The Sickle Cell Disease Coalition Research & Clinical Trials Working Group is focused on distilling key sickle cell disease (SCD) information presented at national conferences and disseminating it to the SCD community. Each summary is written in plain language to ensure comprehension of topics covered. This summary is from the 2020 American Society of Hematology Annual Meeting. The original abstract entitled "Cellular Breakups: Transfusion and Hyperhemolysis In Sickle Cell Disease" is available online as well.

Researchers study why some patients with sickle cell disease have severe reactions after receiving a transfusion

Every year, the American Society of Hematology meets to talk about new research. At its 2020 meeting, researchers and doctors shared what they have learned about why some patients with SCD develop a possibly fatal reaction after receiving a blood transfusion to treat their disease.

Blood transfusion remains an important treatment for SCD and can be life-saving. As many as 90% of persons living with SCD will receive at least one transfusion by the time they are 20. However, some patients develop a reaction called "alloimmunization" against transfusions and reject the transfused cells. It's like your body attacking invaders that are there to help but are rejected. The process of rejecting them can sometimes cause a series of events in some SCD patients that can damage tissues and cause severe symptoms, even resulting in death. These reactions to transfusions are often missed because they sometimes happen up to a month after a transfusion and the symptoms are very much like those of an acute SCD crisis. This reaction is called "delayed hemolytic transfusion reaction, or DHTR".

For many years, scientists have been studying "alloimmunization" and these "hemolytic reactions" in patients who have received multiple blood transfusions, not just SCD patients. "Hemolysis" means breakdown of the red blood cells, which contain "heme." Heme carries oxygen throughout the body to all of our cells and organs. However, when red blood cells break down, hemoglobin and heme escape into the plasma (the liquid portion of the blood). This free-floating heme causes inflammation and disease symptoms. Red blood cells from patients with SCD are themselves fragile and break down. It appears that the extra free-floating heme from this breakdown of transfused red blood cells on top of ongoing hemolysis puts SCD patients at higher risk for developing severe DHTR reactions than other patient populations. Better understanding of why someone develops this severe reaction could lead to ways to prevent it from occurring.

Researchers have learned:

Recent studies have shown that a healthy immune response to hemolysis is to switch off the cells, similar to putting out a fire. However, immune cells from SCD patients who develop this reaction to transfusion are not able to handle any extra free-floating heme, putting these patients at higher risk for developing severe DHTR reactions. Understanding what is different about the immune cells of these patients may help researchers find ways to treat and prevent these types of reactions. In addition, another important part of the blood is called the "complement system," which works with your immune system to protect the body from infections and remove dead cells and foreign material. Free-floating heme can jumpstart the complement system in ways that are actually more harmful than helpful.

Researchers are beginning to test ways to hunt for this free-floating heme to gather it up and slow or prevent the damage it can cause. They are also getting a better understanding of how to slow down the complement system so it does not overreact in its attack against the transfused red blood cells. Some

existing drugs, such as eculizumab, have been shown to slow or stop the inflammatory response. Other strategies include better blood tests that can predict which patients might be more likely to have a bad transfusion reaction.

Keep in mind

The results of research studies are always limited in what they can and can't tell you. This research to date has involved a small number of patients and studies with more people will be needed to know how effective a treatment or predictive test might be.

Always consult your doctor before entering a clinical trial.

Questions to ask your doctor

- Should I consider whether this type of therapy might be important to me?
- Are there clinical trials I could join?

Access the American Society of Hematology Research Collaborative's SCD Clinical Trials Pamphlet to learn more about clinical trials for SCD.