

# Sickle Cell Today

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## Gene therapy for sickle cell disease: A breakthrough treatment for a child

By Hamayun Imran, M.D., and Preethi Marri, M.D.,  
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Sickle cell disease (SCD) is a genetic disorder characterized by the production of abnormally shaped red blood cells, which leads to blockages in blood flow and results in severe pain, organ damage, and reduced life expectancy. It affects nearly 100,000 people in the United States. Traditionally, treatments for SCD have been limited to pain management, blood transfusion therapy, and medical therapy with hydroxyurea or immunotherapy such as crizanlizumab.

Hematopoietic stem cell (HSC) transplantation, although potentially curative therapy, has its own limitations of reduced availability of a potentially matched donor and associated long-term complications. However, recent advancements in gene therapy have brought hope to patients with SCD by offering a potential cure. In 2023, the U.S. Food and Drug Administration (FDA) approved two gene therapies — Casgevy and Lyfgenia — for SCD in patients 12 years and older, marking a milestone in the treatment of this devastating disorder.

Gene therapy for SCD works by addressing the root cause of the disease — the mutation in the HBB gene that codes for hemoglobin, the protein responsible for carrying oxygen in red blood cells. In patients with SCD, a single nucleotide mutation in this gene causes the production of abnormal hemoglobin (HbS), which results in the characteristic sickling of red blood cells. The process of gene therapy begins with harvesting the patient's HSCs, which are the precursor cells that give rise to blood cells.

These cells are then genetically modified in a laboratory to either correct the mutation, thus producing adult hemoglobin, or introduce a modified version of the hemoglobin gene, such as fetal hemoglobin, both of which prevent the sickling. Patients then undergo high-dose chemotherapy to eradicate existing abnormal cells followed by the infusion of the modified cells into the body, where they produce healthy, non-sickling red blood cells.

Both FDA-approved therapies have shown promising results in clinical trials, with patients experiencing



significantly reduced pain episodes and no longer requiring blood transfusions for more than a year. Most side effects experienced during the clinical trials over a period of two years were transient and were related to high-dose chemotherapy. The FDA, however, has a black-box warning for blood cancer that has occurred in some patients who received Lyfgenia. Therefore, it is imperative that patients are followed long term.

The approval of gene therapies has marked a vital moment in the treatment of SCD, as they offer the possibility of one-time, curative treatment rather than lifelong management. The cost of gene therapy is currently high, and access is limited. However, we are hopeful that over time the price tag decreases and more centers are certified to commercially provide this life-changing curative treatment to many individuals with this debilitating disorder.

The Johnson Haynes Jr., M.D., Comprehensive Sickle Cell Center provides consultation for the diagnosis,

*continued...*

management, and treatment of children and adults with SCD. The center cares and advocates for a large number of individuals and their caregivers affected by SCD. The Division of Pediatric Hematology takes pride in sharing with the local SCD community details about our first patient who successfully received gene therapy in 2024.

Addilee Mason was born with SCD and is now a 13-year-old female who has had a tough course, starting with her first painful episode in infancy. Despite the family being very compliant with medications, Hydroxyurea therapy with dose escalations, and regular checkups, she had multiple hospitalizations for pain episodes, sickling in the lungs, bone infections, and blood clots.

After several years of complications and despite optimization of medical and transfusion therapy, we discussed curative options with family during a pediatric sickle cell clinic appointment, and then a consultation with the transplant center took place. Unfortunately, she did not have a suitable matched donor. The transplant center shared information on gene therapy clinical trial participation once she turned 12 years of age.

Fortunately, Vertex Pharmaceuticals Inc. had a spot for her at their research center in Nashville, TN. Addilee qualified for the gene editing trial CTX-151 after a year's wait to meet strict eligibility criteria. Participants in this research study received a single intravenous infusion of CTX001, consisting of cells collected from a patient's bone marrow and modified to produce fetal hemoglobin.

She did not have major complications during chemotherapy and cell infusion. Currently, she enjoys a normal hemoglobin and remains pain-free at the 11-month mark. Her hemoglobin composition continues to show > 55% fetal hemoglobin (HbF). Addilee and her family are very pleased with the outcome. She will continue to have regular monitoring visits for many years.

#### References:

Josiah Ballantine, John F. Tisdale: Gene therapy for sickle cell disease: recent advances, clinical trials, and future directions, *Cytotherapy*, 2024 Dec 26;S1465-3249(24)00925-3.

Alexis Leonard, John F. Tisdale: Gene therapy for sickle cell disease, *Hematology Am Soc Hematol Educ Program*. 2023 Dec 8;2023(1):542-547.



## Blood transfusion therapy utilization and blood donations in sickle cell disease

By Mohammad Barouqa, M.D., AB (Path), QIA (ASCP), Assistant Professor of Laboratory Medicine and Anatomic Pathology and Director of Transfusion Medicine, University of South Alabama

Sickle cell disease (SCD) is a serious inherited blood disorder affecting millions worldwide, particularly those of African descent. The condition leads to painful episodes, organ damage, and life-threatening complications due to the abnormal shape and rigidity of the red blood cells. One of the most critical treatments for SCD patients is blood transfusion therapy, which alleviates symptoms and can be used to prevent severe complications. However, the growing demand for blood donations and persistent shortages pose significant challenges for those who depend on this lifesaving intervention.

To enhance transfusion safety and reduce complications such as alloimmunization, USA Health System Transfusion Medicine Services are incorporating molecular/genetic testing to characterize the blood types and antigens of patients more accurately. This advanced testing allows for better donor-recipient matching, significantly lowering the risk of immune reactions to transfused blood. Additionally, the implementation of the American Society of Hematology (ASH) guidelines, which advocate for a patient-specific approach to transfusion therapy, and review by transfusion medicine physicians, clinicians, and nurses allows each transfusion to be carefully tailored to the patient's unique needs, reducing the risk of alloimmunization, and improving overall health outcomes.

Despite these advancements, blood shortages remain a major challenge, making it difficult for SCD patients to receive timely and compatible transfusions. Several factors contribute to this issue:

**Limited donor diversity:** SCD patients often require blood from donors with closely matched blood types, yet a lack of ethnically diverse donors makes finding compatible blood difficult.

**Fluctuations in blood supply:** Seasonal trends, natural disasters, and global health crises like the COVID-19 pandemic have significantly impacted blood donation rates worldwide.

**High demand for blood products:** Many SCD patients require frequent transfusions throughout their lives, increasing the demand on blood banks.

**Misinformation and fear:** Misconceptions about blood donation and fears about eligibility prevent many from donating, further exacerbating shortages.

To combat these challenges, it is crucial to increase blood donations, especially from diverse communities. By donating regularly, individuals can directly contribute to the well-being of SCD patients and others in need of transfusions.

Public awareness campaigns, community engagement initiatives, and targeted donor recruitment efforts play a crucial role in ensuring a steady and reliable blood supply. Hospitals and advocacy organizations are also working to expand education and encourage more people to step forward as donors.

For our patients with SCD, blood transfusions are more than a medical treatment, they are a lifeline. The integration of molecular testing and clinically personalized transfusion approaches has significantly improved care for SCD patients, but ongoing blood shortages remain a pressing issue. By fostering a culture of regular blood donation and supporting innovative medical advancements, we can make a profound difference in the lives of those battling this challenging disease.





# Reno-protective effects of angiotensin converting enzyme inhibitors or angiotensin receptor blockers on protein wasting nephropathy in sickle cell disease

By Ardie Pack-Mabien, Ph.D., FNP-BC; Jessica King, FNP-BC; and Antwan Hogue, M.D., USA Health Johnson Haynes Jr., M.D., Comprehensive Sickle Cell Center; and Caleb Judges, M.D., and Gideon Dosumuni, M.D., Department of Internal Medicine, and Sabrina Besette, M.D., Department of Internal Medicine-Nephrology

Albuminuria is the most common manifestation of glomerular damage in the adult with sickle cell disease (SCD).<sup>1</sup> Many of the individuals with SCD and sickle cell nephropathy will later develop chronic kidney disease and end-stage renal failure in their lifetime.<sup>1</sup>

Previously published studies revealed most adults with SCD and albuminuria treated with angiotensin converting enzyme inhibitors or angiotensin receptor blockers (ACEI or ARB) demonstrate short-term reductions in the level of protein wasting. However, there is no published long-term, evidence-based data on the efficacy of ACEI or ARB therapy in the sustained reduction of proteinuria in adults with SCD and sickle cell nephropathy.

While previous studies have not provided long-term data on the efficacy of such therapies and gaps exist, the purpose of this observational descriptive study was to evaluate the short- and long-term reno-protective effects of ACEI or ARB in adults with SCD and sickle nephropathy.

A retrospective chart review was conducted on 250 adult patients with SCD evaluated at the Johnson Haynes Jr., M.D., Comprehensive Sickle Cell Center during the 11-year period from Jan. 1, 2011, to Aug. 31, 2022. Urine protein creatinine ratio (UPCR) was examined at baseline, six, 12, 18, 24, 36, and 48 months. Eligibility for study inclusion included: > 300mg of protein/gm creatinine on two untimed consecutive steady-state urine samples; hemoglobin electrophoretic profile diagnostic of HbSS, HbSC, HbS $\beta$ 0-thalassemia, or HbS $\beta$ + thalassemia disease; males and females age >19 years; documented treatment with an ACEI or ARB for a minimum of two years and compliance with ACEI or ARB by patient history; clinic records documenting at least 50% of appointments kept.

Eligibility for exclusion included: clinic records documenting non-compliance with ACEI or ARB, clinic follow-up, and scheduled lab draws; and renal replacement therapy. Of note, intermittent acute, chronic simple, or exchange (chronic or acute) red blood cell transfusions did not preclude study participation nor did use of disease-modi-

fying therapies i.e., hydroxyurea, endari, oxbryta, or crizanlizumab.

A Wilcoxon Sign Rank test was conducted to examine the median reduction in UPCR. There was not a statistically significant reduction in the UPCR after six months of therapy from baseline,  $z = -1.730$ ,  $p = .084$ , with a medium effect size ( $r = .30$ ). However, the median UPCR was reduced from baseline (Md = 624) to (Md = 580) after six months of therapy with ACEI or ARB.

There was a statistically significant sustained reduction in the UPCR for this cohort of adults with SCD after 12 months,  $z = -2.540$ ,  $p = .011$  with a large effect size ( $r = .50$ ); 18 months,  $z = -2.664$ ,  $p = .008$ , with a large effect size ( $r = .50$ ); 36 months,  $z = -2.353$ ,  $p = .019$ , with a large effect size ( $r = .50$ ); and 48 months,  $z = -2.549$ ,  $p = .011$ , with large effect size ( $r = .50$ ).

There was not a statistically significant reduction in the UPCR for this cohort of adults with SCD after 24 months,  $z = -1.548$ ,  $p = .122$ . However, the median UPCR decreased from (Md = 624) after six months to (Md = 422) after 24 months of therapy. The median UPCR decreased from (Md = 580) after six months to (Md = 393) after 12 months, (Md = 282) after 18 months, (Md = 422) after 24 months, (Md = 303) after 36 months, and (Md = 248) after 48 months of therapy. Findings from this study suggest efficacy in the long-term use of ACEI or ARB in the reduction of proteinuria in this cohort of adults with SCD after 12, 18, 36, and 48 months of therapy.

Overall, there was a greater than 20% reduction in the median UPCR from the six-month interval to the 12, 18, 24, 36, and 48 months in this cohort of adults with SCD. However, further research in a larger cohort of adult SCD and sickle nephropathy would yield more generalized findings.

## References:

1. Hariri, E., Mansour, A., El Alam, A., Daaboul, Y., Korjian, S., & Aoun Baho, S., (2018). Sickle cell nephropathy: An update on pathophysiology, diagnosis, and treatment. *International Urology and Nephrology*, 50, 1075-1083. <https://doi.org/10.1007/s11255-018-1803-3>



# Pediatric to adult care transition program: Health maintenance and prevention

By T'Shemika Perryman, RN, PACT Coordinator, USA Health Johnson Haynes Jr., M.D., Comprehensive Sickle Cell Center

Children and adults with sickle cell disease (SCD) are more vulnerable to severe infections because of damage to the spleen, an organ that protects the body against certain types of bacteria, such as *Streptococcus pneumoniae* (pneumococcus), *Meningococcus*, and *Haemophilus influenzae*. As a result of the damage to the spleen, individuals with SCD are less able to clear certain bacteria and are immunocompromised.

According to the Centers for Disease Control and Prevention, individuals with compromised immune systems, such as adults and children with SCD, should receive an annual influenza (flu) vaccine and adhere to specific vaccination schedules for *Pneumococcus*, *Meningococcus*, and *Haemophilus influenzae* type B, which includes all standard childhood vaccinations like the Measles, Mumps, and Rubella vaccine (MMR).

## Why are immunizations so important for children with sickle cell disease?

Immunizations work by helping the immune system develop protection from a specific disease. They are particularly vital for those who are more susceptible to infections like measles, a highly contagious virus that manifests as a high fever, cough, runny nose,

red, watery eyes, and a full body rash. It is mostly spread through droplets when an infected person coughs or sneezes. Very tiny respiratory droplets also come from coughing, sneezing, or talking and can float in the air and travel longer distances. They enter the body through the nose or mouth. Measles was said to be eradicated in the United States in 2000; however, multiple outbreaks have been reported in recent months. As of April 2025, 800 cases have been confirmed in the United States.

## How can you protect yourself and your children?

The most effective way to prevent the spread of measles and other infectious diseases is vaccination. The MMR vaccine is safe and effective and is a part of the pediatric vaccination schedule. Normally a two-dose regimen, the first is given between 12-15 months, and the second is given between 4-6 years of age.

Your doctor will help make sure your child gets the right vaccinations at the right time. This depends on your child's age, timing of earlier vaccinations, and any additional risk factors. Please discuss immunizing your child with your local primary care provider, hema-

tologist, and/or sickle cell expert.

As with any medication, please contact your healthcare provider or sickle cell specialist if you have questions or concerns about the medication being prescribed for the management of your SCD.

### References:

- Cober MP, Phelps SJ. (2010). Penicillin prophylaxis in children with sickle cell disease. *J Pediatr Pharmacol Ther.* 15(3):152-159.
- Halasa NB, Shankar SM, Talbot TR, et al. (2007). Incidence of invasive pneumococcal disease among individuals with sickle cell disease before and after the introduction of the pneumococcal conjugate vaccine. *Clin Infect Dis.* 44(11):1428-1433. doi:10.1086/516781. <https://www.sicklecelldisease.org/2025/03/20/scdaa-statement-on-the-measles-outbreak/>
- Kato GJ, Piel FB, Reid CD, et al. (2018). Sickle cell disease. *Nat Rev Dis Primers.* 4:18010. doi:10.1038/nrdp.2018.10. [www.cdc.gov/measles](http://www.cdc.gov/measles)

# *From the director's desk*

## Thank you to our valued donors for keeping Haynes' legacy alive

By Ardie Pack-Mabien, Ph.D., FNP-BC, and Antwan Hogue, M.D.

The mission of the Johnson Haynes Jr., M.D., Comprehensive Sickle Cell Center is to improve the lives of people affected by sickle cell disease (SCD) through comprehensive individualized clinical care, basic and clinical research, and patient and professional education, proving that there is: Life After Birth with Sickle Cell!

The center provides varying levels of services to over 500 adults and children affected by SCD. The primary faculty and staff consist of two adult internal medicine physicians and three pediatric hematology/oncology physicians, three adult advanced practice providers (one of whom also provides pediatric services as a pediatric-to-adult-care provider to facilitate a smooth transition to adult care), two pediatric advanced practice providers, one adult registered nurse, and three pediatric registered nurses.

As the administrative and medical directors of the center, we recognize the center can be no stronger than the community in which it serves and express sincere gratitude for the community's support.

Over the years, the center has received numerous donations from various individuals across the state of Alabama and local community organizations. We sincerely appreciate the generosity of those individuals and organizations. We especially thank the family of the late Dr. Johnson Haynes Jr.

Dr. Haynes served as the director of the center, mentored numerous medical students and residents (physicians in training), was a true sickle cell warrior, an internal medicine and critical care pulmonologist, was and nationally recognized by U.S. News & World Report as a Top Doctor for several years.

Thank you also to the Classic Corvette Club, whose members have graciously presented the center with monetary donations for nearly nine years, as well as supported the annual Sickle Cell Awareness Month blood drive sponsored by members of the Alpha Phi Alpha Fraternity, Beta Omicron Lambda Chapter; Franklin Memorial Primary Health Center, the Sickle Cell Disease Association of America-Mobile Chapter; and the American Red Cross.

The **2025 blood drive has been scheduled for Sept. 27, 2025**, at Franklin Memorial Primary Health Center Medical Mall. The 2024 drive collected 41 units with the potential to impact 141 lives through blood donations.

Thank you also to the individuals both near and far who are too numerous to list for their monetary donations in honor of Dr. Haynes.

***With your continued support, we will continue the legacy of Dr. Haynes as a center of excellence with a focus of providing educational programs related to SCD and financial assistance for those individuals without the means to meet healthcare expenses in the Mobile community and surrounding areas.***



### **USA Health Johnson Haynes Jr., M.D., Comprehensive Sickle Cell Center announces 2024 and 2025 high school graduates**

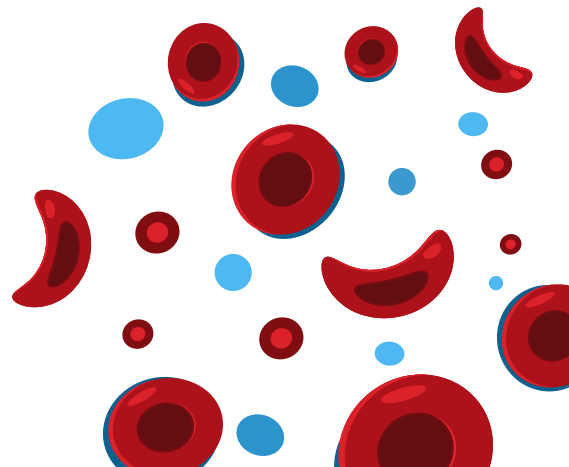
Congratulations to our 2024 and 2025 high school graduates! No matter what comes next, never forget how amazing, unique and wonderful you are.

#### **Class of 2024**

- **Jamya Perry**, Blount High School
- **Zyeiere O'Field**, Blount High School
- **Mylaija Shavers**, McGill-Toolen High School

#### **Class of 2025**

- **Asia Toney**, Blount High School
- **Sonara Dubose**, Choctaw County High School
- **Jamerius Holliday**, Pascagoula High School
- **Oji Bishop**, Linden High School





# Mobile sickle cell chapter advances access, equity and advocacy for patients in region

By Gerald Alfred, Executive Director, Sickle Cell Disease Association of America – Mobile Chapter

The Sickle Cell Disease Association of America – Mobile Chapter, under the leadership of executive director Gerald Alfred, recently launched BeHEARD in collaboration with the Johnson Haynes Jr., M.D., Comprehensive Sickle Cell Center. BeHEARD is an acronym for Bridging Education, Hope, Empowerment, Advocacy, Research and Dedication, and it represents a patient-centered, community-focused approach to reducing disparities in care, expanding access to services, and uplifting the voices of those living with sickle cell disease (SCD).

This bold and community-rooted initiative is transforming how individuals living with SCD are supported across nine counties in southwest Alabama, including Mobile, Baldwin, Choctaw, Clarke, Covington, Conecuh, Escambia, Monroe, and Washington.

BeHEARD offers more than just outreach. It includes building a sustainable network of care and advocacy that includes the following:

## **Sickle Cell Disease and Trait Testing**

- On-site and mobile testing events throughout the nine-county region
- Increased education around sickle cell trait and genetic counseling; case management and counseling
- Personalized case management to assist with healthcare navigation, medications, and social support
- Access to licensed counselors and social workers for patients and families

## **Transportation Support**

- Coordinated rides to and from USA Health and community medical appointments
- Access to screenings, follow-ups, and outreach events
- A dedicated Ride Request Line and future mobile scheduling platform

## **Community-Based Outreach**

- “BeHEARD Town Halls” and Mobile Resource Days in each county
- County ambassadors and grassroots partnerships to extend local impact
- Engagement with churches, schools, and civic organizations

SCDAA-MC is powered by a trained team of social workers, community health workers, and counselors who provide informed, culturally competent support. Their work ensures that individuals and families receive consistent care, reliable information, and the compassion they deserve.

BeHEARD matters because SCD is one of the most underfunded and misunderstood chronic conditions in the United States, with a disproportionate impact on African American communities. Across southwest Alabama, patients frequently face delays in diagnosis and pain management; barriers to reliable transportation and follow-up care; and lack of access to testing, counseling, and coordinated support.

If you or someone you know is living with SCD and needs support, or if you're interested in learning more, volunteering, or partnering with SCDAA-MC, call 251-432-0301 or visit [www.scdmobile.org](http://www.scdmobile.org).



# Make a Gift Today!

Give online at [usahealthsystem.com/give](http://usahealthsystem.com/give)

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**JOHNSON HAYNES JR., M.D.**  
**COMPREHENSIVE SICKLE CELL CENTER**

I am a: (Please check all that apply.)

☐ Friend

☐ Parent

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☐ USA Employee

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Name(s): \_\_\_\_\_

Address: \_\_\_\_\_

City: \_\_\_\_\_ State: \_\_\_\_\_ Zip: \_\_\_\_\_

Phone: \_\_\_\_\_ Email: \_\_\_\_\_

## I wish to make a gift to the University of South Alabama as follows:

### Gift Purpose: (Check all that apply.)

☐ Johnson Haynes Jr., M.D., Memorial Fund

☐ Dr. Cecil L. Parker Jr. Sickle Cell Disease Distinguished Lectureship Endowment

☐ Watson Henderson Higher Achievement Award

☐ This gift is in honor/memory (circle one) of: \_\_\_\_\_

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☐ Please charge my credit card (check one)

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***Thank you for your consideration.***



## Meet the newest member of the Comprehensive Sickle Cell Center team

Santosha (San) Thompson, MSN, APRN, FNP-C, recently joined the Johnson Haynes Jr., M.D., Comprehensive Sickle Cell Center team, bringing a wealth of experience and a strong commitment to exceptional patient care.

Thompson earned a Bachelor of Science in Nursing (BSN) at the University of South Alabama through the Accelerated Nursing Program. Following graduation, she worked as a registered nurse at Children's & Women's Hospital, where she specialized in general pediatric care. Her dedication to advancing her skills and knowledge soon led her to broaden her expertise, gaining invaluable experience in caring for patients across all stages of life, from newborns to adults. She is currently working toward a Doctor of Nursing Practice degree at USA and will graduate this fall.

Throughout her career, Thompson has served as a traveling nurse, where she traveled across 48 states and provided acute care in diverse clinical settings. Experiencing different cultures and lifestyles while gaining insights into healthcare disparities across the nation sharpened her clinical skills and reinforced her commitment to addressing inequities within the healthcare system.

Before joining our team, Thompson served as a family nurse practitioner at a local urgent care center. She is eager to collaborate with the sickle cell center team and leverage her extensive expertise to ensure that every patient receives the highest standard of care.

She is passionate about patient education, advocacy, and empowerment. Her dedication to support patients and their families, along with her commitment to making a positive impact on their healthcare journey, aligns perfectly with our legacy and mission.