have done an amazing job at being able to conduct clinical trials and the way we've done this is through the development of a consortium called the Children's Oncology Group, which really has about 230 institutions across the United States, Australia, New Zealand and Canada and the beauty of this is that as a group then we can, because each individual institution will only have a patient very rarely with a particular type of cancer, we can bring all of us together, and we can then get the numbers to be able to conduct a clinical trial and more importantly, conduct some randomized clinical trials to be able to answer the question of which treatment is the best and most appropriate for these rare cancers. So the children's Oncology Group has existed for a while and we have designed clinical trials on each type of pediatric cancer,
but more recently what is happening that I am very happy to be involved with is that we are now looking at international collaborations. So for example in germ cell tumors because germ cell tumors are again so rare even in the US and Canada and Australia we cannot have the appropriate numbers to do a randomized trial. So currently we are conducting two trials, one for low risk and intermediate risk, and one for high risk. So we’ve collaborated with the UK with India with Australia, New Zealand and we are all running the same trials, so that again we can bring all this information together and be able to make advances for future patients. I think that’s so critical. You know one of the issues that we face in adult tumors, however, is, although all of us know that clinical trials are the drivers of improved care it’s how we make practice changing discovery, is that still there is a reluctance on the part of some patients to participate in clinical trials.
accrual is somewhere South of 5%, and with children I mean I can imagine that parents have obvious anxiety when you talk about clinical trials, but I understand that the rate is much higher for accrual to these clinical trials. Honestly in Pediatrics, the rate is significantly higher, and I think part of the reason at least at Yale, of all the patients eligible for a trial, because sometimes, of course a trial may not be available for that particular type of tumor. at least at Yale, of all the patients eligible for a trial, because sometimes, of course a trial may not be available for that particular type of tumor. But for any eligible patient, we enroll up to 80% of the children who are eligible for a trial. When you're taking care of your child, who has cancer I think the motivation from the parents is very different than maybe the motivation for yourself. I'm not sure, but clearly we all do go above and beyond for our kids. Then we probably even do for ourselves. And I think that that desire especially when we're talking
about rare diseases is so important. And I think the other piece is that parents sometimes have trepidation about what is the right answer to treat my child, especially when all of these cancers are so rare and clinical trials gives you some modicum of this actually might be best practice because, as you say, all of these professionals get together in designing these trials, so they've put in that brain trust of, you know this is potentially best practice or best practice versus what best practice will be and we want to see which is best for patients who are not candidates for a clinical trial where there still may be questions about what is best practice. How do you reassure patients and parents that this really is the way to go? Are there still collaborations where you get together with a consensus, either nationally or internationally, to figure out what might be best practice for these patients? Absolutely. I think one thing is the standard of care in many cases.
But in many cases there is no proper standard of care, but the beauty again of having these close collaborations working together on trials means that we have a really great phenomenal community of oncologists that you can call upon to discuss and get guidance on in really rare cases. So I think that is a really fulfilling part of being able to connect with friends and colleagues across the country, across the world to be able to discuss some difficult cases. What is really fun is we’ve now developed these virtual International tumor boards for some of these really rare cancers, so we have an international tumor board for patients with hepatoblastoma, where experts from across the country meet once a month and you can put in a case and they will review everything and discuss it, just like we do at a local tumor board. Similarly, we have a rare tumor board which is across the country, so again, people do go above and beyond to try and put in their time and effort to bring their
thoughts and their experience to help kids across the country and across the world.

I love the fact that there is such humility among pediatric oncologists to really collaborate with each other and to figure out what’s the best for this child. Which is so important and so heartening for parents going through this.

Now I did promise that we’d spend at least a few minutes talking about your other passion, which is sickle cell disease and sickle cell disease is still rare, but presumably less rare than pediatric cancers.

Is that right?

I think it is rarer than pediatric cancers, and in the US with a changing demographic, we have patients of many different ethnicities who can also have sickle cell disease so it’s definitely something that we see in Connecticut. 24 to 26 new diagnoses of sickle cell disease each year and about 600 new patients with sickle cell trait per year.

Talk a little bit about sickle cell disease and the problems that people can run into.
I mean, when people think about cancer, you really don’t need to say anything more than cancer for it to strike the fear of God into some people. But what problems do people with sickle cell disease run into that are problematic and talk a little bit about some of the new therapies that are out now? So sickle cell disease interestingly, is the first single gene disorder that was described over 120 years ago. It is a lifelong chronic disease that obviously you inherit from your parents and the hallmarks of sickle cell disease are these painful crises, which really mean that patients with sickle cell disease can come into the hospital or have pain at home several times a year. These chronic VS occlusive crises can also lead to multiple complications, including stroke and acute chest syndrome. You can also have a lot of long term chronic morbidity because of this ongoing microvascular occlusion that happens in all your organ systems. So patients with sickle cell disease can have long term problems with their kidneys,
leading to sickle nephropathy. They can have problems with their liver leading to sickle hepatopathy. They can have sickle retinopathy, so it’s a disease which has acute complications which brings someone to the hospital. But also has ongoing long term chronic disease burden which continues to affect pretty much every organ system in their body. So it is a disease where you have to pay attention to obviously the acute management during pain, crisis, stroke, etc. but you also have to take care of these adults and children for preventative care. To make sure that you are monitoring for these long term complications and you are intervening when feasible. But the good part about sickle cell disease or the exciting part currently is that we have a lot of new therapies which have come about in order to improve not only the pain crises, the FDA has now approved several new drugs besides hydroxyurea, which was the only drug available for a long time to modify sickle cell disease and the most exciting thing really is the
advent of bone marrow transplant, which is currently the only curative option for sickle cell disease but also gene therapy and many of you might have seen data on gene therapy, some case reports of gene therapy for sickle cell disease which is exciting and we are looking forward to that becoming more streamlined in the next few years.

Dr. Pashankar is an associate professor of Pediatrics in hematology oncology at the Yale School of Medicine. If you have questions the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at yalecancercenter.org. We hope you’ll join us next week to learn more about the fight against cancer here on Connecticut Public radio. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital and AstraZeneca.