Gene Therapy As A Cure for Sickle Cell Disease

Felicia L. Wilson, MD, FAAP
Professor of Pediatrics, Division of Hematology/Oncology

On March 10, 2019, CBS 60 Minutes reported on an exciting medical breakthrough using gene therapy to cure sickle cell disease (SCD). For 15 months, they followed the scientists and patients who are ushering in this genetic revolution. The concept started nearly 20 years ago when scientists working on the Human Genome Project stunned the world by decoding 25,000 genes that make up a human being. They hoped to use that genetic blueprint to advance gene therapy, which locates and fixes the genes responsible for different diseases. Genes are pieces of deoxyribonucleic acid (DNA) that contain the code or instructions for how the body makes a certain protein. Each protein has a specific job or function in the body. Genetic diseases can be caused by a change in the code called a mutation. SCD is caused by a mutation in the beta globin gene that provides the instructions to make the part of hemoglobin, the protein inside of red blood cells (RBCs) that carries oxygen. Normal RBCs are round, flexible, and flow freely through small blood vessels to carry oxygen to all parts of the body. They have an average life span of 120 days in the blood stream. In SCD, the RBCs become rigid and have an abnormal stickiness to the lining of the blood vessel. Instead of flowing freely, they create blockages in blood flow leading to pain, tissue damage, organ failure, and premature death in some cases. They also have an average life span of only 19 days. New RBCs are constantly being made in the bone marrow to replace those that have reached the end of their life span.

Currently, the only cure for SCD is a bone marrow transplant from a matched healthy donor without SCD. Bone marrow contains the blood stem cells that follow the genetic code and give rise to new blood cells. These hematopoietic stem cells (HSCs) with the sickle hemoglobin code are destroyed by chemotherapy. Then HSCs are removed from the donor’s bone marrow, blood, or umbilical cord, then infused into the patient. If the transplant is successful, the donor’s HSCs produce normal RBCs curing the disease. Donors can be a sibling or someone unrelated with the same tissue type, but less than 18% of people with SCD can find a matched donor.

Gene therapy could provide a cure for many more people because it doesn’t rely on a donor. Instead, HSCs are harvested from the patient’s
Gene Therapy As A Cure for Sickle Cell Disease (continued)

own bone marrow. A therapeutic beta globin gene is inserted into the HSCs using a modified, harmless virus. Then, the genetically transformed cells are infused back into the patient to repopulate the bone marrow producing an anti-sickling hemoglobin. As a further benefit, gene therapy avoids conflict between the donor’s and patient’s cells. After a bone marrow transplant, doctors have to suppress the patient’s immune system to prevent it from attacking the transplant, which leaves the patient vulnerable to infection. Even then, the donor cells might attack the patient’s cells, resulting in graft-versus-host disease — the leading cause of death after a bone marrow transplant. Gene therapy eliminates this concern.

Twelve clinical trials studying gene therapy to treat SCD are now ongoing. It is important to note that clinical trials are research studies that explore whether a medical treatment is safe and effective for humans. They produce the best data available for determining the standard of care. Clinical trials follow strict scientific standards to protect patients and help produce reliable results. For safety purposes, clinical trials start with small groups of patients to find out whether a new treatment causes any harm. In later phases of clinical trials, researchers learn more about the new treatment’s risks and benefits.

Although we cannot draw large conclusions from the few patients who have undergone gene therapy, we are encouraged by the results thus far. Obviously, there is no long term data to determine the feasibility of this cutting edge technology for all individuals with SCD. It’s a very exciting time in the SCD community as gene therapy show great promise for a cure.

Sickle Cell Disease Practical Issues XVII: New & Emerging Therapies & Approaches to Management

On Saturday, May 18, 2019 the USA Health Comprehensive Sickle Cell Center will host its 17th Annual Regional Sickle Cell Conference in Mobile, AL. This year’s meeting will feature national and local experts addressing topics ranging from effective emergency department assessment and management of patients presenting with pain crisis to new and emerging therapies that have either recently been introduced or will likely soon be introduced in the care of patients with sickle cell disease. For more information on the conference visit www.southalabama.edu/colleges/com/research/sicklecell.html, email vgardner@health.southalabama.edu or call 251-470-5893. Register online at: https://www.usa-cme.com

Pediatric to Adult Care Transition (PACT) Program Participant Highlight: Jada Cathcart

The mission of the PACT Program is to improve health and literacy through educational programs and a comprehensive, patient-centered health care delivery system. This system emphasizes self-management, patient-physician collaboration, and interdisciplinary care coordination directed at increasing patient education.

Our PACT Program not only teaches it’s participants about their disease process, it encourages them to be self-advocates, take control of their lives, and not be defined by their disease. Also, it encourages them to use their voices and share their stories with others so that people will have an understanding of what it’s like to live with sickle cell disease. Below you will find a personal story from one of our participants detailing her life from her point of view.

Growing Up with Sickle Cell Disease by: Jada Cathcart

“I grew up sick with Sickle Cell, yet when I think about my childhood, I see
it as happy, even though it was filled with hospital visits and scary procedures. I’m currently still healthy and at 18 years of age will be graduating high school and moving into adulthood. I hope that sharing my story will encourage all, that life can still be filled with enjoyment if you’re sick with any life-altering illness despite the difficulties you may experience.

I don’t know if there was a specific moment when I found out I was diagnosed with Sickle Cell Disease and thought my life was over. I only remember my parents being there satisfying my every need and want. I remember my family always hugging me and telling me that they love me. My first crisis at age 7, in elementary school, not only left me feeling pain but embarrassment that I collapsed in front of my classmates.

As I got older, I started to see my disease as not being routine; I wasn’t in control over it, and I was right. I had been exposed to treatments, daily medication, and a depressive thought that this is all that my life consists of and I wasn’t normal. When I was in my teen years and finally hit puberty, I started to act out so I would fit in but even the slightest actions couldn’t change the fact that my health needed to be taken into serious consideration 24/7.

June 16, 2014, I decided on my own to truly be committed to giving my life to Christ. Since then everything started to change inside physically and mentally, emotionally healing my thoughts and body. You can say it was with better medications, treatments, or home life but only God got me through those hardships.

Growing up I went through so many stages of grief. I managed to get through those with the help of my strict parents. Of course, I appreciate they don’t want anything to happen to me, but I’m already 18 years old and I need to live my life before I regret it. I know my parents are here for me. There are many reasons why my parents are so strict. My parents are overprotective. It honestly frustrates me when half the time when I’m never allowed to go anywhere with my friends or go to places without my parents having to be right next to me.

I understand they want to protect me because they love me, and I appreciate it, but growing up being ill in a strict home with strict morals, I learned what the text book recognizes as “Special Treatment” throughout my childhood meant to my siblings. It took a bad turn on my mental state especially when I started to get bullied. I have been diagnosed with Sickle Cell Disease since birth, so growing up I always could handle whatever obstacles that came my way accept what was happening in my life whether it’s in my control or not. All I ever wanted to do was try to fit in with my peers causing me to be judged at home about my actions. Overall, I look back and think about my childhood and I missed out on a lot. It upsets me knowing what could’ve been, even though sometimes I wanted to commit suicide but I knew that wasn’t the solution to my problems. My life will always be tough but we have to stay strong and get through it the right way.

People were seeing me getting treated like I was lost and needed to be cared for. This also made me take risks for what I considered to be “Love”. The truth is it didn’t matter how anybody treated me and for once I got to call the shots for myself. As I keep going on with life learning and growing, this experience has shaped me in so many ways. I’m the best person I can be and I don’t blame my parents nor myself. I’ve come to learn great lessons out of this, to love all, and to move forward knowing everything happens for a reason, and to not let this interfere with the greatness that is about to become of my life in the future. Talk about sharing my story, this is closure to healing old wounds, said with the most honest and loving regards I can of telling my Sickle Cell Journey.”

Meet the USA Comprehensive Sickle Cell Center’s Newest Addition to their Pediatric to Adult Care Transition (PACT) Program

The USA Comprehensive Sickle Cell Center invites you to join them in welcoming their newest member, Cimone Smith, MHA.

Smith is a native of Beatrice, Alabama and graduated with her bachelor’s degree in Pre-Professional Health Science/Informatics from the University of South Alabama in 2014. As a student at USA, Smith worked at University Hospital as a student assistant in the Department of Radiology where she assisted in keeping the electronic records of diagnostic studies performed using Powerscribe 360. While pursuing her master’s degree she served as a consultant, coordinator, project manager and liaison for the quality department at one of the area hospitals. While there she participated in the development, evaluation, planning, and implementation of new technology and
Meet the USA Comprehensive Sickle Cell Center’s newest addition to their Pediatric to Adult Care Transition (PACT) Program (continued)

educational projects. Smith graduated with her Master’s degree in Health Administration/Informatics from the University of Phoenix in May 2016. As a part of the USA Comprehensive Sickle Cell Center PACT Program team, Smith will function as the Life Skills Transition Coordinator and Facilitator of the Sickle Cell Trevor Thompson Transition Project (ST3P-UP Trial) under the Patient-Centered Outcome Research Institute contract. She will work alongside Drs. Johnson Haynes, Jr., Felicia Wilson, and Ardie Pack-Mabien; T’Shemika Perryman, RN; and the Sickle Cell Disease Association of America, Mobile Chapter case manager, Aisha Davis. In her role as the life skills transition coordinator, Smith will develop and implement innovative technological programs and activities that foster the development of self-management and self-advocacy skills for participants in the PACT Program. She will also serve as the liaison between the pediatric and adult providers and health care team, patients, and caregivers. Ms. Smith may be reached at (251) 471-7714 or (251) 470-5893.

Sickle Cell Disease: Therapeutic Advancements

Hamayun Imran, MD, MSc, Professor and Chief, Pediatric Hematology/Oncology

Sickle cell disease affects approximately 100,000 individuals, primarily African-Americans, in the United States. The therapeutic armamentarium against this chronic illness remains limited. However, ongoing clinical research remains promising. Some of the newer sickle cell disease therapies in development target specific pathways that lead to recurrent sickling with pain crises and organ dysfunction. Some prevent and others are meant to abort the acute painful episodes, commonly referred to as vaso-occlusive crises (VOC), a consequence of enhanced sickling of red cells and obstruction to blood flow. One group of such drugs blocks the selectin molecules. Selectins, a family of adhesions molecules (L-, P- and E-selectin) involved in cell migration and activation, are thought to play an important role in the development of VOC. Their key function is to mediate the adhesion of white blood cells to endothelial cells (inner lining of blood vessels) and platelets in the circulation. Therefore, drugs that block selectins can prevent blockage in small blood vessels and maintain blood flow.

Rivipansel, a pan-selectin inhibitor, has shown encouraging effects on hospitalization time and opioid use. It was tested at 22 US locations in a phase 2 randomized, placebo-controlled, double-blind trial in 76 hospitalized patients, ages 12 and older who had experienced 5 or fewer episodes of VOC in the last six months. Patients were dosed within 24 hours of admission to the hospital with the IV drug that was repeated up to a maximum of 15 doses or resolution of the VOC. The average cumulative IV opioid analgesic use was reduced by 83% in the rivipansel group compared to placebo and the average duration of hospitalization was reduced by 41 hours, a difference that is clinically meaningful yet found to be statistically insignificant. Therefore, RESET, a phase 3 clinical trial with expected accrual of 350 patients, ages 6 and older is further evaluating the role of rivipansel in people with SCD. The USA Health College of Medicine, department of pediatrics participated in the initial portion of the RESET trial and successfully enrolled 3 children.

A P-selectin inhibitor called crizanlizumab is also worth mentioning as a potential preventative therapy. Crizanlizumab was tested in a phase 2, double-blind, placebo-controlled, study (SUSTAIN trial) consisting of 52 weeks of monthly IV treatment. One hundred and ninety-eight patients with or without hydroxyurea, aged 16–65 years with SCD who had experienced 2-10 pain episodes in the previous 12 months were included in the study in sixty US centers. Crizanlizumab significantly reduced the frequency of pain episodes by half, significantly delayed the median time to first pain episode by 2.7 months and second pain episode by 5.2 months. When compared to placebo, it decreased the annualized median rate of days hospitalized by 42% (4.00 vs. 6.87 days), a clinically relevant difference. The adverse events rate was low and acceptable in both groups. Results were published in New England Journal of Medicine. The University of South Alabama, Department of Pediatrics also contributed in this successful endeavor by enrolling 1 child on the trial.

These are just a couple of examples out of the many other drug therapies in the pipeline awaiting results from clinical trials but a discussion of the science behind these novel therapeutics is less meaningful if newer therapies do not reach the people with SCD. Introduction of hydroxyurea into the clinical world exposed barriers to the effective use of the only available disease modifying agent1. This challenge was compounded in a younger population since
the FDA took over two decades to approve its use in children. It is hoped that crizanlizumab’s approval trajectory would be different since the manufacturer has already started the process of FDA filing in less than three years of publication of the successful results. Finally, improvement in access to care to specialized centers is of paramount importance for people with SCD in order for newer therapies to prove their effectiveness in and outside the clinical trial arena.

References:
1. Field JJ. Can selectin and iNKT cell therapies meet the needs of people with sickle cell disease? Hematology Am Soc Hematol Educ Program. 2015; 2015:426-32


ATTENTION Medicaid Recipients

Effective May 1, 2019, Alabama Medicaid will begin implementing changes to their prescription drug coverage of opioids. This will affect some individuals who receive large quantities of opioids for their pain management. For more information log on to the link listed here: https://www.medicaid.alabama.gov/content/4.0_Programs/4.3_Pharmacy-DME.aspx

Traveling Guide for Individuals with Sickle Cell Disease

Jessica King, MSN, FNP, NP-BC

Well folks it is almost that time of year again where everyone is looking forward to summer vacation. For most people a vacation will include traveling by car or plane to destinations within the United States to visit historical landmarks, theme parks, shopping malls, or visit family and friends, while others may choose to travel abroad to another country to explore and experience a different culture or their ancestry. For individuals with sickle cell disease traveling internationally or in the U.S.A., it takes adequate preparation particularly when traveling by air when risk for pain crisis may increase. Therefore, it is always important to contact your health care provider and set up a pre-travel office visit well in advance to discuss you or your families’ concerns for potential health risks, preventative strategies, and contingency planning for illness. I have included a list below of helpful tips for travel preparation:

1. Make an appointment with your health care provider to discuss travel plans, including travel dates, method of travel, destination, and length of stay.

2. Request a travel letter from your health care provider to take on your trip. The letter should include the specific type of sickle cell disease you are affected with, allergy list, medication list, additional health conditions such as high blood pressure, diabetes, past medical history, and surgical history.

3. If you are traveling abroad, check with your local health department and the Center for Disease Control to see if any travel vaccinations are recommended prior to your departure.

4. Make sure you have adequate amounts of all medications you take daily as well as your pain medications, should you need them on your trip.

5. If your plans include air travel, you will need to allow yourself adequate time prior to the planned trip to discuss travel details with your health care provider. This includes dates of departing and return travel, travel destination locations, and approximate length of flight time.

6. If your health care provider deems it necessary that during flight you will need supplemental oxygen, you will need to contact the airline(s) you plan to travel with to determine what the regulations are for in-flight use of oxygen. The Federal Aviation Administration dictates which portable oxygen devices are acceptable, and the required battery supplies needed based on
Traveling Guide for Individuals with Sickle Cell Disease (continued)

the duration of your departure and return travel. You will be responsible for securing the oxygen concentrator and batteries needed for travel.

7. Access the Global Sickle Cell Disease Network (GSCDN) at www.globalsicklecelldisease.org. The network is worldwide and provides information regarding the location of available health care services and treatment centers for individuals with sickle cell disease.

8. Maintain adequate hydration prior and throughout your vacation experience to decrease the risk of potential health complications.

9. Always remember to dress appropriately for the weather and prepare for unexpected weather conditions. Airports are notoriously cold regardless of the season, so definitely bring a jacket!

In closing, the rewards of travel can be substantial for individuals that have lived a lifetime with a chronic illness like sickle cell disease. Travel opens your heart, broadens your mind and fills your life with stories to tell. And with advanced planning and involvement of your health care providers, patients and families can approach their travels safely and well informed.

References:


The Sickle Cell Trevor Thompson Transition Project (ST3P-UP Trial)

PARTICIPANTS NEEDED FOR A RESEARCH STUDY

Are you between 16 and 25 years old and have sickle cell disease?

Are you still getting your sickle cell care from a pediatric clinic?

The USA Health Comprehensive Sickle Cell Center is conducting a research study about how to support young adults with sickle cell disease as they prepare for moving to adult care. We will compare a structured education-based program with a peer mentor to a structured education program alone to see if it reduces how often young adults with sickle cell disease go to urgent care, the emergency department, or get admitted to the hospital.

To participate you will be asked to:

• Complete questionnaires about your quality of life every 6 months
• See your sickle cell provider every three months for at least 30 months
• Your providers will track how often you go to clinic appointments, urgent care, the emergency department, and get admitted to the hospital
• You may be assigned a peer mentor who will contact you regularly to support you during the transition process.

Please contact the ST3P-UP Study Team if you are interested at (251) 470-5893

This research is conducted under the direction of Dr. Ifeyinwa [Ify] Osunkwo, Atrium Health.
USA HEALTH

Make a gift to the University of South Alabama Comprehensive Sickle Cell Center

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