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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 the care of adolescents and young adults with sickle cell disease with Doctor Cece Calhoun.

Dr Calhoun is an assistant professor of medicine and hematology and assistant professor of Pediatrics in hematology at the Yale School of Medicine, where Doctor Chagpar is a professor of surgical oncology.

Cece, maybe we could start off by you telling us a little bit about yourself and what you do.

I like to call myself a lifespan hematologist, and both my clinical and research interests center around the care of young adults with sickle cell disease as they transition from pediatric to adult care.

We know it’s a really high risk time for them. And so all the work that I do both in the clinic and in the research setting is about making that process better.
Is sickle cell disease a cancer?

Tell us more about what exactly sickle cell disease is and why it’s being seen by an oncologist?

That’s a great question, so actually sickle cell disease is an inherited condition of the red blood cells and so many people are familiar with anemia and conditions of that sort, which affect red blood cells and hemoglobin.

And that’s what sickle cell disease is a condition of, and it’s genetic. So patients are born with it, and what it manifests as is a normal red blood cells are kind of squishy. I like to think of them as Jelly doughnuts because I like food.

But when you have sickle cell disease because of a genetic mutation your red blood cells are not squishy and malleable, they can be really stiff and misshapen like a sickle. They can be shaped like a sickle or a banana, and so if you think of your blood cells as pipes, imagine if you had your Jelly doughnuts kind of going through those pipes, bouncing off the walls,
taking oxygen to where it needs to go, and you replace those cells with sticky stuff, fragile misshapen red blood cells like sickle cells that are scratching up the red blood vessels sticking together, causing blockages, impeding flow, and then you can imagine all the complications that patients face. Most saliently or what patients have to really deal with is a lot of pain. That’s the thing that brings them to the hospital. And acute meaning an unplanned basis, but any part of our body where there are blood vessels, those misshapen cells can get clogged up in those blood vessels and cause problems. It’s important for patients with sickle cell disease to have regular care by an oncologist who also understands hematology, to make sure that all their organs are in tip top condition and that we treat anything before there’s a problem. Now, I would think that if you’re a pediatric patient and this is an inherited condition,
0:03:17.39 –> 0:03:19.638 you might have a sense of whether or
0:03:19.638 –> 0:03:21.8 not you have sickle cell disease
0:03:21.87 –> 0:03:24.228 based on whether your parents did.
0:03:24.23 –> 0:03:26.988 But somebody had to start with the
0:03:26.988 –> 0:03:29.049 genetic mutation to begin with.
0:03:29.05 –> 0:03:30.874 So how many of your patients
0:03:30.874 –> 0:03:32.773 actually know that they have sickle
0:03:32.773 –> 0:03:34.633 cell disease from the time that
0:03:34.633 –> 0:03:36.72 they were born
0:03:36.72 –> 0:03:39.942 and how many of them present to you acutely?
0:03:41.67 –> 0:03:43.82 In the United
0:03:43.83 –> 0:03:46.766 States we have the benefit of the newborn
0:03:46.766 –> 0:03:49.587 screen that all babies born in hospitals,
0:03:49.59 –> 0:03:50.965 when they
0:03:50.965 –> 0:03:52.934 get their heel poked and get that
0:03:52.934 –> 0:03:54.548 little spot of blood that can test
0:03:54.55 –> 0:03:56.476 for a variety of genetic conditions
0:03:56.476 –> 0:03:58.165 and sickle cell disease is
0:03:58.165 –> 0:03:59.557 included in those conditions.
0:03:59.56 –> 0:04:02.71 So if a child has an abnormal newborn screen,
0:04:02.71 –> 0:04:04.758 oftentimes the pediatrician will
0:04:04.758 –> 0:04:07.675 refer them to a hematologist for
0:04:07.675 –> 0:04:09.45 further evaluation and work up.
0:04:09.45 –> 0:04:11.628 And sometimes, even if it’s abnormal
0:04:11.628 –> 0:04:14.41 to show sickle cell trait,
0:04:14.41 –> 0:04:16.45 which means that you don’t have the disease,
0:04:16.45 –> 0:04:18.028 but you can be a carrier,
0:04:18.03 –> 0:04:19.85 and if your partner has the disease,
0:04:19.85 –> 0:04:21.369 you can have a child with sickle
0:04:21.81 –> 0:04:23.706 We can figure that out from
So these days we know pretty early on which is critical to the survival of our young children or infants and in other countries the newborn screen isn’t quite as universal, and so sometimes children could present with swelling of the hands and feet. That’s something called dactylitis, which is pretty rare these days as a presenting sign. And then there’s some patients with more milder forms of sickle cell disease that don’t know until they’re older children or young adults, but most of the time we get them in our catchment when they are young because of their newborn screen and can really wrap our arms around them and give them the care they need. Let’s suppose you’re a newborn baby and you had your heel poked and they tell you that you have sickle cell disease. Well, presumably they don’t tell you they tell your parents and you get referred to a pediatric oncologist. If that means that your red blood cells are now more like bananas than squishy Donuts, what can you do about that? I mean, is it reversible?
At this time the only cure for sickle cell disease or way to reverse those cells is by replacing your bone marrow with another person's, but that's pretty rare. Later in the show, you get to talk a little bit more about therapies coming down the pipeline for patients, but right now that's the only way to reverse. However, if you are a little baby and your parents find out that you have sickle cell disease the benefit of coming and talking to a pediatric oncologist and hematologist who knows about this is that you now have a team member, somebody on your team that can help your baby, or you if you're the baby, stay healthy and safe. And what that looks like as a toddler is getting them started on penicillin prophylactically or in advance before there's any problems because we found that as recently as the late 70s, there was kind of a peak in infancy and toddlerhood of death, because patients with sickle cell were getting really bad infections,
but we found that if we vaccinate them and give them prophylactic penicillin, they live well into adulthood.

The challenge becomes, how do we help them when they go from infant to adults? And that’s what I work on in my work.

So just to back up a little bit when you say prophylactic penicillin, do you mean like every day for the rest of their life?

So definitely every day for the first five years of their life. But what it does is it protects them against really bad infections like pneumococcus you know. Patients with sickle cell disease, their spleen doesn’t really work as well as somebody without sickle cell and because of that they are susceptible to certain types of infections and that penicillin every day just like a vitamin helps them to stay healthy and safe.

So why is there this transition then from childhood to young adulthood? What’s the difference in terms of the disease and how it’s managed that requires a specialist like you?

Well, I think it’s a variety of things. It’s not just the disease,
but it’s becoming a young person and learning how to navigate the health care system on your own. Earlier we talked about newborns and if you were a newborn and found out you had sickle cell disease that your parents would help you take you to the doctor. Manage your care, give you that prophylactic penicillin. The beautiful part about being a young adult is you can start to assume some of that care for yourself, so it’s pretty multi-factorial. I always like to use and I like to think that I was a pretty smart young adult like I made some good decisions. I’m a doctor now, but I still did some foolish things as a 16-17 year old and that’s without a chronic disease. So in sickle cell disease, what we can do as lifespan hematologists and as health care providers is really help our patients as they learn to manage themselves. As they’re learning to navigate a pretty complex health care system,
and as they’re just trying to be productive, happy young adults.

What kinds of things do you talk about with your patients?

It sounds like after their five years old, they’re no longer on penicillin, but there’s still no way to reverse the condition, so you’re still at risk of all of those sticky, misshapen blood cells forming clots all over your body, which presumably can cause all kinds of problems.

Is it just a matter of telling your patients what to watch for and when to seek help?

Or are there things that they can do to reduce the risk of clots and other problems that it can cause?

Absolutely, so I want to answer your question in two parts. First, what other parts of the body does sickle cell affect?

How does that show up for patients across their lives?

One of the things that our patients most deal with is pain every single day.

So when those blood vessels get clogged by those sickle cells and those juicy Jelly doughnut cells can’t get through,
that means oxygen isn’t going to where it needs to in our bodies. And because of that, that can result in pretty bad bone pain for patients with sickle cell disease, and this is the thing that really affects their quality of life as young students trying to learn and keep up in school. If you have to be admitted to the hospital several times a year you can imagine how frustrating that can be as a scholar. Other parts of the body that are affected by sickle cell disease are numerous. Though patients with sickle cell disease can have something called acute chest syndrome, which is a really bad infection of the lungs that can be very challenging, they can even have strokes as young people, which is one of the reasons that compelled me as a Med student to pursue hematology was seeing a sickle cell patient eight years old who had a stroke in Pediatrics. And in order to kind of get a jump on these things, we do several things, we do screenings. Something called a transcranial Doppler, which is basically like an ultrasound
of your head where you can look at the blood vessels and make sure you're not at risk for having a stroke. We always make sure that our patients have their eyes checked because sometimes in sickle cell disease you can have vision changes and a regular follow up with a hematologist can help you notice any changes before they cause problems. One of the biggest things and one of the things we know works and helps prolong life in sickle cell patients is a use of a medication called Hydroxyurea. Now, some of your listeners may be familiar, because sometimes this can be used in patients who have certain cancer diagnosis, but in sickle cell disease, the dose that we use is much lower and the way that we use it as a bit different. And we know that it kind of helps you have more juicy fat cells than bananas and so your body overall does better in the long term. So just to follow up on a few things that you just said.

First off taking that last comment about Hydroxyurea making you have more fat and juicy like blood cells rather than sickling bananas,
Is it true that if you have sickle cell disease, not all of your blood cells are bananas and it is possible to increase the number of Jelly doughnut blood cells that you have instead? Absolutely, and that is up until recently, the only FDA approved medication that we have had for our patients is Hydroxyurea to increase the amount of non-sickle cells, Jelly doughnut cells and ensure that you're pain complications are lower and that your organs can really get the oxygen they need to thrive. So an obvious question is why not use more and make all of your blood cells Jelly Donuts? But hold that thought. Because first we need to take a short break for medical minute. Stay tuned to learn more about adolescents and young adults with sickle cell disease with my guest doctor CeCe Calhoun. Funding for Yale Cancer Answers comes from Smilow Cancer Hospital. Fifteen care centers offer access to oncologists committed to providing patients with cancer and blood diseases. Individualized innovative care.
Find us. Milo Care Center near you at yalecancercenter.org.

There are over 16.9 million cancer survivors in the US and over 240,000 here in Connecticut. Completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life changing experience. The return to normal activities in relationships may be difficult and cancer survivors may face other long term side effects of cancer, including heart problems, osteoporosis, fertility issues and an increased risk of second cancers.

Resources for cancer survivors are available at federally designated Comprehensive cancer centers such as the Yale Cancer Center and at Smilow Cancer Hospital to keep cancer survivors well and focused on healthy living. The Smilow Cancer Hospital Survivorship Clinic focuses on providing guidance and direction to empower survivors to take steps to maximize their health, quality of life and longevity.

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 Dr. Cece Calhoun. We're talking about the care of adolescents and young adults with sickle cell disease and bright before the break CeCe was mentioning that while sickle cell disease is completely irreversible, that actually using a drug called Hydroxyurea can help your body to create more of these quote juicy cells which are normal red blood cells and less of these quote banana like cells. So my question to you was, before we had the break, is why not just give more Hydroxyurea? I mean if it helps your body to produce more normal cells and less sickle cells, wouldn't that be a way to kind of reverse it? I would love if it could be totally reversed by Hydroxyurea but we know that when our patients are awesome, take their medications every day as prescribed, there's still an upper limit to how many of those juicy fat
cells they can replace. They can produce to replace the banana cells, so there’s a threshold of how effective the drug can be, but it can really help enough to help your organs stay healthy. So this Hydroxyurea is something that you’re taking every day? And the other thing that you mentioned before the break was this concept of pain and the fact that many of these patients they present with pain and they have pain every day which impairs their ability to concentrate at school or maybe place boards so what do you do about that? I mean, are these patients treated with daily painkillers? Or do you tell them to simply wait until they have pain and then prescribe pain medication? I mean how do they get through their day to day life if they’re in pain everyday? Yeah, so sickle cell patients are warriors and you’ll often see that described because despite having pain of variable severity, they managed to live life and be productive. That’s one of the most awesome things
about working with sickle cell patients.

So in terms of pain prevention,

Number one Hydroxyurea and get more juicy

cells around so you have less pain.

And recently there are a couple

of medications on the market

that help with pain prevention.

Also just keeping yourself well hydrated.

My patients are so wonderful in

that they often know their bodies.

They know their triggers.

And what situations make their pain worse.

And what kind of things can

make their pain better.

So really being attuned to those things

in terms of addressing pain acutely

when it happens and it’s not planned,

we have a couple of things in our toolkit.

Yes, pain medication is something

that we give frequently for pain,

but we can also use red

blood cell transfusions if we need to.

If somebody is having pain often,

but many times we can’t predict

when the pain will come,

or how severe it will be,

and so because of that our patients

have to get care in the ED sometimes

to get treatment for their pain.

You mentioned something
0:17:57.06 –> 0:17:59.29 that I found kind of intriguing.
0:17:59.29 –> 0:18:01.474 You said that we have medications
0:18:01.474 –> 0:18:03.74 for pain prevention, like what?
0:18:04.27 –> 0:18:07.006 Hot off the press I know,
0:18:07.01 –> 0:18:10.565 so recently there’s been
0:18:09.565 –> 0:18:11.609 an FDA approved medication,
0:18:11.61 –> 0:18:13.78 Adakveo or crizanlizumab
0:18:15.9 –> 0:18:18.716 but I try not to say
0:18:18.716 –> 0:18:20.7 that because crizanlizumab,
0:18:20.7 –> 0:18:23.724 but that can be used to prevent pain
0:18:32.01 –> 0:18:33.87 And another medication that’s recently been
0:18:33.87 –> 0:18:36.449 approved is something called Oxbryta
0:18:36.45 –> 0:18:38.9 and really, what that does is increase
0:18:38.9 –> 0:18:40.779 patients with sickle cell disease,
0:18:40.78 –> 0:18:41.512 their hemoglobin,
0:18:41.512 –> 0:18:44.44 and so the thought is if their
0:18:44.52 –> 0:18:46.75 hemoglobin is better they
0:18:46.75 –> 0:18:49.025 may in turn have less pain,
0:18:49.03 –> 0:18:51.61 but the primary medication that
0:18:51.61 –> 0:18:54.75 is out there for pain
0:18:54.75 –> 0:18:56.68 prevention is Adakveo.
0:18:57.49 –> 0:18:59.225 That sounds like a
0:18:59.225 –> 0:19:00.621 pretty good deal, right?
0:19:00.621 –> 0:19:02.727 If instead of having pain everyday,
0:19:02.73 –> 0:19:05.018 if you had an infusion once a month,
0:19:05.02 –> 0:19:07.092 does that infusion kind of really get
0:19:07.092 –> 0:19:09.458 rid of the chances of having pain?
0:19:09.46 –> 0:19:10.54 Or not really?
0:19:11.51 –> 0:19:14.59 I think that the medication is pretty
0:19:14.59 –> 0:19:17.925 new and patients themselves are
are individuals, and so I’ve had some patients who it’s worked great for. I’ve had some patients that we just have to try other things. I think the wonderful thing about being a physician and sickle cell, or even being a patient right now who has sickle cell is that it is such a fertile time for discovery. In terms of sickle cell disease, how to prevent complications and how to cure it. So you just have to work with your hematologist to find the right regimen for you. So I want to pick up on that discovery and some of the new advances that are going on in terms of sickle cell research. But before that I had one other question about the complications you had mentioned before the break. One of the impetuses for you to become a pediatric climatologist was an 8 year old who had a stroke, which just I mean is heartbreaking to me. But clearly if you think about these sickle cells, it makes sense, right? These sickle cells kind of glom
together and they cut off blood supply to a part of your brain that’s called the stroke. Now when we think about older patients who may be at risk of stroke or who may be at risk of heart attack or who may be at risk of other clotting, whether it’s in their lungs or in their legs or whatever, we often use blood thinners, so are sickle cell patients put on blood thinners to prevent these complications? Since we know that they’re at risk of getting clots. So the blockages that occur in sickle cell disease are a little bit different than your normal blood clot, which is caused by a different series of events, and so for patients with sickle cell disease, though they are at an increased risk to have those traditionally, what we think of blood clots, we don’t put them on blood thinners to try to prevent complications with sickle cell disease. We know those blockages can be stuck like a clot, or they can be transient, they come and go because of the cells sticking together.
It’s not like the other proteins in your body are swimming over there, making a huge clot.

What we do in our young people to maximize stroke prevention is we do screenings like the Transcranial Doppler I mentioned. And if we notice any kind of abnormality at all, we have a couple of options. One we can start them on chronic transfusion to decrease the amount of sickle cells circulating in their blood and give them more normal cells. Or if somebody has been on transfusions, their transcranial dopplers looks fine, we can switch them to again Hydroxyurea put more Jelly Donuts around, have less sickle cells, decrease the risk of complications, and that’s again why it’s important to connect with your friendly hematologist so we can help you on that journey. Yeah, but presumably you would have already been on the Hydroxyurea so if that transcranial Doppler finds that you’re at increased risk I guess the transfusion is your only alternative,
but the issue there is if you keep getting transfusions on a regular basis, doesn’t that increase your risk of transfusion reactions and potentially ultimately developing antibodies such that there are fewer and fewer blood types that you can actually take?

Absolutely. For patients who have chronic transfusions, they’re a variety of risks that come along with that. There’s obviously a clear benefit in that it keeps you safe and protects you against stroke and may decrease your pain. But you’re absolutely right, our bodies recognize things that aren’t foreign, and that’s why we really work in tandem and together with our transfusion medicine colleagues to do extended typing in patients with sickle cell disease to prevent that risk of developing antibodies. Another big risk is something called iron overload, where excess iron from the blood deposits in different organs like your liver, your heart, or your eyes. So we measure that regularly and again, medicine is so cool because we’re
always ideally moving forward and there’s also a procedure called Erythrocytosis which I don’t too much mind saying five times fast, but I like it, which can help decrease that risk of iron overload. Let’s talk a little bit about some of the exciting advances in terms of sickle cell disease. Tell us about what you think are the most exciting things that are on the forefront that you think are really going to make a difference for your patients. I think there are a lot of medications in the works to address pain and complications of sickle cell disease. But one of the things I think that is most exciting is the idea of a cure through gene therapy, and that’s pretty awesome. There’s been some media, the New York Times has published about it and the Washington Post as well about how we can use different scientific technologies like CRISPR technology or use different vectors like viral vectors to take somebody’s stem cells and correct that defect in their DNA that caused them to be making sickle cells and then
give it back to them in a safe way, and then when those new and improved cells from their bodies replicate they are no longer affected by sickle cell disease. They may still make some sickle cells, but will effectively be cured or be like somebody who just has the trait and that’s one of the things I think that’s most exciting. The possibility of a cure in our future. And is that 10-15, 30-50 years from now? No, the time is totally now, so there are clinical, active clinical trials going on to better understand the safety and efficacy of this process for patients and so that’s happening now. Wow, that’s super exciting. What else is going on? So I think the other main things are the development of oral medications to improve pain and to decrease complications from sickle cell disease. That one medication, Adakveo, the way that it works, it’s something called a B selection inhibitor.
And so they’re more medications coming around that look at that. And there’s some additional oral medications coming that target different mechanisms and other blood problems like thalassemia and they want to see if those medications can work well in patients with sickle cell disease. So I think that fact that we are shining a light on this community of people with sickle cell disease and that we as a scientific community have committed to making their quality of life better, that’s the thing that’s most exciting to me, because oftentimes I think my patients feel unseen and unheard, and so it’s great to see so many people, brilliant people standing up for them and helping to make their lives better. That’s awesome. I guess the last question that I have is really with regards to clinical trials. I mean, it sounds like there’s so many great things on the horizon. Do you find that young people adolescents are interested in clinical trials and willing to participate? Are there barriers to participation? How has that been going along? Yeah, so anybody who has lived
with sickle cell or chronic pain,
I think is enthusiastic about finding a way to have a better life and to come have a better quality of life and to find a cure.
When it comes to clinical trials, there’s a careful balance between understanding clinical studies and not wanting to feel like an experiment and understanding how the medical system can wrap around you to keep you safe. As we understand more about how to help you have a cure. And so when I think about my young people, are they interested in clinical trials? I think that they have a lot of excellent questions about the benefits and risks of participating in clinical trials. But many of them ultimately, when we sit and talk and take the time, they understand that it is their contribution to not only their health, but the community of sickle cell patients. And that’s the beauty of having providers that have known you through the lifespan. You have a relationship. They know that I care for them.

And so when I offer them this option,
then there’s a little bit more willingness to enroll.

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If 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 Astra Zeneca.