News from ASH: Research and Treatment for Sickle Cell Anemia
ASH Conference Coverage
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Introduction

Andrew Schorr: Hello and welcome to our live broadcast from the American Society of Hematology meeting where all the blood experts get together from around the world. I’m Andrew Schorr, and you’re listening to our Patient Power special edition broadcast, and we’re talking about sickle cell anemia. Joining us is a widely respected expert, Dr. Kim Smith-Whitley. She’s Director of the Sickle Cell Center at the Children’s Hospital of Philadelphia, which consistently seems to be ranked the number-one children’s hospital in the country if not the world. So thank you for being with us.

There were a bunch of studies presented, one by a colleague of yours from “CHOP” as you say. So first of all for people concerned and their families and about their children, first an overview. What’s the sense of the research being presented here and what it could mean to families touched by sickle cell?

Dr. Smith-Whitley: There’s wonderful information being presented at this meeting. The overwhelming number of presentations is numerous, over a hundred in the area of sickle cell disease. There are therapeutic interventions that are important to patients and their families that are being presented. There are studies that look at the survival of individuals with sickle cell disease, and the impact that certain complications have on the quality of life of patients. It’s a very important meeting.

Andrew Schorr: Okay, any new treatments or monitoring that seems to be; now I know you lead the way in a lot of what you do in Philadelphia, so maybe there are things you’ve been doing already that now the rest of the world is hearing about, but help us understand about that for people really worldwide even.

Dr. Smith-Whitley: Initially when sickle cell disease was first mandated by the government for comprehensive sickle cell centers, there were large studies where over four thousand individuals with sickle cell disease were followed to try to determine what the complications were of sickle cell disease, the survival of individuals with sickle cell disease, and those studies early on
let us know that the life expectancy for individuals with sickle cell disease was shortened compared to African Americans without sickle cell disease. So anywhere between forty-two to forty-eight years of age was the life expectancy at that time.

The complications that were life-threatening were primarily due to infections and lung complications. There is data being presented at this meeting by Charles Quinn and the group from Texas that implies that survival is improving, and estimates now are that 94% of individuals born with sickle cell disease will make it to the third decade of life. That’s wonderful, and it can be due to the early diagnosis and recognition of sickle cell disease, patients getting in to see their doctors and getting medications to prevent infections early, and then chronic therapeutic interventions such as transfusion therapy and hydroxyurea therapy I’m sure have had an impact on the survivability of individuals with sickle cell disease.

**Andrew Schorr:**
Now I know you mentioned that last drug, hydroxyurea. I saw the Greek specialists had presented some studies there where they’re using that and having success.

**Dr. Smith-Whitley:**
Yes, and hydroxyurea trials were done in adults with sickle cell disease now approximately a decade ago, and what we’re trying to do is to increase awareness about the benefits of hydroxyurea therapy in individuals with sickle cell disease. So now we know that individuals with sickle cell disease who have pain and a lung complication that can be fatal called acute chest, which is a pneumonia-like illness, that once they start this medication the frequency of pain and the frequency of acute chest episodes decrease, and we’ve been able to demonstrate that same benefit in children with sickle cell disease with very limited side effects.

**Decreasing Risk of Stroke**

**Andrew Schorr:**
Now of course one big concern is also stroke. What about monitoring to see if someone might be at serious risk of that?

**Dr. Smith-Whitley:**
I think that the identification of risk factors for stroke and treatment of stroke has been revolutionary in the last decade. We have really determined that transcranial Doppler ultrasonography, which is a noninvasive test to determine the speed of blood as it flows to the brain; if you can imagine for example just taking a water hose and you have your water flowing freely from the opening of the hose. If you put your finger on the opening the water spurts out faster.

**Andrew Schorr:**
More pressure.
Dr. Smith-Whitley:
Yes, it’s narrowed. So we know that individuals with sickle cell disease have strokes because the sickle cells cause damage to the lining of the blood vessel. That damage then forms a scar and narrowing occurs, and when the narrowing becomes severe enough to decrease the blood flow and the oxygen delivery to the brain, that results in a stroke, and that stroke risk is greatest in children with the SS form of sickle cell disease between two and nine years of age. Bob Adams and others discovered that by this noninvasive test where they can just place a small probe by the side of the temple...

Andrew Schorr:
Ultrasound?

Dr. Smith-Whitley:
Yes, ultrasound, they can determine the speed of the blood as it flows to the brain, and that individuals with rates above a particular cutoff are at increased risk for stroke, and that transfusion therapy, routine transfusion therapy every three to four weeks, can markedly decrease that stroke risk in patients, so we can predict those who are at greatest risk for stroke, start an intervention, and prevent the stroke before there are any other outward symptoms.

Andrew Schorr:
I heard of another study that was presented here too, and I think it was Dr. Quinn, with using the little thing that you put on your fingertip, the pulse oximeter just on the end of your finger, no pricking or anything, to look at the oxygen saturation of the blood, that that can be used in a valuable way too.

Dr. Smith-Whitley:
Right, when you use transcranial Doppler ultrasonography and pulse oximetry monitoring in children with sickle cell disease, we know that those with low steady state oxygen values by that noninvasive method have a greater risk for having abnormal TCD values than those with normal oxygen.

Andrew Schorr:
Okay, so for families listening we’ll talk a lot more. We’re visiting with Dr. Kim Smith-Whitley who’s Director of the Sickle Cell Center at the Children’s Hospital of Philadelphia.

Now let’s back up for a second just to make sure everybody understands. Sickle Cell is really what the cell looks like, right? It looks like a sickle, kind of a crescent, and we’re talking about red cells. If you don’t have a whole big, full-bodied red cell, that red cell can’t do its job very well, right?

Dr. Smith-Whitley:
Correct.
Andrew Schorr:
And one of them is carrying oxygen. So when we talk about oxygen to the brain and all these needs, if those red cells are shaped like sickles they have a tough job.

Dr. Smith-Whitley:
As you know, sickle cell disease is an inherited blood condition. You can’t catch it from anyone. You’re born with it, and the only cure right now is stem cell transplantation. So individuals with sickle cell disease have an increase in the level of sickle hemoglobin in their blood, and that sickle hemoglobin is caused by a protein that’s different between normal adult hemoglobin A and hemoglobin S, or sickle hemoglobin. That one change makes the hemoglobin susceptible to stacking when it’s deoxygenated, and the stacking of the hemoglobin polymers causes a conformational change in the shape of the red cell making it stiff and sticky and difficult to navigate small capillaries, so it leads to the lining of the blood vessels being damaged to the point that oxygen delivery is compromised. So pain is a result of lack of oxygen to a muscle or bone is a common feature. Stroke, lack of oxygen to the brain, and acute chest syndrome possibly due to lack of oxygen delivery to the lungs are frequent complications of sickle cell.

Stem Cell Transplantation

Andrew Schorr:
You mentioned stem cell transplant. Now, there’s been research presented at this meeting related to cord blood transplant, okay? So the stem cells that would otherwise be thrown away from the cord when a baby is born, and there seems to be a lot of exciting research there and certainly stem cells that could help a child. So where are we with that? Is that helpful because certainly in the African American community there’s often been a shortage of donor cells?

Dr. Smith-Whitley:
That’s correct, and right now the standard of care for stem cell transplantation in individuals with sickle cell disease requires that you have a brother or a sister who has bone marrow cells that match yours and that that brother or sister does not have sickle cell disease. So you can imagine that the likelihood of finding appropriate stem cell donors is very difficult, but you are correct in that umbilical cord blood is a wonderful source for these very immature red cells, white cells, platelets, and that that these cells can go into somebody just through an IV and know where to go, to go to the bone marrow, and then can produce normal hemoglobin A.

Andrew Schorr:
And they’re more forgiving as far as trying to make a perfect match.

Dr. Smith-Whitley:
That is interesting, yes, they are more forgiving, we’re hoping that because of stem cell transplantation improvements over the last ten to twenty years that individuals with sickle
cell disease may be able to receive stem cells from an unrelated donor without a lot of increase in complications, and that’s an investigational project that is ongoing right now.

**Andrew Schorr:**
We’re going to take a brief break. When we come back we’re going to be asking Dr. Kim Smith-Whitley from the Children’s Hospital of Philadelphia and the Sickle Cell Center there about what are our other treatments besides, you mentioned a couple, but also in transplant where are we headed and what can we give hope to for people? So we’ll be right back with much more of our live broadcast on the latest from this big medical meeting on sickle cell anemia. We’ll be right back.

We are back live from San Francisco where I’m sitting across from Dr. Kim Smith-Whitley who is the Director of the Sickle Cell Center at the Children’s Hospital of Philadelphia.

Doctor, one of the things that I was impressed with was there was a news conference here with some of your colleagues, some you’ve mentioned, on sickle cell the other day was that we have other conditions, and not to put this one down at all, hemophilia where there are Centers of Excellence around the country and we’re getting pretty well organized, we haven’t quite gotten there with sickle cell even though it’s not an uncommon condition and certainly in the African American community although not exclusively African Americans, and there was evidence that patients who get to a center, and it makes sense to me, do better.

**Dr. Smith-Whitley:**
One of the challenges I think for all individuals with chronic illness is access to medical care, and these Centers of Excellence or Comprehensive Sickle Cell Centers have been in existence in many regions for two or three decades now. What is very, very exciting is newborn screening has been adopted by states for hemoglobinopathies so that we can tell parents within two weeks of a child’s birth whether or not that child has sickle cell disease or not. We can get that child to someone who understands the complications of sickle cell disease, start them on medications to prevent infections, and hopefully improve their quality of life. You’re exactly correct. There is data that has been presented at this meeting that implies that those who live closer to centers may get better medical screening and care.

For example, at the Children’s Hospital of Philadelphia, Dr. Janet Kwiatkowski has just presented her study that details the impact of transcranial Doppler ultrasound, or TCD screening, for stroke prevention in children with sickle cell disease. Before we had the capability of using TCD, individuals with sickle cell disease were at increased risk for stroke and actually sickle cell disease was one of the number one reasons for childhood stroke.

With the impact of TCD screening, we have seen now a ten-fold decrease as demonstrated by Dr. Kwiatkowski who looked over a sixteen-year period, eight years before TCD screening and eight years after TCD screening, and looked at the numbers of
individuals followed at Children’s Hospital of Philadelphia with sickle cell disease and their stroke rate, and what she determined was in the eight years prior to TCD screening compared to the eight years after that strokes had reduced more than tenfold in individuals with sickle cell disease. So that lets you know that access to these centers who understand the importance of using these tools for screening, have the personnel that are trained in how to use these screening tools, greatly benefit our geographic patient population with sickle cell disease. You wonder what children who have sickle cell disease who do not live close to these centers experience. So my colleagues and I are advocating regional programs so that individuals with sickle cell disease can have access to the expertise of hematologists who care for individuals with sickle cell disease regardless of where they live geographically in reference to a center.

Andrew Schorr:  
Well I wish you well with that. Now let’s mention someone gets the news that their baby has sickle cell and that maybe there could be that going on in their family. That’s very scary. What can you say today, doctor, to give people hope of a better life and hopefully leading to a longer life?

Dr. Smith-Whitley:  
I think the data that Dr. Quinn has demonstrated that shows that individuals with sickle cell disease born in the last two decades have a greater than 93% chance of surviving to beyond 20 years of age. In the 1960s and 1970s we lost children who had sickle cell disease from overwhelming bacterial infections. Now we have been able to decrease that risk with the use of penicillin prophylaxis, special immunizations, and now it appears that acute chest syndrome, the severe lung complication that I mentioned that is very common in adults, is also not so uncommon in children and can be fatal.

Andrew Schorr:  
All right, now let’s put this in perspective too because I’m a leukemia survivor, Dr. Smith-Whitley, and when I was first diagnosed you’d open a book, and you’d look up my leukemia, and it would say it was an always fatal condition. I thought, okay, I’m dead, like tomorrow.

So now you’re saying the hope is people will live into their 20s at least, okay, but that’s what we’re saying today. So now let’s, I know it’s crystal ball-ish, and we don’t know what’s going to happen, but if you see a mother with a child today and they’ve been diagnosed with sickle cell, what hope, no guarantees, but what hope can you give for looking ahead so that that can be extended?

Dr. Smith-Whitley:  
Sure, and I think that what we know is that that rate of the median age of survival, 42 to 48 years of age in individuals with the SS type of sickle cell disease, was an estimate that was made over 25 years ago. So since that estimate we’ve had hydroxyurea therapy,
chronic transfusion therapy; those two therapies have demonstrated, have shown to decrease complications in individuals with sickle cell disease, acute complications, or those that are unexpected and short-lived.

Now what we’re trying to do is address the long-term or chronic complications, and as you suggest pulmonary hypertension is a chronic complication in individuals with sickle cell disease that can be life threatening. We now know that it exists, we know how to screen for it, and now we’re looking for methods to treat it. So what I can say to that mother of a patient with sickle cell disease in the newborn period is that if we make sure that we take care of infection, if we make sure that we attend to warning signs for acute problems and do screening to make sure that we identify chronic or long term problems early and start interventions, then I think that we will eventually within the next decade approximate the survival of African Americans as we would hope in this decade so that we can hopefully see that these children will survive into their 60s and 70s.

There’s also a report at this meeting about sickle cell disease in the elderly out from the UNC Chapel Hill Duke group, Dr. de Castro and Dr. Telen, and it’s wonderful to see that they have a substantial patient population greater than 55 years of age, which is their definition of an elderly individual with sickle cell disease, and that these individuals have great quality of lives, that they’re being followed closely for lung and other complications, and that this patient population in that age group is increasing.

So we have these intermediate indicators that things are getting better. We just don’t have the solid data to demonstrate the survival change right now.

**Andrew Schorr:**
Well, and it’s also great to hear of the collaboration. I went to UNC and we didn’t get along with Duke very well, so I’m very delighted to hear them working together. That’s good.

**Dr. Smith-Whitley:**
Well, as a Duke graduate...

**Andrew Schorr:**
Oh, you are, and we’re collaborating, okay.

**Dr. Smith-Whitley:**
<laughing>

**Andrew Schorr:**
And I think Dr. Jordan, if I’m not mistaken, from the Sickle Cell Association was from UNC.
Dr. Smith-Whitley:
Yes, she did her medical training there, and she’s now in Hollywood, Florida, and I really do want to mention the Sickle Cell Disease Association of America.

Andrew Schorr:
Yes, please.

Dr. Smith-Whitley:
It’s a wonderful organization that is designed to empower individuals with sickle cell disease through their member organizations. Individuals with sickle cell disease if they have access to these member organizations then I know they have access to good information, ways to address barriers to medical care, and ways to make sure that they have access to some of the most current medical interventions through the resources that the Sickle Cell Disease Association of America provides.

Andrew Schorr:
Right, I want to give the website, and that is www.sicklecelldisease.org. and of course their phone number is on there and people to call so you’re not alone then, right?

Dr. Smith-Whitley:
Yes.

Genetic Testing for Sickle Cell Disease

Andrew Schorr:
You can find out, and I know there are families touched by it. Let’s back up now. Are there tests to know whether you marrying a certain person or that maybe you are carriers of this? My family is Jewish, and so we worry about a genetic condition Tay-Sachs, and I actually know a family where they weren’t tested, and then they gave birth to a child with Tay-Sachs who only lived a couple of years as you know. So is there a way to make choices wisely?

Dr. Smith-Whitley:
Yes. As you have implied, sickle cell disease is a disorder that more commonly affects individuals of African descent, although that is not the only subpopulation of patients that we see that have sickle cell disease. It is an inherited condition, and it is inherited by having a gene from one parent with sickle cell trait being transmitted and another sickle gene from another parent with sickle cell trait or some other abnormal hemoglobin trait, and that gives that couple a one-in-four chance of having a child with sickle cell disease. As you know with anything, with population and statistics, it doesn't mean anything specifically for a couple, that they cannot predict whether or not the their child will have sickle cell disease or not, and so what we recommend is for individuals who are planning on having children, particularly if they're of a racial group that that may be at increased risk, to speak to their OB/GYN to get the appropriate testing.
The appropriate testing is for both parents to have something called a hemoglobin electrophoresis. That is a method that allows the hemoglobins to be separated and identified appropriately. We have these old tests in place called the Sickledex or the “shake test” where we try to manipulate the sickle hemoglobin in a way to give clues about whether or not it exists, but as I already mentioned individuals who have sickle cell disease may or may not have two parents that have sickle cell trait because there are many forms of sickle cell disease.

There’s the SS, which is the more common form, where you inherit two sickle genes from your parents, but you also have SC or S beta-plus or zero thalassemia where that other parent has a trait for C or beta thalassemia, and so that Sickledex test is not able to show those other traits, so it’s very important that individuals know the right testing to request, and that’s a hemoglobin electrophoresis.

**Andrew Schorr:**
Okay, so who would be the couples who should get the test? Should this just be anybody or if you’ve had someone with sickle cell in your family?

**Dr. Smith-Whitley:**
I think that you need to be concerned if you have anybody with sickle cell trait or sickle cell disease in your family. I think you also need to be concerned if you’re from a racial or ethnic group where sickle cell disease or the gene, the frequency of the sickle gene, is more common.

**Andrew Schorr:**
And that’s which?

**Dr. Smith-Whitley:**
So that’s in people of African descent, so primarily in the U.S., African Americans, Latino Americans, individuals from the Mediterranean; there is a small pocket in Italy and Greece of the sickle gene, and so those individuals may be affected, and also in parts of India, and of course in the Afro-Caribbean countries.

So it’s very important that if you have ancestry where you know that you may be at risk for having a child with sickle cell disease that you get tested.

**Andrew Schorr:**
Okay, we’ve learned a lot. I’m Andrew Schorr. Remember, knowledge can be the best medicine of all.