Aaron Leech, MD:

Welcome to the latest installment of Paradigm Shift, the official podcast of the National Foundation of Emergency Medicine. The purpose of this podcast is to create visibility for young and soon to be prolific academic emergency physicians by highlighting their research and their vision for their field. We hope to introduce these ideas to you, the listener, and to expand, and maybe even redirect your thinking toward the forefront of both science and philosophy and emergency medicine. Today, Dr. Peter Rosen and I are joined by a Dr. Gentry Wilkerson. Dr. Wilkerson is an assistant professor of emergency medicine at the University of Maryland Medical Center in Baltimore, Maryland. Amongst other things, he is the assistant program director for the emergency medicine residency program. He is the co-chair on the opioid task force for his hospital and is involved in multiple areas of research, including opioids, angioedema, congestive heart failure, and today's topic, sickle cell disease. Dr. Wilkerson, welcome.

Gentry Wilkerson, MD:

Thank you so much. It's a pleasure to be here.

Aaron Leech, MD:

So you have several research interests but the primary one we're going to be talking about today is going to be sickle cell disease, and you've distilled three different paradigms you want people to shift in their mind. We'll just kind of go over them before we start the discussion. But the first is to have a restoration of empathy for patients with sickle cell disease as they present to the emergency department. The second one is to recognize the burden that the care of sickle cell disease patient has on the healthcare system. And the third is recognizing that the vaso-occlusive episodes associated with sickle cell disease are a diagnosis of exclusion. So, before we get into these, can you tell us a little bit about how you became interested in this field of research?

Gentry Wilkerson, MD:

Sure. Sickle cell disease is something that's not uncommon. There's 100,000 people in the United States that have sickle cell disease. I think every emergency physician is pretty familiar with the patients that come in with this. I did medical school at University of Miami in Florida. We had a fair number of sickle cell patients that would present there. And then I did residency at Kings County Hospital, SUNY Downstate in Brooklyn, New York. And there, I was exposed to a number of patients with sickle cell disease. And I think that at times you get called into a rut with sickle cell and just sort of treat them on a conveyor belt of, let's just give opioids and if they fail we'll just get them admitted to the hospital and really not thinking too much about it. And sometimes it can be a very frustrating venture.

Gentry Wilkerson, MD:

I don't think too many BD docs are jumping up excited, "Oh, there's a sickle cell patient that's come in." I was kind of in that realm, and then I realized that this was a patient population that there really was given short shrift and they've got a terrible disease, their life expectancy's going to be shortened by 20 to 30 years on average, although that's improving. They they've got a life of pain in front of them and I could do more to help them out. That's how I kind of started with that first paradigm shift, the restoration of empathy for patients with sickle cell disease. And I realized that I could do a lot more with that. So, I did start looking into it more and started developing different projects with it which we can get into as we go through this podcast.

Gentry Wilkerson, MD:

So, when thinking about restoration of empathy, we need to recognize that the medical system often doesn't treat sickle cell patients very fairly. They come into the emergency department often as a last resort. They don't want to come into the hospital. There have been plenty of studies that have shown that it is something that they fear having to do. They've experienced all sorts of long waits and inadequate treatment. So, they really don't want to come in in general, but when they do come in, we could do better taking care of them. I noticed it at University of Maryland, that there was a lot of practice variation between the providers in how we were treating these patients. And I know that there are some guidelines that were published in 2014, the NHLBI guidelines. That was one of the first things that I did with sickle cell disease was looking at the guidelines and looking at the way we're caring for patients at the University of Maryland. And I just developed a set of guidelines for the use in our emergency department to help streamline the care of these patients.

Aaron Leech, MD:

I think that it's an entity that we know what causes this, we know that this is a real disease. And yet somehow as we just see patient upon patient with the same presentation, we become almost numb to it. Even though, we can't turn away from the fact that these are patients that are in need of our help, it's very easy to become numb to the fact that this is like you mentioned another sickle cell patient. And the approach to I think a lot of what we do in emergency medicine, as I've heard Peter say before is that the patient's not here to entertain you. It's not a fascinating disease. It's not even sometimes a satisfying disease to treat because the pain control is so difficult. So, I can certainly attest to even in Tucson where we don't have a very high sickle cell population, when patients come in, it can be very difficult when you see the same patient that by name and that they come in with the same complaints. It can be difficult to say, "How am I making any progress, any headway, and trying to get this patient treated."

Dr. Peter Rosen:

One of the things I noticed was that when I worked in Denver, we didn't have many sickle patients probably because of the altitude. But because of that, every time they came in, they were treated like drug addicts seeking drugs. And I think that in part, one of the problems in treating a disease that has chronic pain we tend to forget there's a disease that's causing the pain. And I noticed that in San Diego, again, we still didn't have very many sicklers because there aren't all that many blacks who live in San Diego. Things changed drastically when we developed a program of assistance with our hematologists, so that there was a special problem that had a special response as opposed to here's another pain seeking drug addict.

Gentry Wilkerson, MD:

Yeah, there's definite reasons why the emergency physicians start to develop this sense of this is just another patient that's seeking drugs. The overall population of sickle cell doesn't have a rate of addiction that's any higher than on average. However, if you look at the subset of patients that present to the emergency department you're starting to see a little bit higher of a rate. And then everybody kind of has this bias where they focus on the few patients that come in over and over again with behavioral disturbances or aberrant behavior. And those are the ones we kind of fixate on. And those patients are usually easily recognizable and shouldn't be too big of a dilemma and how to manage them, although they still are. But it's the rest of the sickle cell patients that we tend to lump in with those others that have displayed that aberrant behavior in the past. And we always just focus on that.

Aaron Leech, MD:

Now, I'm curious because you have overlap in working with an opioid task force in some of your research that you've done with opioids. Can you describe a little more of the patients that come in with more opioid seeking behavior? Is it similar to the patients that have any other illness or any other opioid seeking behavior that they kind of have the same attitudes where if they're rejected from opioids or if they're tried to scale down a little bit on their treatment, they tend to get more upset? I mean, some of the things that are described usually in even the ABM tests of what to be looking out for.

Gentry Wilkerson, MD:

Yeah, it's difficult trying to describe what drug seeking behavior is because anybody that has an unmet need is going to do something to try to meet that need. And if they have pain, they're going to do something to try to get that resolved. Now, that gets into kind of a loaded statement because you're starting to touch on this idea of pseudo addiction. That's a loaded term that has a lot of controversy associated with it, mostly because it was pretty much put forth by drug companies. But I do recognize that if somebody has unmet analgesia requirements, they're going to act out, but the patient that comes in time and time, again, they have multiple pot infections because of self-injection or there's evidence of drug diversion, seeking care from multiple providers. These are kind of typical behaviors that we will see in different disease states that we sometimes will see in our sickle cell population.

Gentry Wilkerson, MD:

But again, it's fairly recognizable. I'm a big fan of the prescription drug monitoring program that we have available here. And I think 49 out of the 50 States now have some form of this. And it's great because you can very easily get a sense of what the patient's history of opioid, at least the outpatient use is. Well, we use Epic and that has care everywhere where we can access other hospitals records. And then we have something called CRISP where, again, we can access other hospital records. So, we can see that patient that's gone from hospital to hospital. And sometimes we see it in the sickle cell patients, but in other chronic conditions like gastro-paresis or other conditions where they're coming in with painful episodes that are difficult to evaluate and treat, it's kind of the same thing over and over.

Aaron Leech, MD:

I think you mentioned that the rate of addiction is no different in this disease than any other disease. And just looking at those 2014 sickle cell guidelines that you mentioned, there's good evidence that patients get relief from opioids. And this seems like a condition that really necessitates opioids, both in children and adults. And it's interesting because we had a recent podcast where one of the paradigms we kind of addressed was try to keep opioid patients naive of trying not to get people started down that pathway, if you can, but this is a different patient population. Would you agree?

Gentry Wilkerson, MD:

I would agree. The primary treatment of a vaso-occlusive episode, which is 95% of what we're going to see in the emergency department is opioids. However, I do support the notion in general of keeping opioid naive patients naive to opioids. I love that idea. I do think that there's a lot of work that can be done in the sickle cell population early on. And I think that sometimes we miss the boat if we haven't sort of set expectations and developed coping skills and other pain management skills early on. I think one of the toughest transitions that sickle cell patients have is when they transition from childhood care to adult care. They tend to get lost in that transition and then all of a sudden they're reaching out in any way they can to manage their pain. But I think that by developing skills early on, then we can help them out so that their reliance on opioids is a little bit less. I'm also in favor of all kinds of research that can be done on finding other ways to treat vaso-occlusive episodes with things other than opioids. But currently we don't have much to offer.

Dr. Peter Rosen:

Gentry, there's a couple of things I wanted to ask you about. We tend to make complex problems simple because it's easy to think about. And the current simplicity to the difficult problem is that patients who have chronic pain shouldn't receive opioids, whereas patients who have acute pain are entitled to them. And that seems to be back with from what we have to do to treat the sickle patient accurately since they're not really having simple acute pain, they're having recurrent acute pain.

Aaron Leech, MD:

Acute exacerbations of a chronic illness that normally we would say that's not something that's going to get better with opioids, but in this case, that seems to be exactly what we need to do.

Gentry Wilkerson, MD:

The problem lies in the fact that we don't have a test for the patient that's in acute crisis. There's no vital signs, there's no lab tests, there's no imaging, there's no physical exam finding that can truly determine whether it's an acute vaso-occlusive episode or whether it's an exacerbation of their chronic pain. Now, we all know that it's probably some overlap of all of this. Is it a manifestation of their avascular necrosis, the chronic pain because of that. And I agree for run of the mill chronic pain patients, opioids are not the best thing for them. But with sickle cell patients, because we just don't know what's going on with them, the prevailing thought is we've got to take them at their word that this is an acute crisis and that we treat it like it is.

Aaron Leech, MD:

I'm curious, just from your perspective as this was the first paradigm that you put forth that we need to change in our minds. Was there a specific patient encounter or something that happened that really made you see that this was a problem? Was there kind of a light bulb that went off for you at a certain shift or anything that really prompted this? Or is this just the culmination of seeing time after time that we're not doing the best that we can?

Gentry Wilkerson, MD:

I don't think that there was a light switch that got turned on for me with this, I think it was something that slowly developed where I realized I was probably being a jerk to some of these patients, freely admit that, and then realized that I could do a lot better. We've had a number of sickle cell patients who have died because of complications here in the past few years. So, realizing this is not a simple disease, this is a pretty bad disease. That with my involvement in the opioid crisis, I kind of like thinking that my sickle cell work and my opioid work is if you look at a Venn diagram, there's a lot of overlap with it. And I think that by working on both those things, I can improve the care of many of my patients.

Gentry Wilkerson, MD:

I have spoken about it previously, but I was a pain patient at one point when I broke eight ribs in multiple places and ended up having titanium plates put on my chest. I've now had the experience where I had pain issues. And luckily I had resources that most patients don't have. After I got flown back to Baltimore, I was able to get into interventional pain management right away and had great family and support at home. This is not what most people have. So, I was luckily able to get off of opioids much faster than they thought I was and get back to work and be productive. So, I think the drawing on my experience as a post-traumatic pain patient, that helps me get a lot more empathy with these patients.

Aaron Leech, MD:

I appreciate you sharing that. I think that lends a lot of perspective to the approach of this. And I think it's easy for those of us that haven't had to go through that to take kind of a different approach to patients that come in with that. Thank you.

Dr. Peter Rosen:

I have another direction to send you. I grew up in an age in medicine when Demerol was considered a great drug, and literally, millions of doses were successfully used to treat patients' pain. One of the things that I discovered in my interaction sicklers is that they prefer Demerol to other forms of opioids. So, then we have the combination of refusing to give them what they need in the first place and refusing to use what works best for them in the second place. Do you have any experience with why they like Demerol and find it useful and whether or not it's still and that's why they use it?

Gentry Wilkerson, MD:

I kind of feel fortunate that all my practice has been in the era post Demerol, pretty much been removed from the armamentarium in most emergency departments. Demerol or meperidine is a great analgesic. There's no doubt that it's got great analgesic properties. One of the problems with it is it had a large euphoric effect which some patients preferred. If you're experiencing lots of pain, getting a little euphoria, probably wouldn't be something that you're really averse to. You probably would welcome a little bit of relief in that regard. But one of the main problems with meperidine is that it's renally excreted in in-patients that are presenting with sickle cell pain. They may not be able to excrete the active metabolite, which is normeperidine. The accumulation of normeperidine lowers the seizure threshold. And that really was the driving force for why it got removed in general from emergency departments, and in sickle cell patients in particular, because up to 30% of adult patients will have some degree of sickle cell nephropathy.

Gentry Wilkerson, MD:

It was generally thought that that's just too high of a risk population to continue to use that medication. Now, we went through that era of Demerol and then Demerol getting removed, but now we're in an era where a lot of emergency departments are moving away from hydromorphone or Dilaudid. You often hear about these Dilaudid-free EDs or opioid-free EDs, which I kind of don't like the idea of that, because I think that what that is doing is it's broadcasting the stigma of Dilaudid-free ED. When you're promoting that, you're basically saying, "Most patients that present with pain are probably pain seeking, and we're just not going to give that at all." So, I don't like the approach that that has. I think that it leads to a lot of biases and I think it's kind of unfortunate. What's your experience at the hospitals that you were working at? Are you using Dilaudid or?

Aaron Leech, MD:

So, I'll say that in Tucson, we have Dilaudid. We try to do morphine first. We try to address patients that have allergies that are minor with Benadryl, some of the other Diphenhydramine, some of the other adjuncts to try to get them appropriate morphine equivalents. But the most interesting thing I've seen over 10 years is that nurses are really hesitant to give eight milligrams of morphine, but they have no problem pushing two milligrams of hydromorphone, not realizing that it's way more than they're actually giving. I've found that we tell the nurses to dilute it, put it in a 10 ml flush, push it really slowly because I think a lot of what they get is patients get from a high, whether that's a pleasant or an unpleasant experience for them is that you can't help, but push two milligrams really quickly compared to eight.

Gentry Wilkerson, MD:

Right. We experienced that. I've worked the overnight shift this weekend, Friday and Saturday night, and Saturday night, we had that exact experience. We had a nurse who came in questioning an order of eight milligrams of morphine for a patient. It wasn't a sickle cell patient, but it was a 90 kilogram male who had some painful episode going on. So, eight milligrams of morphine is a completely appropriate dose. And the nurse just wasn't familiar with it, even though for our sickle cell patients, we regularly give two milligrams or even four milligrams of Dilaudid, which as you point out is a much higher morphine milligram equivalent.

Dr. Peter Rosen:

I think many of our residents don't understand the difference. And I believe that was the source of some of the reluctance to keep using Dilaudid is it seems like you're being bruten when you order two milligrams as opposed to the usual dose of morphine. So, they tend to underdose morphine and overdose the Dilaudid.

Aaron Leech, MD:

I think this gets to the point that you're trying to make with how we treat patients with sickle cell and anyone with chronic pain if we can't have it be an us versus them of, "Well, this is what the patient wants." And that means that it must be wrong, "I'm the doctor, I'm the one who decides what's right for you and what's not." And I think it's a very dangerous approach to some of these patients. And that's how we miss some of the stuff which you bring up in the next paradigm, which is that vaso-occlusive episodes or a diagnosis of exclusion. That's how we get to anchoring. This is yet another patient with sickle cell disease coming in with pain, load them up on the pain pathway, walk away, see the next patient. And that can be incredibly dangerous.

Gentry Wilkerson, MD:

Yeah, these patients have had however many episodes in the past, and have had to present to hospital after hospital for the treatment of this. It's understandable that over time they have figured out what works for them. And when they say, "Doc, my pain is usually controlled with this regimen," well, right there, that's one of the red flags for drug seeking behavior. However, this is somebody that knows more about their disease than we know about it. We have to be careful just ascribing that to drug seeking behavior and kind of take them at their word. You mentioned the fact that we underdose their pain crises all the time, that's absolutely true. We did a small study looking at our patients and we basically dichotomized them into two different groups where we looked at what dose of opioids previously controlled their pain during vaso-occlusive episodes.

Gentry Wilkerson, MD:

And we said for the next episode when they came in, "Did they get at least 50% of that morphine milligram equivalent? Or did they get less than 50%?" And we found that patients that got underdosed less than 50% of the previously effective dose, the rate of admission was significantly higher than those that got treated, what we consider appropriately. So yeah, I think that one of the things when they come in, look at what was effective for them previously, talk to them, ask them what works for them, and then try to dose them appropriately. You may decrease the rate of admission in that regard.

Dr. Peter Rosen:

Are there other devices that could be used? We've started using ketamine instead of opiates in a lot of painful situations? Has that been tried?

Gentry Wilkerson, MD:

Absolutely, I think that this goes back to where I was saying, I think we need to do a lot of research in alternative methods because right now opioids is the tried and true, that's the recommended first-line agent. But you mentioned ketamine, that's a great idea. There are a number of case reports and case series so far, there is no published randomized controlled trial looking at ketamine in sickle cell patients. There was one trial that was underway in Brooklyn, not at the hospital that I worked at, but it was discontinued. And I don't know the reasons why it was discontinued. I believe that there's another study going on maybe in Florida, but so far nothing published.

Gentry Wilkerson, MD:

So hopefully, somebody will work on that. I have tried to use ketamine at my facility, although we had some limitations because it was still being treated as a moderate sedation. So, there's all sorts of ... I mean, the burden on doing that is really high because you've got to get consent, the airway box, the monitoring. It's just not that simple, even when you're giving a sub-dissociative dose for pain management. So yeah, that's definitely an area that needs to be researched. IV lidocaine, another thing to consider. So, there are things out there, we just don't have the evidence yet.

Aaron Leech, MD:

So, tell me a little more about how people are viewing vaso-occlusive crises on their own and kind of missing some of the other things. Is this your typical anchoring bias that, well, the patient has a vaso-occlusive crisis. This is what they always come in with, and so this must be yet again? Or is there something specific about sickle cell disease that people are missing the boat on on a regular basis?

Gentry Wilkerson, MD:

So sickle cell disease affects every organ system. These patients have complications related to skin, joints, spleen, liver, heart, kidneys, brain, et cetera. So, you always have to think about, "What kind of complication can be happening with this patient?" When the patient comes in and they're saying, "I'm having a pain crisis, I'm having pain in my arms, legs," that's fine. Most of the time that's probably going to be their vaso-occlusive crisis, but you got to do a good physical exam and you have to keep in the back of your mind. Could this be something else? Could this be a septic joint? Could this be a DVT? The incidents of septic arthritis, the incidents of DVT, all of these things are increased in sickle cell patients. So, our level of concern for these other diagnoses should be raised, and we need to do a good history and a good physical exam and not just a cursory one and get them on that pain pathway as we talked about.

Gentry Wilkerson, MD:

There was one example, the patient that we had. Probably, 30 year old patient with sickle cell who was a ... We're now calling them MVPs or multi-visit patients. He came in frequently for sickle cell pain difficult to manage. He had some behavioral issues. And I would say that his treatment was often not the best. And he came in multiple times with a joint pain, which he said was typical of his crises. And one day, I was fortunate to take care of him. And I'll say I probably got lucky, but I did a pretty good thorough exam. Noticed that his joint that he's been bothered by was swollen. It was red, it was inflamed. And turns out ... Well, at that visit, he left AMA, but on the next visit, he came in and it was floridly septic arthritis.

Gentry Wilkerson, MD:

He ended up getting massive infection there. It got disarticulated. He had a lot of complications. He ended up dying later on that year from other complications related to a sickle cell disease. But that was something that probably was missed multiple times on presentations. And I don't want to fault everybody for it. And I think that I got fortunate in recognizing it, but we have to keep this suspicious nature in the back of our mind for all these different complications that can happen.

Dr. Peter Rosen:

What other adjunctive treatments are you using? I remember there was a wave of enthusiasm for IV urea, which didn't seem terribly useful over time.

Gentry Wilkerson, MD:

So, other treatments, we talked about other pain medicines, ketamine, lidocaine, there's really not much that's been studied and proven to be effective. I personally, am not a fan of nonsteroidal anti-inflammatories in sickle cell vaso-occlusive episodes. It actually is recommended by the NHLBI not a consensus recommendation, it's actually a moderate recommendation with a low level of evidence. I started to do a systematic review on this. I'm not done, it's one of the many things that it's taken a back burner a bit, but basically, what we were finding was it didn't reduce the rate of admission, it didn't reduce the opioid requirement, it didn't necessarily reduce the pain levels of these patients. And the potential for harm is really great. We talk about patients that have a 30% risk of developing chronic kidney disease, by the time they're an adult they're presenting in their most vulnerable time during a vaso-occlusive episode, and then we're going to give a nefrotoxic agent.

Gentry Wilkerson, MD:

To me, it just never made any sense why we would give a medicine that hasn't been shown to benefit and has a great potential to harm these patients. Now, that the life expectancy is getting better and better for patients with sickle cell disease, they're going to have an accumulation of chronic issues and things that we're doing when they're 10 years old, 20 years old, 30 years old, that could be really affecting them 15, 20, 30 years down the road, so we have to keep that in mind. NSAIDs really, in my opinion, they're not part of my treatment of sickle cell patients during a vaso-occlusive episode. Other things that have been looked at, steroids, this hasn't panned out too well. There was some evidence that it did reduce admissions, but then the bounce back rate was high and the outcome of the patients that bounced back wasn't so great.

Gentry Wilkerson, MD:

That really didn't get put forward. I think there's some work by Jeffrey Glassberg up in New York looking at that. Again, I don't know where he is with that or what's going on, but I think that as of right now, steroids are not really the thing to do. There are some other treatments that are being investigated, some industry funded stuff, and I've been involved with that. And I think it's kind of exciting to be in part of the evaluation of these new medicines. There's a smaller biotech company called Fulong Pharmaceuticals and they created this drug, the brand name is SANGUINATE which is a bovine carboxyhemoglobin, which sounds pretty cool, but basically the gist of it is it increases the oxygen carrying capacity of the blood by giving this medicine.

Gentry Wilkerson, MD:

So, I was part of a small randomized blinded trial, and we don't know the outcome of it yet. We enrolled a small sample of patients and it's up to the sponsor to do all the data analysis and we're still waiting for the outcome of that study. That'll be interesting. And then I'm involved in a larger study on a medicine called rivipansel, which is a pan selectin inhibitor. This is a study that's sponsored by Pfizer. And the idea of a pan selectin inhibitor is it reduces the inflammation that's experienced in sickle cell disease. Sickle cell disease, it's not just the sickling of red blood cells, it's an activation of all sorts of things, including the inflammatory cascade by blocking the selectins, which are present on pretty much every blood cell. You're reducing that inflammatory component, at least that's what it seems to show in mice and in preliminary studies.

Gentry Wilkerson, MD:

Right now we're involved in the larger phase three study, and it's an ongoing study. I think there's 50 patients left to be enrolled in it and the results would be forthcoming. But there's a number of other medicines that are being developed in research. Hopefully, we get some more stuff out there because this is a disease process that I think research has largely left behind for decades. When you look at the drugs that are approved for sickle cell disease, right now there's two. It's Hydroxyurea which was approved, I believe in 1998 in adults and it just got approved in kids in 2017, and then L-glutamine, which was approved in July of 2017.

Gentry Wilkerson, MD:

And that's it. That's it for approved drugs for the indication of sickle cell disease. So definitely, an area that has not been met. I do a lot of work with angioedema and hereditary angioedema. This is a disease process that only affects one in 50,000 people, yet there's now lots of medicines that are approved in many more that are coming down the pipe for this really rare disease. But then with sickle cell where it's a much greater incidence of disease, we still have very few drugs available to us.

Dr. Peter Rosen:

Has anybody tried hyperbarics for acute crisis?

Gentry Wilkerson, MD:

I have seen some literature on that. I'm not familiar with too much on that. I don't think that it's anything that's gotten a lot of press or popularity. But yeah, I know that there's been some small stuff done on that, but I don't know enough about it to really speak to it. That's a good question.

Aaron Leech, MD:

When we're learning about sickle cell disease, especially in Tucson where we have a fairly sizable African refugee population, but not a huge sickle cell population. So we try to train our residents about acute chest syndrome and splenic sequestration and stroke and all of the big dangerous things. But the day in and day out of what you're going to see is going to be the vaso-occlusive crisis. And I think that having some medication and some research and medication directed towards that is very promising and something that you actually could make a difference on. I think when we started the podcast at the beginning, we said this is a disease entity that affects so many people. And as an emergency doctor, it's so easy to be jaded by seeing this day in day out and feel like I don't have any hope for it. So, this is very hopeful to see that people are starting to look more into, how can we treat the more common problem rather than just honing in on waiting until there's an emergency?

Gentry Wilkerson, MD:

Right. I agree. I mean, I'm excited to be a part of the development of this, and hopefully our efforts are going to pay off and we'll find some additional medications to use in vaso-occlusive episodes, which as you point out, are the bulk of what we're going to see as emergency physicians. It's probably about 95% of the presentations of sickle cell patients that other 5% we have to be extra careful about.

Aaron Leech, MD:

Right. And you mentioned earlier that a lot of patients that are underdosed in their treatment of vaso-occlusive crisis, they end up being admitted and you've actually done a little research in this area to see what happens and how that kind of affects our hospitals, our EDs and the healthcare system at large. Can you expand on that a little bit?

Gentry Wilkerson, MD:

Sure. This goes back to the whole idea of a lot of practice variation at my facility and I think every ED doc probably has a different way of doing these things. And every emergency department has its own issues with patient flow, getting patients in quick enough, comfort level with administration of what tends to be high doses of opioids. At University of Maryland were significantly challenged with patient flow and have probably one of the worst boarding issues in the country. It's not uncommon for our sickle cell patients to wait in the waiting room for six, eight, 10, 12 hours before they get seen by a provider which violates every notion of acute pain management that can be imagined. One of the NHLBI guidelines is that patients with sickle cell disease should be given a ESI triage category of level two which kind of puts them towards the front of the line, not necessarily the front of the line, but it definitely encourages the rapid assessment and treatment.

Gentry Wilkerson, MD:

This is something that we haven't been able to accomplish at University of Maryland yet. They're still typically given the ESI-3 unless they have some other obvious thing going on with abnormal vital signs or some other presentation that's concerning. That means that they tend to wait. And one of the things that I did when I read the guidelines was I wanted to look at, did the implementation of these guidelines reduce the time to evaluation of the patients? I wasn't able to get the ESI category changed, but with the implementation of the guidelines and this focus on quick assessment and treatment, I was hoping that our providers were getting more involved in it. And unfortunately, did not show any significant change. The average time from registration to administration. The first analgesic went from roughly, I think it was three and a half hours to just under three hours, which there was nothing significant about that.

Gentry Wilkerson, MD:

Not even close to significant decrease in the time. And then I looked at time from first dose to the second dose and there was no significant change there. Our admission rate didn't go down. None of the metrics that I looked at with implementation of this guideline actually improved, which was a little disappointing because put a lot of work into the guideline. But I'm still happy that the guidelines there. I'm constantly teaching about it, educating our providers that it exists, encouraging them to use it. We created an order set in Epic based on the guidelines to help streamline what providers were going to be ordering. And now I'm excited to say that I now have a sickle cell disease nurse navigator program that it's taken a lot of work to get that implemented, but our nurse navigators started work one week ago.

Gentry Wilkerson, MD:

And I'm excited to see how this is going to change things. This is a ... I have to give a shout out to the American College of Emergency Physicians and Pfizer who gave the seed money for this with a grant. And then the hospital, I went to the hospital and said, "I've got this grant money. It will, in no way cover the entire salary of a nurse for a year. Can you give me some additional money?" And the hospital saw the value in it. And I was able to get a large amount of funding to help fund this program. Hopefully, we're able to show the value of the nurse navigator program. And it remains to be seen. We're one week into it.

Aaron Leech, MD:

It's very exciting to get buy-in from a lot of different sources to try to do something that matters.

Dr. Peter Rosen:

One of the disappointments of the human genome project is that a little differences made in the management of genetic diseases. I think sickle cell is high on that list. Has there ever been any work in trying to end the disease by say a bone marrow transplant with non sickler?

Gentry Wilkerson, MD:

Yeah. So, hematopoetic stem cell transplant is the curative option for sickle cell disease. This has been something that's been around for a while now. I don't know exactly, but certainly one or two decades. The problem initially was in order to match somebody, in the past that had to be a sibling that had great matching. And so that limited it, and then the complications of the stem cell transplants were kind of high, so it really wasn't recommended in the run of the mill sickle cell patient, because I think the two year survival I think it was 79% at one point. So, the cure could be worse than the disease. Now, again, there's selection bias because they were probably only doing that in the truly sick patients.

Gentry Wilkerson, MD:

So, I don't know that much about all the data on stem cell transplants, because it's not much in the realm of what I do in the emergency department, but I do know that they're starting to expand the pool of potential donors. That's something that as they're honing their skills in stem cell transplants, we're probably going to see more of that and better outcomes. So definitely, something that's in the future, but yeah, it'd be great if we could figure out some cure, because sickle cell disease comes from a point mutation. It seems like it would be such an easy thing to fix, but not yet, we're not there yet.

Aaron Leech, MD:

It seems like if I can summarize, the best thing that emergency doctors can do to aid in the care and kind of decrease some of the burden that sickle cell disease puts on just the entire system is to make sure that we adequately aggressively treat pain and don't put these patients on a pathway that we never check on them again, but to really look a little bit deeper as we would with somebody that has any chronic illness. The COPD patient that we need to make sure it doesn't have a pneumo, the asthmatic that we have to make sure isn't having anaphylaxis. I mean, these are conditions that are chronic and you said, we see 90% of the time, it's going to be vaso-occlusive crisis.

Aaron Leech, MD:

But just a little bit extra diligence in looking to make sure we don't miss anything else, how much reliance do you put in a patient's history when you ask them, "I think of a migraine as a corollary. Is this your typical pain crisis?" And if they say, "Yeah, this feels exactly like normal." Okay, well then we're going to put you into the pain pathway. And I'm just going to make sure everything else is squared away versus the patient that says, "Normally, I have pain in my back and my arms, now I have pain just on the left side, just in my legs, just in my head."

Gentry Wilkerson, MD:

Yeah. I take that into account greatly if these patients know their disease process better than we know. So when they say that there's something different about this, it makes me really think, "Okay, are we missing something?" If they're saying, "I typically get back pain, but now I've got left arm pain." "Okay, well, did you have a PICC line recently in that arm? Is there something that I need to worry about which could have increased your risk of having upper extremity DVT? Are you having any fevers? Are you having a hard joint too? What do I need to think about?" And as long as I've thought about these other bad things that can happen and I've evaluated it appropriately, then okay, they can kind of just be managed like a vaso-occlusive episode.

Aaron Leech, MD:

It sounds kind of silly of like, "All right, the paradigm shift has to be, make sure you don't miss the simple stuff," but it's the simple stuff that we tend to gloss over. But the exciting thing that you're doing with some of this research, I think that hopefully, it pans out and that it has some great potential to make a big difference. Is there anything else that you want to highlight about some of the work that you're doing right now? This kind of new and up and coming things?

Gentry Wilkerson, MD:

Mostly with the sickle cell navigator program, which is a ... It's a quality improvement project that said, "I'm still going to be looking at outcomes because I can't help, but look at that sort of thing." But I think that it has a great potential to reduce the healthcare utilization, which is when these patients get admitted, because we have not met their needs for analgesia, there's a huge burden on the healthcare system. The patients, once they get admitted, the average length of stay for sickle cell patient is five days. The downstream effect is that's going to increase the number of patients that stay in your hospital. That's a bed that's not going to be able to be used for another patient. And there's a cumulative problem with that. I get a report every day of our multi-visit patients who are admitted to the hospital for sickle cell disease.

Gentry Wilkerson, MD:

And the report today is astonishing. There's a dozen sickle cell patients who are currently admitted to the hospital. So, these are patients that are taking a bed. If I could have helped their pain earlier on and gotten them out of the hospital, maybe that's going to reduce the crowding. The benefit to me is immense. If I am not admitting a sickle cell patient, I'm able to admit another patient that has some other disease process going on. So, there's a great benefit to me in trying to adequately treat these patients and find other ways to utilize healthcare resources that may not be inpatient admission or emergency department.

Aaron Leech, MD:

And clearly a benefit to them as well. Do you find that there's a window that we have in the ED that if we get a patient's pain controlled within a certain amount of time, we can probably abort the admission versus sending them into almost a status of just pain of where now it's going to take a long time to get this broken.

Gentry Wilkerson, MD:

I don't have the data to definitively say it, but I agree with that statement. I think that when a patient presents with a vaso-occlusive episode, the clock is kind of ticking, and if you can get their pain managed earlier, you can avoid that admission. However, if they're sitting in the waiting room for six to 10 hours that ship has sailed. They're probably not going to be able to get appropriate analgesia. And even if they do have appropriate analgesia, they probably have some level of fear of being discharged with this idea of, "What if my pain comes back and I have to sit another six to 10 hours in the waiting room before I get treated." So, they're probably gonna be hesitant to be discharged. And I can't say blame them, we failed them when we parked them in the waiting room for so long.

Dr. Peter Rosen:

I was very impressed with how different the management of these patients were once the hematology department set up a pain program for them, and I hate to admit it, but I think a lot of that is biased racism. When the hematologist calls you and says, "Here's the dose of medicine you need to give Mr. Jones," he gets it faster. And nobody thinks about whether this is another black patient painkiller seeking. Before that, we had the same issues you do, patients sits in triage and sits in triage, and maybe finally gets evaluated by someone. So, maybe we have to overcome our own unknown bias in order to do a better job with sickle disease.

Gentry Wilkerson, MD:

Yeah, absolutely. There's lots of work that's been shown that not only is there explicit bias where people are outright racist, sometimes even in the medical community which is just so sad to think that that exists. There's implicit bias. I think all of us have to recognize that we have implicit biases and studies have shown that patients that present with other acute painful episodes like biliary colic or renal colic, they get treated faster than patients with sickle cell disease, even without any evidence of explicit bias. So, the only reasonable explanation is there's an implicit bias going on. So, you mentioned when a hematologist calls up and says, "Oh, the dose that this patient should get is this." And it greases the track to have that appropriately given. I like the idea of a lot of indigent individualized care plans.

Gentry Wilkerson, MD:

And that's one of the things that the nurse navigator role is going to help establish developing care plans for our individual patients so that there isn't a lot of kind of wondering what's the right thing to do for this patient when they come in. And I think that once we get those established, it's going to make it a lot easier to have all the providers on board with the various treatments that are recommended. It makes it easier with nursing as well. You can say to nursing, "This is their care plan." They're like, "Oh, okay, that's fine."

Aaron Leech, MD:

I find that when the provider is not comfortable with the disease in front of them, it really makes ... I can speak for myself, it makes me question a lot of what I do, "I'm the one who's treating this condition, I'm not particularly comfortable with this condition. I don't know enough about it. Therefore, I'm hesitant to do what the patient is telling me to do. What maybe I've read about in books or papers or have been trained, but I just don't have the level of comfort that I should. And you get a specialist on the phone that you may or may not have ever met in person, and they tell you to do something.

Aaron Leech, MD:

Well, now I've transferred that discomfort onto a specialist. So, I'm just going to spread this around a little bit more." And I think that just a little bit of what you've done and educating people on the podcast hopefully increases people's comfort and now it's all spread upon you of, "Well, I heard Dr. Wilkerson say this," so it's probably a good idea. But it really does help though to have somebody say like, "It's okay if you need to treat this pain aggressively," because this is what the patient needs.

Gentry Wilkerson, MD:

Sure, thank you. [inaudible 00:53:06].