Informed Consent

The Effects of Phosphotidylserine Expression on Older Red Cell Units in Adults with Sickle Cell Disease

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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

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IRB Study # 21-0018
Title of Study: The Effects of Phosphotidylserine Expression on Older Red Cell Units in Adults with Sickle Cell Disease
Principal Investigator: Matthew Karafin
Principal Investigator Department: Pathology and Lab Medicine - Clinical
Principal Investigator Phone number: (919) 966-4676
Principal Investigator Email Address: matsco@email.unc.edu
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CONCISE SUMMARY

Purpose: To assess the affect the age of a unit of blood has on individuals with sickle cell disease

Length: You will be in this research project for 4 months, or until you receive 3 transfusions in the outpatient setting.

Procedures: There are 2 groups in this project. You will be randomly enrolled into one of the 2 groups. You will have 10 total study-related visits.

Risks: Study potential risks include infection, bruising, itching, or dizziness.

Benefits: We do not know if participation in this trial will help you.

Other options: You do not have to join this study. Your options include: joining a different study protocol, continuing your routine care, or getting no treatment for your condition.

If you are interested in learning more about this study, please continue reading below.

What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary.

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There

also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

Red cell transfusions are one of the best treatments available for patients with sickle cell disease. It has been shown to be effective in preventing stroke and in reducing the acute and chronic pain experienced from frequent painful crises. While units of blood can be stored for up to 42 days, the most effective storage age to improve health in sickle cell disease remains unknown. Currently at our hospital, 50% of all units received by sickle cell patients are stored longer than 18 days.

The sickled red cells in your body have increased concentrations of a lipid (a type of fat) known as phosphatidylserine or PS, which has been shown to contribute to the removal of these red cells by your immune system and perhaps increased inflammation and symptoms of your disease. It is also known that older stored red cells have increased concentrations of this same lipid and therefore older stored units may not help you to feel better over time. No study has yet evaluated the effect that PS content in your routine red cell transfusions has on your health. However, the effect is likely subtle, as no study to date has shown any differences based on red cell storage age. Due to the potential importance of PS in sickle cell disease, our goal is to better define the effect these lipids on your immune system and on your health after a red cell transfusion. Ultimately, our goal is to maximize the benefits of red cell transfusion therapy for all patients with sickle cell disease.

You are being invited to participate in this research because you are between the ages of 16 and 60, you have sickle cell disease, and you receive red cell transfusions as part of your routine health care.

Are there any reasons you should not be in this study?

You should not be in this study if you:

1) have a history of severe reactions to transfusion therapy
2) have a history of multiple red cell alloantibodies
3) are currently receiving hydroxyurea therapy
4) are currently participating in another therapeutic trial for SCD

5) are pregnant
6) have a history of HIV infection

How many people will take part in this study?
Approximately 40 people at UNC and Emory University will take part in this study.

How long will your part in this study last?
You will be in this research for about 4 months, or until after you receive 3 study transfusions in the outpatient infusion clinic.

What will happen if you take part in the study?
After signing this consent form, the following will take place:

You will be randomized into one of the two study groups.

Study Group One – blood stored in the blood bank 10 days or less

You will receive 3 study transfusions in the infusion clinic. If you need a transfusion and the blood bank does not have enough red cell blood units stored at 10 days or less, you will be given red blood cells stored the shortest amount of time among all the available units. You will only receive blood transfusions that your doctor orders for you. You will not receive more or fewer blood transfusions because you are in this study.

Study Group Two – blood stored in the blood bank 30 days or more

You will receive 3 study transfusions in the infusion clinic. If you need a transfusion and the blood bank does not have enough red cell blood units stored at 30 days or more, you will be given red blood cells stored as close to 30 days as are available among all the available units. You will only receive blood transfusions that your doctor orders for you. You will not receive more or fewer blood transfusions because you are in this study.

Summary of Study Procedures:

Medical chart review: Your medical chart will be reviewed by the study investigators. As part of the review, the study investigators collect information from your medical record including diagnoses, medications, and information about how many blood transfusions and hospitalizations you have received. All of your information will be kept confidential.

Blood draws: You will have **one study blood draw** around 4 weeks prior to your first transfusion. You will then have **two study blood draws** on the day of your blood transfusion. Blood samples will be drawn by inserting a needle into a vein in your arm or through your medi-port. Each sample obtained will be approximately 2-3 teaspoons. You will have a blood draw before your transfusion and as close to 2 hours after the end of your transfusion as possible.

Urine sample: You will be asked to provide a **urine sample** in a sterile cup for analysis. This will occur one time prior to each transfusion.

Physical exam: Similar to a usual clinic visit including an evaluation of your clinical health, and measurements of your weight, blood pressure, and other vital signs. This exam will take place in the infusion clinic where your transfusion will occur. Since the tests described above are part of a research study, you will not be notified of the results and they will not become part of your medical record. The exception would be if results from one of the standard blood tests indicate a condition that may be harmful to your such as a critically low hemoglobin or platelet count. In this case, your regular physician will be notified of the results. The other lab test besides the blood count are done for research purposes only. You will continue to have routine medical tests ordered by your physician and those test results will be entered into your medical record as usual.

After these tests, you will receive your normally scheduled blood transfusion. However, unlike normal (you would usually receive a mix of units), you will either receive only red cell units stored ≤ 10 days or only units stored ≥ 30 days. You and your physician will not know which one you will receive. This will occur over the next 3 blood transfusions that you receive in the infusion clinic.

When you are finished receiving your blood transfusion…

- **Clinical Diary**- You will be asked to complete a diary of your daily pain symptoms, any infection symptoms, and your medication needs. You will be given specific instructions on how to do this. This is a very important part of the study, and a study nurse or coordinator will call you at regular intervals to help you and answer any questions that you have.
- **Follow-up lab visits**- You will also be asked to return to the lab for additional blood samples to better track the change in your sickled red cells over time after the transfusion. These samples will be obtained a day after the transfusion and then two weeks after your transfusion. These lab visits will be scheduled ahead of time with your study coordinator.
- **Follow-up physician exam**- After your final study transfusion, a study nurse or coordinator will call you about 3 weeks after your last transfusion and schedule a time for a final physical exam. This exam will be similar to the other exams that you received during the study. This follow-up can occur at an already scheduled future outpatient appointment.

Research study groups

Because no one knows which of the interventions is best, you will be "randomized" into one of the two groups. One group will receive newer red blood cell units and one group will receive older red blood cell units. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in either group. Neither you

nor the research doctor can choose what group you will be in. Since the expectations of patients and doctors can influence the results, neither you nor your research doctor can know which intervention you will get until the research is over. A computer program chooses which group you are in, and the infusion in each group will look the same. In an emergency, your research doctor can find out which group you are randomized too.

Summary of Each Visit:

Transfusion Visits:
- Physical Exam
- Blood Draws
- Urinalysis
- Diary Review/Administration

24 Hour Post Transfusion Visits:
- Blood Draws
- Diary Review

2 Week Post Transfusion Visits:
- Blood Draws
- Diary Review

End of Study Visit (can occur the same time as the 2 week post final transfusion visit)
- Physical Exam
- Collection of Diary

What are the possible benefits from being in this study?
Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

What are the possible risks or discomforts involved from being in this study?
The blood transfusion, regardless of the storage age provided, is given as part of your regular clinical care. The risks are no different than that presented to you as part of your routine red cell transfusion consent. Blood does change during refrigerated storage, but no studies have evaluated these changes on chronically transfused patients with sickle cell disease. In other populations (1 in patients with acutely ill sickle cell disease patients, and 2 in other populations), published randomized clinical trials have demonstrated no adverse effects. If you do not participate in this study, 50% of your transfusions would be older than 18 days.

There is also no increased risk of blood borne infections from the transfusion in this study. While there was a small study that showed a decrease in your body's ability to fight infections after blood transfusion, most research shows no increased risk.

Blood Tests

Additional blood will be taken for various lab tests. The phlebotomy has a risk of slight discomfort as well as bruising and a very small risk of infection. If you have a mediport, the port will preferentially be used. The amount of blood taken for these study labs (if not done as part of routine care) will be no more than 6 teaspoons on any one day.

Loss of Confidentiality.

Every effort will be made to keep your study records confidential but we cannot guarantee it. Depending on the kind of information being collected, if your study information were accidentally seen, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have question, you can talk to the study director about whether this could apply to you.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

If you choose not to be in the study, what other treatment options do you have?
You do not have to be in this research study in order to receive treatment. Your regular transfusion therapy will continue regardless of your decision to participate in this study.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?

- Your data will be stored in locked and password protected files.
- Only the researchers and study staff who run the trial will have access to individually identifiable data.
- Your name or ID number will not be used to store study data. A number will be assigned for data collection purposes. The link between your identifiable information and the data collected for this study will be protected on a password protected file that will only be accessible to the PI and study staff involved in the data collection process.

Participants will not be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

By signing this informed consent document, you agree that some of the information generated by participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you. This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study. Additionally, the information may be shared with your medical insurance plan if the research services provided are billed to your insurance.

You will be asked to sign a separate form ("HIPAA Authorization") to allow researchers to review your medical records.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal.

Will you receive anything for being in this study?

You will receive $50.00 for each study transfusion you participate in for this study. If you discontinue the study, you will receive compensation for the number of transfusions that you did participate in. You will receive a total of $150.00 for completing the study. Any payment may be reportable as income on your taxes.

IF you participate and make an attempt to stay after your transfusion you will also be given a lunch voucher at each study transfusion.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

Who is sponsoring this study?
This research is funded by the National Institutes of Health (NH). This means that the Dr. Matthew Karafin and the research team are being paid by the NIH for doing the study. The researchers do not, however, have a direct financial interest with the NIH or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent

_____
Signature of Witness if applicable; e.g. literacy issues, visually impaired, physically unable to sign, witness/interpreter for non-English speaking participants using the short form)

_____
Date

_____
Printed Name of Witness