Blood Bank Practices for Sickle Cell Patients in North Carolina

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A Master's paper submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Public Health in the Public Health Leadership Program.

Chapel Hill
2004

ABSTRACT

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Sickle cell disease (SCD) remains an important public health problem. Predominantly affecting African Americans, SCD is associated with significant health, financial, and psychosocial costs. Therefore, it is vital to find new ways to improve delivery of care to this patient population.

The hospital blood bank plays a key role in delivering transfusion therapy to SCD patients. Because transfusion therapy represents the mainstay of treatment for most SCD patients, we hypothesized that a systematic review of blood bank practices for these patients might uncover new opportunities to improve this care. Current blood bank practices for SCD patient have not been previously described.

This paper discusses blood bank practices for SCD patients in North Carolina. The layout is as follows. First, the underlying cause, history, and costs of sickle cell disease are described. Next, evidence supporting the use of transfusions for SCD management and its associated risks are considered. Data from a cross-sectional study of NC blood bank practices for SCD patients are then presented. Finally, the significance and implications of this research are discussed.

INTRODUCTION

Sickle cell disease (SCD) is a heterogeneous group of inherited disorders, characterized by the vaso-occlusive episodes with end organ damage, chronic pain and hemolytic anemia*. Replacement of a single amino acid (i.e. point mutation) in both β-subunits of the hemoglobin (Hgb) molecule causes a conformational change of red blood cells (RBCs) under low oxygen tension, resulting in the characteristic "sickle cells" observed microscopically in a peripheral blood smear for which this disease is named. Clinically, SCD varies in severity both within and between specific genotypes; however, all SCD patients have abnormal RBCs that 1) are poor carriers of oxygen, 2) break easily creating a state of chronic anemia, and 3) lodge in small caliber vessels further preventing oxygen delivery to the tissue.

Approximately 70,000 to 80,000 Americans have SCD making this one of the most common genetic disorders; an additional 2.5 million carry the sickle cell trait.[1, 2] Although SCD occurs in a variety of racial/ethnic groups, this disease disproportionately affects African Americans, an already vulnerable population. In the United States, health disparities clearly exist for patients in racial/ethnic minorities and those with lower educational attainment and socio-economic status. SCD patients typically fall into all of these categories.[3] An important national goal is the reduction and elimination of these health disparities.[4]

More than thirty years ago, SCD was formally recognized as a national health priority.[2] In 1972, the National Sickle Cell Anemia Control Act was signed into law providing for the establishment of screening and counseling

programs, health education for both health providers and the public, and finally, research and research training. Shortly thereafter, the Secretary of Department of Health and Human Services (formerly known as the Department of Health, Education, and Welfare) created a National Sickle Cell Disease Program under the direction of the National Heart Lung and Blood Institute (NHLBI) within the National Institutes of Health (NIH)*. Since then, NHLBI has devoted over 923 million dollars for research in SCD.[2] Through the Blood Diseases Program, under the Division of Blood Diseases and Resources, NHLBI develops and disseminates materials on SCD, supports research on the use of blood and blood components in the treatment and prevention of disease, and leads a national multidisciplinary program of basic, clinical and applied research through NIH funded Comprehensive Sickle Cell Centers.[5] Although these efforts have dramatically improved the lives of SCD patients, this chronic disease still remains an important public health issue today.

In addition to disease morbidity and mortality, there are significant societal and individual costs for persons affected with SCD. Annual total health care costs for SCD patients exceed $3 billion dollars[6] due to frequent interactions with the health care system. Inpatient admissions occur at a rate of 0.9 per patient per year (75,000 hospitalizations annually) with an estimated cost in excess of 475 million dollars.[7] Outpatient visits occur at a rate of 8 visits per patient per year.[8] Total hospital and physician charges are estimated to be in the order of $8,000 dollars per patient per year.[8] Nearly all SCD patients rely on government support through national and state programs to pay for these high medical

expenditures.[9-11] Individual costs include financial strain, mood disorders such as anxiety and depression, drug abuse, developmental delays, frequent interruptions in school and work, and inability to work secondary to chronic disability. All of these factors present a tremendous burden to patients, their families, and society. In addition to these costs, SCD patients remain at risk for early mortality and significant disease morbidity.

Once a uniformly fatal disease of childhood, today > 85% of children with SCD survive past 18 years of age.[2, 12] This contrasts with 1974 autopsy data that showed the average life span of a person with SCD in the United States was approximately 14 years.[13, 14] Today, the average life expectancy for African American males affected by SCD is 42 years and 45 years for affected African American females. [15] Although sickle cell patients now live into late adulthood, their life expectancy is still decreased by approximately 25 to 30 years as compared to their African American counterparts in the United States. Risk factors for early mortality include frequent pain episodes, renal failure, stroke, and acute chest syndrome, all of which represent significant disease morbidity.[16]

Disease morbidity is secondary to the chronic occlusion of vessels causing painful "crisis" and end organ damage as described above. Commonly affected organs include the spleen, brain, lungs, kidney, and joints. Complications in SCD patients include painful crisis, aplastic anemia, acute chest syndrome, stroke, and renal failure. Surgical complications, even for minor surgeries such as tonsillectomy and cholecystectomy, occur in up to 35% of patients.[17, 18] These complications are potentially life threatening.

An important advancement in the management of this disease has been use of transfusion therapy, which has been a key component of improved survival rates in SCD patients.[19] For the great majority of SCD patients, transfusion therapy represents the mainstay of care. By age 20, approximately 70-80% of patients will have been transfused.[18, 20-23] The underlying rationale for using RBC transfusions is to improve tissue oxygenation by decreasing the proportion of HbS red cells and suppressing further production of HbS through replacement of sickle cells with blood from normal donors.

The benefits of transfusion therapy, which include decreased morbidity and mortality, have been demonstrated in a few randomized control trials (RCT) and several observational studies. The first RCT to demonstrate a dramatic reduction in disease morbidity and mortality with the use of transfusions was a 1998 study comparing the incidence of stroke among children with SCD identified as high risk by transcranial Doppler ultrasound. The authors of this study found a greater than 90% reduction in the incidence of first stroke in children who received periodic prophylactic transfusions (chronic transfusions).[24] This trial was stopped after only 18 months due to overwhelming morbidity for patients in the non-transfusion arm. Other studies have shown that chronic transfusions also reduce the risk of recurrent stroke in children.[25, 26] Studies in both children and adult patients receiving chronic transfusions have shown a reduction in hospitalization rates, emergency room visits, recurrence of acute chest syndrome, and severity and frequency of severe pain episodes.[27-30] A RCT comparing the use of aggressive vs. conservative transfusions in SCD patients

undergoing surgery showed a decrease of some peri-operative complications.[18] Based on these and other studies, transfusion are recommended for the acute management of life threatening and organ threatening vaso-occlusive episodes such as acute chest syndrome, multi-system organ failure, splenic sequestration, and stroke and prevention of disease complications.[26, 31-35]

Transfusion therapy however, is not without risks. Potential complications of transfusion therapy, as for any patient, include transmission of infectious diseases, allergic reactions, and hemolytic and non-hemolytic transfusion reactions. Sickle cell patients however, are at increased risk for hyperviscosity, iron overload, painful episodes, alloimmunization, and severe hemolytic transfusion reactions (delayed and acute).[36-38]

Alloimmunization is the most frequent and problematic complication of transfusion therapy. Rates of alloimunization for SCD patients in the published literature vary from 18 to 36%.[21, 22, 39-41] These are significantly higher than those in other chronically transfused populations such patients with β-thalessemia (5%).[41-44] On average, 1/3 of SCD patients who receive transfusions develop alloantibodies to RBC antigens that are not present on their own RBCs. Figure 1 illustrates the mechanism by which alloimmunization occurs. The risk of alloimmunization also increases with each transfusion episode.[40] The mean number of units a chronically transfusion SCD patient receives is approximately 30 units/year (range= 17-42 units/year).[45] The consequences of alloimunization include difficulty obtaining compatible blood for transfusions. In the past 2 decades, SCD patients have been the single largest users of national rare donor

blood*.[46]

Differences in antigen frequencies between blood donors and SCD patients, particularly of the Rh and Kell blood groups, are thought to constitute a major reason for the high rates of alloimmunization observed in this population.[22, 40, 47] Because the frequency of red cell antigens vary by racial/ethnic groups, the probability of transfusing a SCD patient with blood of a similar antigen profile is several times greater if blood from an African American donor is used. The probability of finding a compatible unit of blood is dependent upon the number of antigens required to be absent on donor red cells and the demographic composition of the donor pool. For example, the probability of finding a compatible unit lacking the three most common antigens missing on the red cells of African Americans (C, E, and K) is 1/33 in the typical donor pool composed of 90% Caucasians and < 10% African American. In contrast, finding these same units screening only African American donors is 1/4, an 8 fold difference.[48] More recently, Castro et al. showed that one is 24 times more likely to find a compatible unit lacking nine of the most common antigens causing alloimmunization in SCD patients if blood is selected from an African American donor.[49] However, the small number of African American blood donors relative to the entire donor pool.[50, 51 52] makes this approach impractical. Prophylactic antigen matching, that is providing SCD patients with blood from donors who lack similar major and minor red cell antigens before antibody development, is an alternate strategy to decrease alloimmunization rates and prevent associated hemolytic transfusion reactions.

Hemolytic transfusion reactions in SCD patients range from mild to life threatening. Delayed hemolytic transfusion reactions occur days to weeks after being transfused with red cells containing antigens absent on their own red cells. Although usually mild, these reactions can severe and also precipitate more serious SCD related complications.[32, 53, 54] Life threatening reactions include acute transfusions reactions. One atypical reaction that occurs in SCD patients is the "hyperhemolysis phenomenon" where the patient destroys transfused donor red cells as well their own red cells.[55, 56] This cycle of destruction is potentially fatal.

Alternatives to transfusion therapy include medication (hydroxyurea) to decrease the frequency of disease related complications[57] and bone marrow transplantation for potential cure.[58] Most patients however will still rely on transfusion therapy for treatment. Therefore, managing the risks of transfusion therapy by judicious use of transfusions in clinical practice and identifying new opportunities to improve delivery of this therapy remain critically important to improving the health of this patient population.

BACKGROUND

North Carolina (NC) is "a national model for innovation and excellence in the diagnosis, treatment, and research of SCD".[59] This is due in part to two important factors, the large number of persons affected by SCD in the state and its longstanding comprehensive state sickle cell program. African Americans comprise 22% of the NC's population.[60] Of the 1.7 million African Americans in North Carolina, about one out of every 294 is born with SCD and approximately 12,730 newborns carry sickle cell trait.[61] About 2400 children and adults have been diagnosed with SCD; an estimated 500 remain unidentified.[59] The North Carolina Sickle Cell Program (NCSCP) was one of the first state programs in the country.[59] Created in 1973 in the Department of Health and Human Services, Division of Maternal and Child Health, it serves to promote the health and well being of persons with SCD through the reduction of mortality and morbidity. It accomplishes this mission through free newborn screening, genetic counseling to those with sickle trait, education to health professionals and the public, financial assistance for medical services, and coordinated care through a multidisciplinary program of four (4) community based centers and six (6) academic and regional medical centers in the state.[59, 61] The latter includes a NIH-funded Comprehensive Sickle Cell center shared between two large academic centers, Duke University and The University of North Carolina. Studies suggest that SCD patients receive better quality of care through comprehensive sickle cell centers.[12, 62, 63]

One aspect of care that has not been the focus of much attention is the

practices of blood bank as a component of the delivery of transfusion therapy. Specifically, blood banks provide laboratory testing of patient samples, special transfusion services, blood products for transfusion, and clinical oversight for the management of transfusion complications. Despite these functions, blood bank practices for SCD patients have not been well studied. To date, there have been no studies that provide a comprehensive overview of the way blood banks are currently managing SCD patients.

Two important sources for transfusion management guidelines for SCD patients are the updated NIH monograph "The Management of Sickle Cell Disease"[14] and a consensus document from an international workshop of hematologists held in 1999, published in Seminars in Hematology.[64] Both describe the appropriate indications for transfusions, blood product use and administration techniques, and the diagnosis and management of transfusion related complications. Despite the existence of these sources, some aspects of managing SCD patients remain unclear.

One example of this is the use of antigen matched RBCs for all SCD patients. Several authors have promoted the widespread use of this practice; others support its use in a more limited fashion.[38, 39, 47, 65] Recent studies describing the use of antigen matched RBCs for SCD patients among blood banks confirmed that no single standard of care exists for this practice.[66, 67]

Based on review of the literature, anecdotal evidence, referral patterns, and expert opinion, our research team hypothesized that signification variation exists in blood bank practices for SCD patients. To test this hypothesis, we developed

and performed a cross-sectional survey of hospital-based blood banks in North Carolina, with the following specific aims:

1. To describe the current practices of hospital blood banks providing transfusion care to sickle cell patients;
2. To describe factors that may influence these practices, and;
3. To describe the use of NIH transfusion guidelines.

The study described below attempts to provide new information to those caring for SCD patients, particularly blood bankers. We hope this study will serve to provide information to blood bankers about how their practices might differ from their peers and evidence based literature and identify new opportunities to improve the delivery of transfusion therapy to this patient population.

METHODS

Sample

In order to conduct this cross-sectional survey of hospital-based blood banks in North Carolina (NC) to assess their current blood bank and transfusion practices for SCD patients, we first constructed a database of NC hospitals that potentially provide services to this population. Using the data from the state hospital licensure files, the American Hospitals Association (AHA) directory, and the Medicare On-Line Certification and Reporting (OSCAR) files, we identified 153 hospitals in NC. Hospitals that did not provide on-site blood banking, apheresis services, or both within their facility were excluded (N=19). This included regional and local blood centers that provided contractual arrangements with hospitals for these services. Based on these criteria, 132 of 157 hospitals were initially selected for inclusion. We then excluded government-associated hospitals such as Veteran's Administration and Armed Forces hospitals and specialty hospitals providing care to only select, limited patient groups, i.e. Women's Hospital of Greensboro (N=26). The former were excluded because we hypothesized that standardization within these systems could potentially mask the variation in practice we sought to describe, the latter, as they were as they were unlikely to care for sickle cell disease patients. Finally, we also excluded the two academic hospitals, University of North Carolina Hospitals and Duke University Hospitals, which comprise a national NIH Comprehensive Sickle Center. Rather, these hospitals were included in a subsequent study of blood bank practices at NIH-funded Comprehensive Sickle Centers. Therefore, the final survey sample

was composed of 106 hospitals.

Next, we used the membership roster of the American Association of Blood Banks (AABB), and information provided by the American Red Cross, Carolinas Region to obtain contact information for each hospital blood bank, the blood bank medical director, and laboratory supervisor. For each hospital, we selected two possible respondents, the blood bank medical director and the laboratory supervisor. The rationale for having two respondents per institution was based on our a priori hypothesis that each of these informants could provide unique and specific expertise relevant to different areas of the survey. We believed the blood bank medical director would provide the most accurate information on questions pertaining to clinical management and decision-making, while the laboratory supervisor could provide the most accurate information on questions relating to the day-to-day operations. Figure 2 illustrates the sampling methodology.

The final mailing list contained the following identifying information: hospital name, phone number, and address; medical directors and laboratory supervisors' name, phone number, mailing address, and email address. Telephone screening of each hospital was performed to confirm the currency and accuracy of the contact information.

All medical directors and laboratory supervisors at hospitals meeting the study criteria were mailed a self-administered, written survey accompanied by a cover letter describing the purpose of the survey, assuring confidentiality, and inviting participation. Each study participant was assigned a unique identification

number allowing data to be linked to an individual subject and the institution. The prefix "ND" was used to indicate the North Carolina medical director; "NS" was used to indicate the North Carolina laboratory supervisor.

Survey Design and Content

The 30 minute, 35 item survey questionnaire was designed to assess six general content areas: 1) background demographic information of the hospital and blood bank, 2) respondent demographic characteristics, 3) the sickle cell population serviced by the hospital/blood bank, 4) blood banking, transfusion, and apheresis practices and available services, 5) clinical management of SCD patients, and 6) availability and utilization of educational resources. To maximize the quality of information obtained on this wide range of topics, we used several response formats, including yes/no responses, single-item and multi-item responses, 4 and 5 point Likert-scale items, and open-ended responses. Additional information about the clinical management of SCD patients was collected using clinical vignettes that only the medical directors were asked to complete. The survey also collected information about individual respondent characteristics such as education/training, familiarity with NIH SCD Management guidelines, and opinions about consensus with transfusion guidelines.

Pre-testing

A draft survey instrument was pre-tested to address face validity, content, clarity, individual item format, and overall questionnaire format. For pre-testing, we selected a non-random sample of ten (10) large community based and

university hospital blood banks in Michigan and Virginia. These sites were selected based on previous experience with the medical directors at these institutions (principal investigator) in the former, and hypothesized regional similarities in patient population and practice patterns in the latter. Each potential participant was called by the principal investigator and asked to participate in the pre-testing of the survey instrument. After obtaining verbal agreement to participate, each participant was mailed a packet containing a cover letter explaining the purpose of the survey and pre-testing, the draft survey instrument, and an evaluation/feedback form (APPENDIX A). Responses were received from 5/10 participants (50% response rate). In summary, respondents indicated the content, format, and length of the survey instrument was appropriate but several questions were confusing.

Next, the principal investigator contacted six national experts on the management of SCD patients (by telephone and email) to gather additional feedback on the clinical vignette section. These vignettes were composed of four case scenarios designed to assess different areas of clinical management of SCD patients. Medical directors were asked to select the single best response based on 1) the information provided and, 2) how such a patient would be managed in their own hospital. Feedback from these experts confirmed the appropriateness of the content, format, and clarity of these four vignettes.

Based on all of the pre-testing information, a final survey instrument was drafted. As a result of feedback, the entire lay out of the survey was revised, several items were deleted, the order and grouping of items were changed, and

responses categories were simplified. The final survey instrument and cover letters accompanying each wave of data collection can be found in Appendix B.

Survey Administration

A summary of the procedures for administration of this survey is described below. A survey packet containing a cover letter, survey, and return postage-paid envelope was sent to the blood bank medical director and laboratory supervisor at each of the 106 hospitals. One hospital had two laboratory supervisors so a total of total of 213 surveys were mailed initially. Two weeks later, non-respondents were mailed a postcard reminder asking them to complete the sent survey. One month later, non-respondents received a second mailing of the survey packet. Two months after the first mailing, non-respondents received a third and final mailing of the survey packet.

Coding and data entry were performed as the surveys were returned. Detailed information on survey tracking, coding, and data entry can be found in Appendix B-3. The principal investigator ensured that all appropriate policies and procedures are followed. This study was approved by the Schools of Medicine and Public Health Institutional Review Boards at the University of North Carolina at Chapel Hill.

Measures

The following variables were selected from the NIH monograph, The Management of Sickle Cell Disease, as measures of blood bank practices: 1) use of leukocyte-reduced RBCs and 2) sickle trait negative RBCs, 3) performing

patient RBC phenotyping, 4) providing this information to the patient or family, and 5) use of antigen matched RBCs. These measure were selected as concrete and directly measurable. NIH guidelines were used as our source because it was felt that they not only reflected the opinions of the authors of the earlier consensus but also other health professionals involved in the care of SCD patients. Specifically, NIH guidelines state the following:[14]

1. All blood should be screened for the absence of sickle cell trait.
2. Prestorage leukodepletion of red cells is standard practice to reduce febrile reactions, platelet refractoriness, infections, and cytokine induced complications.
3. The antigenic phenotype of the red cells (at least ABO, Rh, Kell Duffy, Kidd, Lewis, Lutheran, P, and MNS) should be determined in all patients older than 6 months of age.
4. A permanent record of the phenotyping should be maintained in the blood bank to optimize matching, and a copy of the record should be given to the patient or family.
5. Limited matching for E, C, and Kell [sic] antigens is usually performed, unless patients have antibodies.

Figure 3 describes each guideline and its corresponding survey item(s).

Next, we developed a model of the delivery of transfusion care to SCD patients in which the blood bank was an independent factor (Figure 2). We hypothesized both external (hospital level) and internal (blood bank level) factors might affect the blood bank's ability to deliver transfusion care to SCD patients. Figure 3A-B illustrates these possible factors. The survey instrument measured The survey instrument measured the following external factors: hospital type (academic, community, other), presence of a trauma center and number of RBC units transfused/year (surrogate markers of hospital size/complexity), identification of a sickle cell patient to the blood bank prior to transfusion. Internal blood bank factors measured were specific policies/procedures for SCD patients; blood bank capabilities measured by offered services such as simple transfusions, exchange transfusions and a chronic transfusion program, testing (perform phenotyping of patient RBCs and communication of results to patient or family), blood product selection (age of RBC, special RBC products), clinical management of SCD patients in that institutions (clinical vignettes), opinions on whether clear consensus exists on the management of SCD patients, and finally, training and educational resources (availability, conference attendance, sources of SCD information).

Analysis

Because the hospital was the unit of analysis, survey responses received from either the blood bank medical director or the laboratory supervisor were considered a positive response. If responses were received from both respondents at a single institution, we preferentially selected the medical director's survey for inclusion. This method allowed us to include clinical management of sickle cell patient as an independent variable. We also excluded surveys with > 10% missing data. In that case, the more complete of the two responses was selected for analysis.

The descriptive analyses are reported as percentages of the total number of surveys used in the analysis for categorical variables; normally distributed continuous variables are reported as means and ranges. For non-parametric continuous variables, medians and ranges are reported for a more accurate depiction of the data.

Finally, in order to provide a general assessment of use of NIH transfusion guidelines by blood banks in NC, we re-categorized the five measures selected from the NIH monograph into dichotomous variables based on clinical significance or positive (affirmative) and negative responses. Descriptive analyses were performed using a standard statistical software program (STATA, 8.0, Stata Corporation, College Station, TX).

RESULTS

Of the 106 hospital blood banks surveyed, 76 returned completed or nearly complete surveys, 9 returned invalid or incomplete responses, and three surveys (3) were returned undeliverable, for a final response rate of 80.4% (85/106). Excluding invalid/incomplete surveys, a total of 76/106 surveys (70% of sample) were included in the analysis. The individual response rate was 55.4% (115/213). Characteristics of the hospitals, blood banks/transfusion medicine services, respondents, and sickle cell population are reported in Table 1.

Nearly all of the hospitals in our sample were community-based (90%); approximately 5% were university or university-affiliated hospitals. The majority of hospitals (82%) did not have a trauma center. Of those that did, only 5% were Level 1 trauma centers. Hospitals in our sample were representative of hospitals in NC.

As described in the methods, we sampled two respondents per hospital, the medical director and the laboratory supervisor. On average, laboratory supervisors responded twice as frequently as the medical directors (70% vs. 30%). All medical directors had doctorates in medicine or osteopathy; a minority also had an additional graduate degree (5%). The majority had medical training in hematology/oncology or pathology (91%). One fourth of these physicians also had subspecialty training in blood banking/transfusion medicine. Nearly all of the laboratory supervisors were medical technologists (85%) and about one quarter had obtained sub-specialty certification in blood banking (SBB) (22%).

Hospital blood banks transfused a median of 1943 RBC units per year

(range = 30-26,000 units). North Carolina blood banks provided services for 0-30 SCD patients per month (median=1). The percentage of sickle cell patients younger than 21 years of age, ranged from 0 to 100% (median = 15%). Thus, most blood banks transfused a small number of RBC units per month, and encountered few SCD patients per month. The majority of these were adults patients

Blood bank practices such as specific policies/procedures, offered services, and testing, are reported in Table 2. About one third of hospitals had specific policies/procedures for the work-up of a sample from a SCD patient and for the distribution of blood products to SCD patients. These practices did not appear to depend upon whether a patient was new or already known to the blood bank (88.3%). All blood banks offered simple transfusion of RBCs. Few offered manual RBC exchange transfusions (16%) and even fewer offered automated RBC exchanges (6.6%) or chronic exchange transfusion programss (6.9%). Although the majority of NC blood banks performed patient RBC phenotyping (69%), few patients or families received the results of this testing (16%).

Table 3 shows the frequency and types of RBCs routinely used for SCD patients. The majority of our sample typically provided RBCs that were less than or 14 days old to their SCD patients. About 16% provided RBCs less than 7 days old. The vast majority of blood banks in our sample routinely provided leukocyte reduced RBCs to SCD patients (91% always or sometimes). Few routinely provided washed, irradiated, or frozen RBCs. Finally, nearly two-thirds of NC hospital blood banks did not routinely provide, antigen-matched RBCs to SCD

patients (62%). Of those that did about half provided these units before a patient was transfused.

Respondents indicated that several external factors affected their practices for SCD patients. These included the frequency in which SCD patients were identified to the blood bank prior to transfusion, availability of compatible units, and cost. Identification of SCD patients to the blood bank prior to transfusion was fairly poor. In our sample, 52% indicated patients were always or often identified, 21% sometimes identified, and 27% rarely or never identified. When asked how difficult it was to obtain compatible RBC units for SCD patients, 9% indicated that it was very difficult, 57% indicated it was somewhat difficult, and 34% indicated it was not difficult at all. Finally, only 16% of the respondents indicated that cost affected their practices. When asked if cost were not an issue would their practices change, the overwhelming majority said no (83%).

Internal factors, measured in the survey were clinical management of sickle cell patients, consensus with transfusion guidelines, training, and availability/utilization of educational resources. There was significant item non-response for these questions. As previously described, only medical directors were asked to complete the section on clinical management of SCD patients within their institutions. Only 50% of medical directors completed this section. Therefore, these results were omitted from this paper. Approximately 75% of hospitals provided information on consensus, training, and education. Although results are not available for 25% of hospitals, we examined these items to identify possible trends and opportunities for future interventions. These results are

described below.

We originally postulated that blood bank practices could be influenced by the perception that clear consensus existed for different aspects of managing SCD patients. Approximately 50% of respondents indicated that there was clear consensus with the selection of blood products for SCD patients, indications for transfusion therapy, and the use of phenotypically matched (antigen matched) RBCs. However, the majority (70%) did not feel there was clear consensus on the use of a chronic transfusion program. The actual percentages of respondents who agreed and disagreed as well as their level of agreement/disagreement for each of these items can be found in Table 4.

Similar results were found for items related to education and available resources (Table 5). Half of the respondents felt their training had prepared them to manage the needs of SCD patients and that blood bank/transfusion information for SCD patients was readily available. The majority of respondents (65%) were not familiar with the NIH monograph, Management of Sickle Cell Disease. This finding is not surprising given the fact that no study respondents cited the NIH as a source of information about the management of SCD patients.

The most frequently listed resources for blood bank/transfusion information on SCD patient management by respondents in this sample are described in Table 6. Pathology professional societies were the most utilized source (39%) of information for blood bankers; the American Association of Blood Banks represented the bulk of this category. Consultation with hematologists and other hospital blood banks was cited as the next most common

source (21%). The remainder of sources (in decreasing order of frequency) included the American Red Cross (17%), the Internet (11%), conferences (6%) and other (5%). No respondents cited the NIH as source of information about SCD.

Finally, a few respondents provide feedback about their concerns in managing SCD patients via responses to open-ended questions. A sample of these written comments follows:

- "if we knew what the consensus was on what to do" and "we see so few patients"
- "if we know specific needs of our sickle cell patients we'd want to do all that we can to help"
- "currently we have very few sickle cell patients with time and info, we would perform prophylactic antigen typing"
- "We have a very low number of sickle cell patients. Most are referred out."
- "We have no protocol, are not consulted. For the most part, SS patients are transferred."
- "Patient management [is] under control of hematologist, not BB Medical Director"
- "Would love to be informed of continuing education re: SCD."
- " These patients would most likely be transferred to a larger facility."
- "Our hospital is very small; we would always try to get these patients to a larger facility."
- "Need guidelines for transfusion selection/crisis management/diagnosis.

Standards change per region."

- Provide special units "if ordered by MD." "Provide leukocyte reduced units if certain physicians order them."
- "May look at current practice of local area and see if we need to update our policy."
- "Antigen negative blood from ARC [American Red Cross} is too expensive to phenotypically match every sickle cell patient. Would phenotypically match sickle cell patients if antigen blood from ARC wasn't so expensive."
- "Computer system doesn't display patient diagnosis; we don't know we are transfusing a SCD patient."
- "Heme/onc docs manage our rare HbSS patients."
- "Test patient for Fya, Fyb, Jka, Jkb, S, s but do not provide units negative due to cost/availability."
- "Adult and peds [patients] are treated differently"
- "Blood Bank doesn't know if patient has SCD; patients managed by their MD's."
- "Never had a SC patient. Only have 1 family of African Americans in our community."
- "I would like to know what the best practices are for management of sickle cell patients."
- "If they have antibodies, they are going to another area."

DISCUSSION

This descriptive study provides the first comprehensive glimpse of how blood banks are currently managing transfusion therapy for SCD patients. Findings from this study support the notion that the hospital blood bank is a source of variation in the delivery of transfusion care to this patient population. In addition, they further strengthen our contention that opportunities exist to improve this care by interventions designed to address factors that affect the blood bank's ability to deliver transfusion therapy. This study also suggests that NIH transfusion guidelines are not a source of information for blood bank personnel. These results provide important and useful information to consider in the design of future interventions to improve the delivery of transfusion therapy to SCD patients

Our study confirms previous findings that variation exists in the use of specific blood products for SCD patients. Blood banks appear to uniformly provide leukocyte reduced RBCs (92%) to these patients but not antigen matched blood. In our sample, approximately 30% of blood banks provided antigen matched at any time to SCD patients. This finding is consistent with the results of a 2004 College of American Pathologists' survey of 1172 accredited laboratories in the US[67] but contrasts with another that showed 73% of academic medical centers in the US and Canada provide antigen matched blood to SCD patients prior to transfusion.[66, 67] Availability of these units has been cited as a limiting factor to this practice.[49] Nearly two-thirds of our sample indicated that getting compatible, antigen matched blood was very or somewhat difficult. Given the

fact that nationally, over the past 30 years the percentage of African American donors has remained at less than 10%[50, 68-70]the use of antigen matched blood for SCD patients may still not be feasible for most blood banks. Costs associated with routinely providing antigen- matched blood to SCD patients have also been cited as a barrier to widespread implementation of this practice.[39] It is estimated that antigen matched units are on average 1.5 to 2 times the cost of a usual RBC unit.[47] In this study, cost did not appear to be a barrier as only 16% of our sample described cost as influencing their practices.

Although there is no published data that we are aware of to compare with our finding that 52% of blood banks in NC always or sometimes provide sickle cell trait negative blood, anecdotally we know that it is standard practice among many blood banks to only screen RBC units for sickle cell trait when providing these units for manual or automated exchange transfusions (7% in our sample). In this case, pre and post transfusion monitoring of HbS is important to determine if the goals of therapy were met. With the current composition of donors, roughly 9 out of 10 RBC units will be negative for sickle cell trait. In light of this fact, the utility of screening every blood unit of for sickle cell trait becomes questionable. Therefore, our results may represent a significant underestimation of the frequency in which SCD patients actually receive sickle trait negative blood.

Our study also suggests that communication between patients, clinicians, and blood bank personnel could be improved. Our finding that less than 1/3 of blood banks who phenotype patient's RBC then provide these results to SCD patients and/or their families has not been previously reported. This is alarming as

SCD patients are already at high risk for alloimmunization and potentially severe transfusion reactions. Documentation of these results in patients' medical records may not be inadequate protection for SCD patients who receive care at multiple institutions. More frequent identification of SCD patients to the hospital blood bank prior to transfusion may help ensure that the blood bank utilizes all available resources for these patients.

As in other areas of medicine, little is known about the use of practice guidelines. In our study blood bankers, did not consider the NIH to be a definitive source of information about managing SCD patients. In addition, most felt that consensus did not exist on how to managing these patients. One possible reason for this finding may be disagreement about the evidence for various practices. This has been true for the practice of prophylactically providing antigen matched RBCs. Some authors have suggested the need for a randomized control trial comparing outcomes in patients receiving prophylactic antigen matched RBC vs. those who do not.[38] Our findings support the need for this future study. Additional reasons for our findings may include 1) a lack of involvement by blood bankers in the development and dissemination of information pertaining to transfusion therapy, 2) lack of participation in educational activities about SCD, and 3) lack of knowledge about the practices of their peers. Further work is need to elucidate whether increased awareness of the NIH guidelines will result in increased us by blood bankers. exists for management of SCD patients. for the latter may include Practice guidelines are.

Limitations

Our study has several limitations. First, these results are only descriptive and should therefore be considered preliminary. Further planned analyses will include testing for non-response bias, assessment of correlation between variables, and multivariate analysis. The small sample size relative to the number of variables will likely preclude the use of modeling data for a specific outcome. The results of these analyses will provide a more complete view of our study findings. Furthermore, the study design, a cross-sectional survey, provides only limited information about this complex issue. An inherent limitation of this design is that causality cannot be assessed.

As previously mentioned, NC is a unique state for the treatment and management of SCD patients. Therefore our results may not generalizable to other states. The effect of having a longstanding statewide program and an NIH Comprehensive Sickle Cell Center on blood bank practices was not assessed in this study. However, we know from discussions with the state program manager that education to health professional in this state has not included blood bank personnel. The large SCD population in NC may also have affected the quality of our data. Our sample was possibly already attuned to the needs of SCD patients so interest in participating in this study was much higher than could otherwise be expected.

Next, our selection of NC hospitals may have also affected the quality of our data. Hospitals that currently provide transfusion care to sickle cell patients may have been inadvertently excluded based on our inclusion/exclusion criteria.

We intentionally excluded the two large academic centers that comprise NIH Comprehensive Sickle Cell Center to minimize bias in our data. As a consequence, blood bank practices for nearly 1400 SCD patients who receive care through this combined center are not represented in our study. In addition, we do not know the extent to which practices these two institutions reflect those in the rest of the state.

Finally, the quality of our data may also have been affected by our sampling strategy of two possible respondents per hospital. Based on our a priori hypothesis that the medical director was the better of the two informants, we preferentially used data from this respondent. In actuality, medical directors were more often non-respondents and more likely return incomplete survey, which in turn, hindered our ability to obtain information about clinical management of SCD patients in each institution. Therefore, data from these respondents may not accurately reflect those of the laboratory supervisor. However, several of the surveys sent to the medical director were completed and returned by the laboratory supervisor; comments on a few of these surveys were "it was felt that only one response was necessary." Accurate comparison of the responses by blood bank medical directors vs. laboratory supervisors may not be possible. Our response rate and rate of item non-response, may have due to the length and comprehensiveness of the survey instrument of survey. This most likely required respondents to actively seek out information they may not have already known or had readily available.

Despite these limitations, our study provides the useful information about

the delivery of transfusion therapy to SCD patients in NC. Variation in blood bank practices may be factor in the quality of transfusion care SCD patients receive. Further studies are needed to confirm whether our findings are representative of state, regional, and national practices. Additional studies should also attempt elucidate the possible impact of this variation on patient outcomes. Finally, improved collaboration and communication among all health professionals caring for this patient population may be one unrealized, yet important, opportunity to improve the delivery of transfusion care.

Figure 1. Mechanism of Alloimmunization

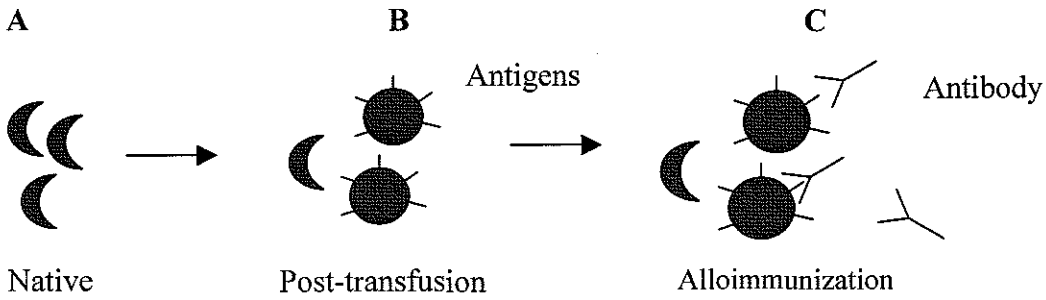


Figure 1. Schematic diagram of alloimmunization in SCD patients. (A) Native sickle cells tend to lack red cell antigens. (B) After transfusion, two populations of red cells exist. The normal (donor) red cells have surface antigens. (C) The body then recognizes the antigens on these cells as foreign and develops antibodies against them.

Figure 2. Patient Interactions with Health Care System

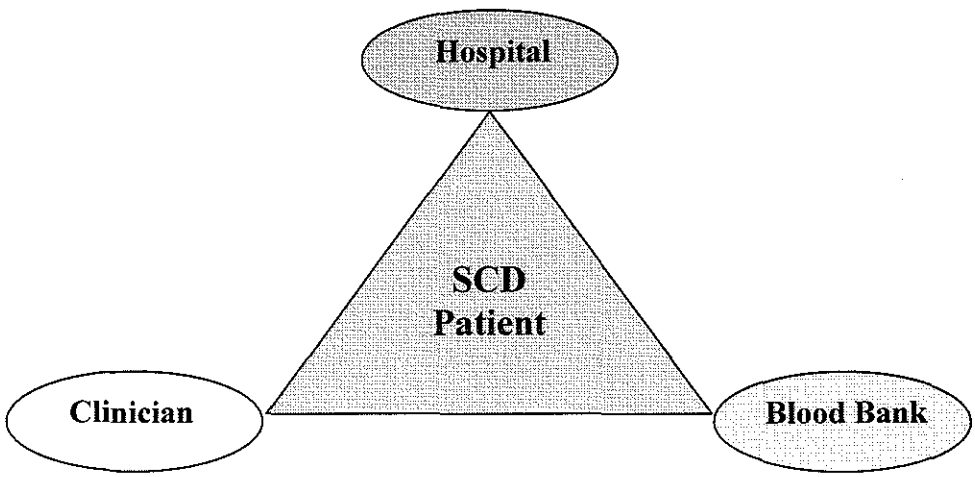
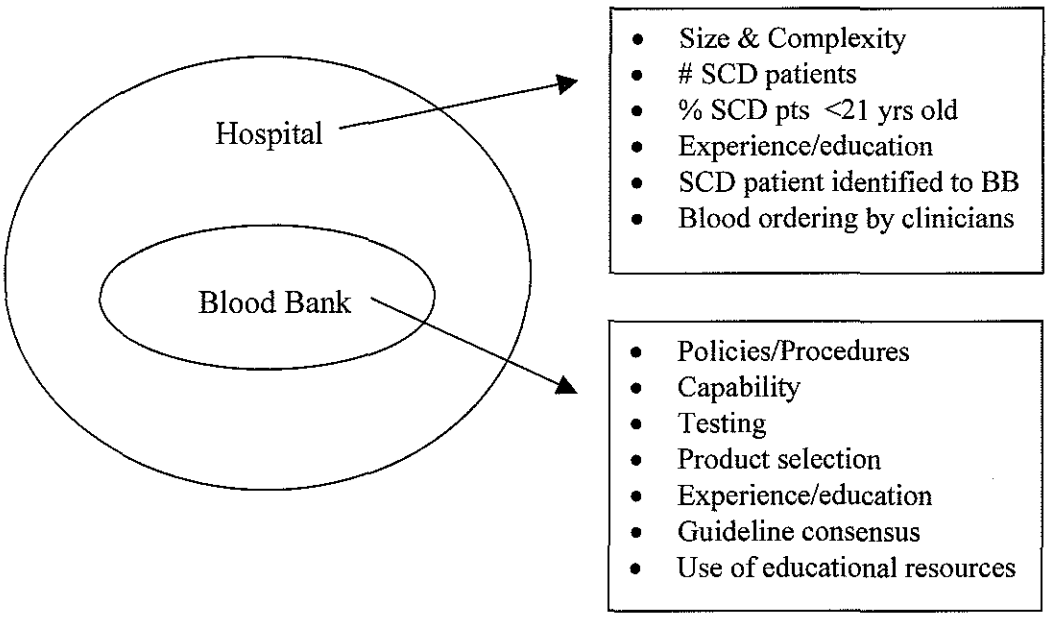


Figure 3. Factors Affecting Transfusion Delivery to SCD Patients

3A. Hospital and Blood Bank Level Factors



3B. External and Internal Factors

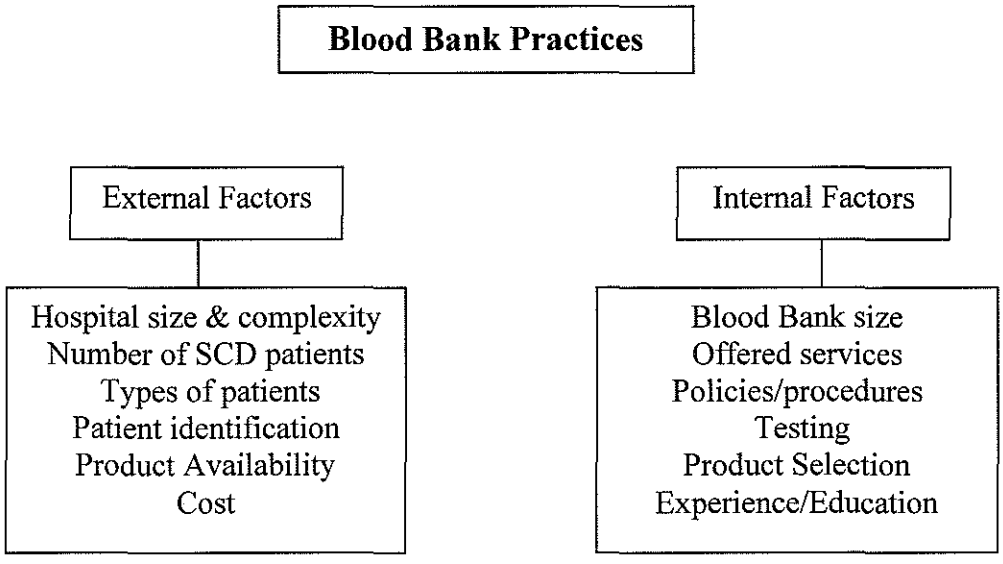


Figure 4. Sampling Methodology

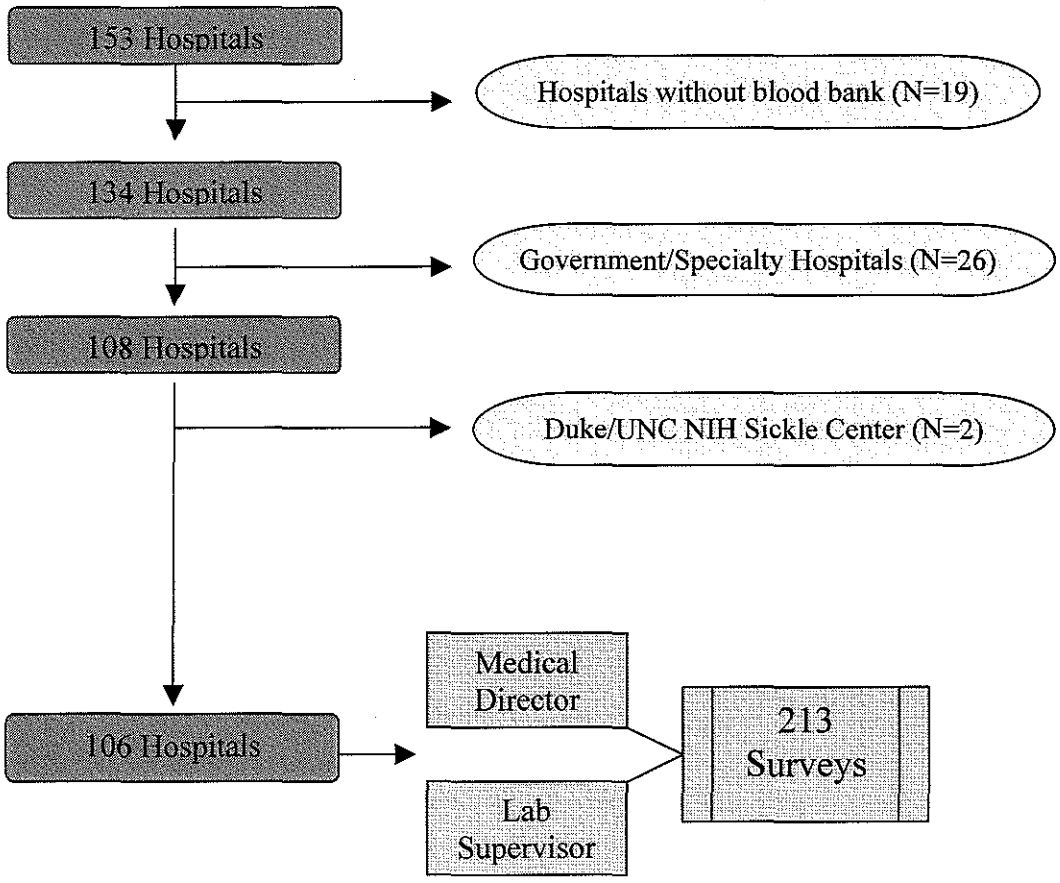


Figure 5. Guidelines with Corresponding Survey Items

- **NIH Guideline: All blood should be screened for the absence of sickle cell trait.**

- **NIH Guideline: Prestorage leukodepletion of red cells is standard practice to reduce febrile reactions, platelet refractoriness, infections, and cytokine-induced complications.**

Corresponding Survey Items:

The following is a list of RBC products that a Blood Bank might provide for a sickle cell patient. Please indicate how often each of the following products is provided for a sickle cell patient in your hospital.

Blood Product	Always	Sometimes	Rarely	Never
a. Non-leukocyte reduced RBCs	3	2	1	0
b. Leukocyte Reduced RBCs	3	2	1	0
c. Irradiated RBCs	3	2	1	0
d. Washed RBCs	3	2	1	0
e. Sickle cell trait negative RBCs	3	2	1	0
f. Frozen RBCs	3	2	1	0
g. Other: _____	3	2	1	0

- **NIH Guideline: The antigenic phenotype of the red cells (at least ABO, Rh, Kell, Duffy, Kidd, Lewis, Lutheran, P, and MNS) should be determined in all patients older than 6 months of age.**

Corresponding Survey Item

Do you perform patient RBC phenotyping…? *(Choose one)*

1. Before transfusion of blood products
2. After transfusion of blood products
3. After development of an antibody
4. No typical procedure
5. Not performed

NIH Guideline: A permanent record of the phenotyping should be maintained in the blood bank to optimize matching, and a copy of the record should be given to the patient of family.

Corresponding Survey Item

Do you provide this phenotyping information to the patient?

0. No
1. Yes → please describe how

- **NIH Guideline: Limited matching for E, C, and Kell [sic] antigens is usually performed, unless patients have antibodies.**

Corresponding Survey Items

C-8. Does your Blood Bank routinely provide phenotypically matched RBCs for sickle cell patients? (Choose one)

1. Yes, perform **pre-transfusion** prophylactic antigen matching.
2. Yes, perform prophylactic antigen matching **after** patient makes an antibody.
3. No, **do not perform** prophylactic antigen matching. (i.e. only honor antibodies patient has already made) --> *Skip **to question C-10***

C-9. Please *circle* the specific antigens that your blood bank prophylactically matches for.

Blood Groups	**Specific Antigens**				
Rh	**D**	**C**	**c**	**E**	**e**
Kell	**K**	**k**			
Duffy	**Fya**	**Fyb**			
Kidd	**Jka**	**Jkb**			
MNS	**M**	**N**	**S**	**s**	**U**
Others:	*Please list*_____				

Table 3. Sample Characteristics (N=76)

Hospital Characteristics	**N**	
Practice Setting		
Community Hospital	68	89.5%
University or Affiliate Hospital	4	5.3%
Other	4	5.3%
Trauma Center	13	18.0%
Level 1 Trauma Center	4	5.3%
Blood Bank/Transfusion Service		
Number of RBC units transfused per year (median) (range)	69	1943 817-3977
Respondent Characteristics		
Medical Director (MD or DO)	22	30%
Education & Training		
Pathology		
Anatomic pathology only	20	90.9%
Anatomic and clinical pathology	18	81.2%
Other graduate degree (PhD or Masters)	1	5.5%
Sub-specialty training		
Blood Bank/Transfusion Medicine	5	25%
Hematology/Oncology	20	90.9%
Laboratory Supervisor	53	70%
Education & Training		
Medical Technologist degree	49	92%
Specialty training in Blood Banking (SBB)	12	22%
Other degree or certification	1	1.8%
Sickle Cell Population		
Number of sickle cell patients seen per month (median) (range)	70	1 0-30
Percentage of sickle cell patients < 21 years of age (median) (range)	68	15% 0-100%

Table 4. Blood Bank Practices (N=76)

	N	%
Policies/procedures		
Have policies/procedures for the work-up of SCD patients	22	29
Have policies/procedures for blood distribution to SCD patients	25	33
Practices differ if new patient	9	12
Offered Services		
Simple transfusion	76	100
Manual exchange transfusion	12	16
Automated exchange transfusion	5	7
Chronic transfusion program	5	7
Blood Bank Testing		
Perform patient RBC phenotyping	52	69
Provide phenotyping information to patient/family	11	16

Table 5. Types and Frequency of RBCs Used (N=76)

	Always	Sometimes	Rarely	Never
RBC Product				
Non-leukocyte reduced RBCs	3.2%	6.5%	3.2%	87.1%
Leukocyte Reduced RBCs	86.1%	5.6%	4.2%	4.2%
Irradiated RBCs	0%	16.4%	31.2%	52.5%
Washed RBCs	0%	4.9%	44.3%	50.8%
Sickle cell trait negative RBCs	41.5%	10.8%	9.2%	38.5%
Frozen RBCs	0%	13.3%	30.0%	56.7%

Table 7. Use of Transfusion Guidelines (in decreasing order of frequency)

Guideline	N	%
Leukocyte reduced RBCs (always/sometimes)	71	92
Perform patient RBC phenotyping	74	69
Sickle cell trait negative RBCs (always/sometimes)	39	52
Provide antigen matched RBCs for C, E, and Kell	23	30
Provide phenotyping results to patient	69	16

Table 8. Agreement with Consensus (N=55)

	Strongly Agree	Agree	Disagree	Strongly Disagree
There is clear consensus on…				
…the selection of blood products for sickle cell patients.	9.3%	35.2%	48.2%	7.4%
…indications for transfusion therapy for sickle cell patients.	5.5%	41.8%	50.9%	1.8%
…phenotypic matching of blood products for sickle cell patients.	12.7%	34.5%	47.3%	5.5%
…the use of chronic transfusion (i.e. hypertransfusion) programs for sickle cell patients.	2%	28%	66%	4%

Table 8. Agreement with Education and Training (N=55)

	Strongly Agree	Agree	Disagree	Strongly Disagree
Education/Training				
My training prepared me to manage the needs of SCD pts.	10.9%	38.2%	47.3%	3.6%
Blood bank/transfusion information for SCD pts. is readily available.	8.9%	42.9%	42.9%	5.4%
I am familiar with the NIH publication, *Management of Sickle Cell Disease.*	5.5%	29.1%	54.6%	10.9%

Table 9. Sources of Information about SCD (in decreasing order of frequency)

	N	%
Source (N=53)		
American Association of Blood Banks	18	34
Peer-Reviewed Literature	18	34
Consultation (hematologists/other hospitals)	11	21
American Red Cross	9	17
Internet	7	11
Conferences	4	6
College of American Pathologists	3	5
Other	3	5

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APPENDIX A-1: Draft Survey

TRANSFUSION MANAGEMENT OF SICKLE CELL PATIENTS SURVEY

ROBERT WOOD JOHNSON CLINICAL SCHOLARS PROGRAM,
UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
and
UNIVERSITY OF FLORIDA HEALTH SCIENCE CENTER IN GAINESVILLE

STATEMENT OF CONFIDENTIALITY

The identification number allows us to keep track of the questionnaires as they are returned. Any information that would permit identification of an individual or a practice organization will be held strictly confidential, will be used only for the purposes of this study, and will not be disclosed or released to other persons or used for any other purposes.

Which of the following services does your hospital provide (Circle only *one*)

1. Blood Banking Only
2. Blood Banking and Therapeutic Pheresis Services
3. Therapeutic Pheresis Services Only

Please continue with the survey

4. None of the Above → Please indicate who provides these services for your hospital.

_____

If you circled item # 4, **do not answer** any further survey questions. Return this survey in the enclosed self-addressed envelope to ensure that you are removed from our list. We thank you for your time.

APPENDIX A-1: Draft Survey

A. Background and Professional Practice

A-1. **What is the zip code of your facility?** _____

A-2. **Which of the following best describes your practice site?** (Choose **one**)

1. University Hospital
2. University Affiliate
3. Community Hospital
4. Local Blood Center
5. Regional Blood Center
6. Other (Please describe)_____

A-3. **What is your current position?**

1. Medical Director
2. Assistant Medical Director
3. Laboratory Supervisor
4. Medical Technologist
5. Other (Please describe) _____

A-4. **Which of the following describes your professional training?** (Circle **all** that apply)

a. MT b. SBB c. MD or DO d. PhD e. Other:_____

A-5. **If you are an MD or DO, which of the following best describes your medical training?** (Circle **all** that apply)

a. Hematology/Oncology
b. Anatomic Pathology Only
c. Anatomic and Clinical Pathology
d. Blood Banking/Transfusion Medicine
e. Other (please describe)_____

B. Facilities and Sickle Cell Population

B-1. How many units of Red Blood Cells (RBCs) did you transfuse at your hospital last year?

_____ units/year

B-2. Are you a Trauma Center?

1. No 2. Yes, (please indicate what level _____)

The following questions refer only to patients with known Sickle Cell Disease (SCD), including patients with genotypes such as HbSS, HbSC, HbS-thal, etc.

B-3. Please estimate the **number** of sickle cell patients your service supports each month.

_____SCD pts /month

B-4. What **percentage** of your sickle cell patients are under 21 years of age

_____%?

C. Blood Banking Practices

C-1. Do you have policies/procedures specific for…(Please circle YES or NO for each item)

a. the Blood Bank work-up of sickle cell patients?	0. NO	1. YES
b. the distribution of RBCs to sickle cell patients?	0. NO	1. YES

C-2. Do your practices differ if a sickle cell patient is…(Please circle YES or NO for each item)

a. **New** to your hospital?	0. NO	1. YES
b. **Known** to your hospital?	0. NO	1. YES

C-3. How frequently are sickle cell patients identified prior to transfusion? (Choose **one**)

a. Always b. Often c. Sometimes d. Rarely e. Never

C-4. Do you perform patient RBC phenotyping…? (Choose **one**)

1. **Before** transfusion of blood products
2. **After** transfusion of blood products
3. After development of an antibody
4. No typical procedure
5. Not performed

C-5. The following is a list of RBC products that a Blood Bank might provide for a sickle cell patient. Please indicate how often each of the following products is provided for a sickle cell patient in your hospital.

Blood Product	Always	Sometimes	Rarely	Never
a. Non-leukocyte reduced RBCs	3	2	1	0
b. Leukocyte Reduced RBCs	3	2	1	0
c. Irradiated RBCs	3	2	1	0
d. Washed RBCs	3	2	1	0
e. Sickle cell trait negative RBCs	3	2	1	0
f. Frozen RBCs	3	2	1	0
g. Other_____	3	2	1	0

C-6. **What is the average age of the RBCs your Blood Bank provides to sickle cell patients?** (Choose **one**)

1. <2 days 2. 3-5 days 3. 5-7 days 4. >7 days 5. > 10 days 6. >14 days

C-7. Does your Blood Bank routinely provide phenotypically matched RBCs for sickle cell patients?

1. Yes, limited matching
2. Yes, extended matching
3. No, not until the patient makes an antibody (**Skip to question C-9**)

C-8. Please **list** the antigen groups that your Blood Bank matches for in each case.

C-8a. Limited matching: _____

_____

C-8b. Extended matching: _____

_____

C-9. How difficult is it to obtain phenotypically matched blood for SCD patients?

1. Very Difficult 2. Somewhat difficult 3. Not difficult at all

C-10. Does cost influence your current practices/policies?

0. No
1. Yes (please describe)_____

_____

_____

D. Transfusion Therapy

D-1. Which of the following are performed at your hospital? (Circle all that apply)

a. Simple transfusion
b. Manual Exchange Transfusion
c. Automated Exchange Transfusion

D-2. Do you have a Chronic Transfusion Program at you hospital?

1. Yes 0. No → **Please skip to section E**

The following questions refer to patients who are enrolled in your Chronic Transfusion Program.

D-4. What types of patients are in your Chronic Transfusion Program? (Circle all that apply)

a. Sickle Cell Disease
b. Thalassemia
c. Other inherited RBC Diseases
d. Acquired RBC Diseases
e. Other _____ (please indicate)

D-5. Please indicate the ***types of therapy*** and ***average frequency of therapy*** provided to patients in your Chronic Transfusion Program. (Circle **all** that apply)

a. Simple Transfusion.....Every _____ weeks
b. Manual Exchange Transfusion.....Every _____ weeks
c. Automated Exchange Transfusion.....Every _____ weeks
d. Other _____(please indicate).....Every _____ weeks

APPENDIX A-1: Draft Survey

E. Transfusion Practices: Clinical Vignettes

This section of the survey is to be completed by the medical director. If you are a laboratory supervisor, please skip ahead to Section F.

E-1. A 16 y.o. with sickle cell anemia is scheduled for laparoscopic cholecystectomy. The baseline CBC reveals Hct 22% and the Hgb electrophoresis reveals 95% Hb S, 2% Hb A2, and 3% Hb F.

You recommend the following…(Circle one)

1. Perform an exchange transfusion to reduce the Hb S fraction to 30%.
2. Transfuse RBCs to a Hct of 30%.
3. Transfuse RBCs to a Hct of 36%.
4. No transfusion is indicated.

E-2. A 7 y.o. girl with known sickle cell anemia (Hb SS disease) presents to the Emergency Department with a 12-hour history of abdominal pain, nausea, vomiting and lethargy. Physical examination reveals an easily palpable and tender spleen. The CBC shows a WBC count of 29,000/uL with 80% neutrophils and 12% bands, Hct 12%, PLT- 88,000/uL. The physician in charge requests assistance in transfusion recommendations.

You recommend the following…(Circle one)

1. Simple transfusion of packed RBCs
2. Perform an automated exchange transfusion
3. Perform a manual exchange transfusion
4. Transfusion is not indicated

E-3. A 28 y.o. woman with Hb SC disease has acute chest syndrome with progressive hypoxemia. The ICU physician caring has requested transfusion of RBCs for the patient. Review of the CBC reveals WBC 22,000, Hct 28%, platelet count 530,000.

You recommend the following…(Circle one)

1. Simple transfusion of 3 U PRCs
2. Exchange transfusion with target Hct 36%
3. Exchange transfusion with target Hct 28%
4. No transfusion is indicated

E-4. Eight days ago a 29 y.o. African American man with sickle cell anemia (Hb SS) was transfused 2 units of RBCs for treatment of hypoxia. He was discharged from the hospital 4 days ago and now returns complaining of severe pain of his arms, legs, and back. On physical exam his sclerae are icteric and his abdomen is mildly tender in all quadrants. His Hct upon discharge was 26% and now it is 14%. He was previously known to have anti-C and anti-K antibodies and on this evaluation there is a newly identified anti-S antibody.

You recommend the following…(Circle one)

1. Transfuse 2 units of compatible RBCs
2. Perform therapeutic plasmapheresis
3. Perform an exchange transfusion with compatible RBCs
4. Supportive care and avoid RBC transfusion

F. Educational Resources

F-1. My training has prepared me to manage the transfusion needs of sickle cell patients.	0. NO	1. YES
F-2. There is a clear consensus on the management of sickle cell patients.	0. NO	1. YES
F-3. Information on the management of sickle cell patients is readily available.	0. NO	1. YES
F-4. In the past 2 years, I have attended at least one conference or presentation on the management of sickle cell disease.	0. NO	1. YES
F-5. I am aware of the Management and Therapy of Sickle Cell Disease guidelines provide by the National Institutes of Health	0. NO	1. YES

F-6. How do you obtain current information on the management of sickle cell patients?

_____
_____
_____

F-7. Is there anything else about your care of sickle cell patients that you would like to share with us?

_____
_____
_____

Please indicate below if you would like to receive a summary of the study results.

_____ Yes, I would like to receive a copy of the study results.

Thank you for completing this survey!

Please return this survey in the enclosed, prepaid envelope to:

Araba Afenyi-Annan, MD
Robert Wood Johnson Clinical Scholars Program
University of North Carolina at Chapel Hill
5034 Old Clinic Building, CB# 7105
Chapel Hill, NC 27599-7105

Phone: (919) 966-3798 Fax: (919) 843-9237 Email: nyaniba@med.unc.edu

APPENDIX A-2: Cover Letter and Evaluation Form

Dear Colleague,

Thank you for agreeing to participate in this pilot test. Your feedback is very important to us; it will be used to reshape and refine the final survey instrument. Your candor and suggestions for improvement will help us ensure the quality of data we obtain from this study.

This study is being conducted by researchers at the University of North Carolina Robert Wood Johnson Clinical Scholars Program/Department of Pathology, Transfusion Medicine Service, the Cecil G. Sheps Center for Health Services Research at the University of North Carolina, and the University of Florida, Gainesville, Department of Medicine, Division of Hematology/Oncology. The purpose of this study is to assess the practice variation that occurs in the blood bank/transfusion medicine management of sickle cell disease patients and identify areas for future interventions. The target audience of this study is blood bank/transfusion medicine medical directors and/or assistant medical directors as well as the blood bank laboratory supervisors. We intend to survey all hospitals in the state of Florida and North Carolina.that provide service to sickle cell patients. This study is currently awaiting IRB approval.

Please see enclosed a draft survey, a comment sheet, and a self-addressed, postage paid envelope for your convenience. The identification number on your survey is used to track the questionnaires as they are returned. Your responses and feedback will be held strictly confidential and no identifying information will be disclosed or released to other persons or used for any other purpose. Finally, the information that you provide will not used in our data analysis.

Thanks again for your help on this project. If you have any other questions or concerns, please do not hesitate to contact me.

Sincerely,

AAA (please leave room for my signature)!

APPENDIX A-2: Cover Letter and Evaluation Form

Now that you have completed the survey, we would appreciate your feedback. Your comments will help us learn how we can alter the survey to best serve our purposes. This is your opportunity to help us improve care to sickle cell disease patients.

1. How long did it take to complete the survey?

2. Is the survey… (Circle one)

   too long? too short? appropriate length?

3. Is the survey understandable?

   Yes No

4. Are the questions clear? (Circle one)

   Yes No

5. Is the content appropriate for the intended audience?

   Blood Bank Medical Director Yes No
   Laboratory Supervisor Yes No

6. Is there additional content you feel should be included in the survey?

   No

   Yes (please indicate) _____

   _____

7. What is your preferred method for receiving this survey? (Circle one)

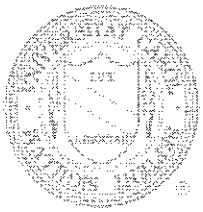
   Mail Log in to secure website No preference

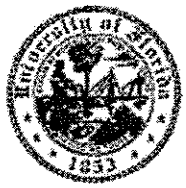
8. Do you have any suggestions that might improve our response rate?

9. Do you have any additional comments?

APPENDIX B-1: Final Survey Instrument

TRANSFUSION MANAGEMENT OF SICKLE CELL PATIENTS SURVEY





ROBERT WOOD JOHNSON CLINICAL SCHOLARS PROGRAM,
UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
and
UNIVERSITY OF FLORIDA HEALTH SCIENCE CENTER IN GAINESVILLE

STATEMENT OF CONFIDENTIALITY

The identification number allows us to keep track of the questionnaires as they are returned. Any information that would permit identification of an individual or a practice organization will be held strictly confidential, will be used only for the purposes of this study, and will not be disclosed or released to other persons or used for any other purposes.

Which of the following services does your hospital provide (Circle only *one*)

1. Blood Banking Only
2. Blood Banking and Therapeutic Pheresis Services — Please continue with the survey
3. Therapeutic Pheresis Services Only
4. None of the Above → Please indicate who provides these services for your hospital.

_____

If you circled item # 4, do not answer any further survey question. *Please return this survey in the enclosed self-addressed envelope to ensure that you are removed from our list.*

WE THANK YOU FOR YOUR TIME.

APPENDIX B-1: Final Survey Instrument

A. BACKGROUND AND PROFESSIONAL PRACTICE

A-1. What is the zip code of your facility? _____

A-2. Which of the following best describes your practice site? (*Choose one*)

1. University Hospital
2. University Affiliate
3. Community Hospital
4. Local Blood Center
5. Regional Blood Center
6. Other (Please describe)_____

A-3. What is your current position?

1. Medical Director
2. Assistant Medical Director
3. Laboratory Supervisor
4. Medical Technologist
5. Other (Please describe) _____

A-4. Which of the following describes your professional training? (*Circle all that apply*)

a. MT b. SBB c. MD or DO d. PhD e. Other:_____

A-5. If you are an MD or DO, which of the following best describes your medical training? (*Circle all that apply*)

a. Hematology/Oncology
b. Anatomic Pathology Only
c. Anatomic and Clinical Pathology
d. Blood Banking/Transfusion Medicine
e. Other (please describe) _____

B. FACILITIES AND SICKLE CELL POPULATION

B-1. How many units of Red Blood Cells (RBCs) did you transfuse at your hospital last year?

_____ units/year

B-2. Are you a Trauma Center?

0. No 1. Yes, (please indicate what level _____)

B-3. Which of the following services do you provide at your hospital? ***(Circle all that apply)***

a. Simple transfusion

b. Manual Exchange Transfusion

c. Automated Exchange Transfusion

The remaining questions in this survey refer only to patients with known Sickle Cell Disease (SCD), including patients with genotypes such as HbSS, HbSC, HbS-thal, etc.

B-4. Please estimate the <u>number</u> of sickle cell patients your service supports each month.

_____ SCD pts /month

B-5. What <u>percentage</u> of your sickle cell patients are under 21 years of age?

_____ %?

B-6. Do you have a Chronic Transfusion Program at you hospital?

1. Yes 0. No *→ Please skip to section C*

B-7. What types of patients are in your Chronic Transfusion Program? *(Circle all that apply)*

a. Sickle Cell Disease
b. Thalassemia
c. Other inherited RBC Diseases
d. Acquired RBC Diseases
e. Other _____ (please indicate)

C. BLOOD BANKING PRACTICES

C-1. Do you have policies/procedures specific for…(*Please <u>circle</u> YES or NO for each item*)

a. the Blood Bank work-up of sickle cell patients?	**0. NO**	**1. YES**
b. the distribution of RBCs to sickle cell patients?	**0. NO**	**1. YES**

C-2. Do your practices differ if a sickle cell patient is… *(Please <u>circle</u> YES or NO for each item)*

a. <u>New</u> to your hospital?	**0. NO**	**1. YES**
b. <u>Known</u> to your hospital?	**0. NO**	**1. YES**

C-3. How <u>frequently</u> are sickle cell patients identified <u>prior</u> to transfusion? (Choose <u>one</u>)

1. Always 2. Often 3. Sometimes 4. Rarely 5. Never

C-4. **Do you perform patient RBC phenotyping...?** *(Choose one)*

1. **Before** transfusion of blood products
2. **After** transfusion of blood products
3. After development of an antibody
4. No typical procedure
5. Not performed

C-5. **Do you provide this phenotyping information to the patient?**

0. No
1. Yes → please describe how _____

_____

C-6. **The following is a list of RBC products that a Blood Bank might provide for a sickle cell patient. Please indicate how often each of the following products is provided for a sickle cell patient in your hospital.**

Blood Product	Always	Sometimes	Rarely	Never
a. **Non-leukocyte reduced RBCs**	3	2	1	0
b. **Leukocyte Reduced RBCs**	3	2	1	0
c. **Irradiated RBCs**	3	2	1	0
d. **Washed RBCs**	3	2	1	0
e. **Sickle cell trait negative RBCs**	3	2	1	0
f. **Frozen RBCs**	3	2	1	0
g. **Other:** _____	3	2	1	0

C-7. **What is the average age of the RBCs your Blood Bank provides to sickle cell patients?** (***Choose one***)

1. 1-5 days 2. 6- 7 days 3. 8-10 days 4. 11-14 days 5. > 14 days

C-8. **Does your Blood Bank routinely provide phenotypically matched RBCs for sickle cell patients?** (*Choose **one***)

1. Yes, perform **pre-transfusion** prophylactic antigen matching.
2. Yes, perform prophylactic antigen matching **after** patient makes an antibody.
3. No, **do not perform** prophylactic antigen matching
   (i.e. only honor antibodies patient has already made)-->***Skip to question C-10.***

C-9. Please *circle* the specific antigens that your blood bank prophylactically matches for.

Blood Groups	Specific Antigens				
Rh	**D**	**C**	**c**	**E**	**e**
Kell	**K**	**K**			
Duffy	**Fya**	**Fyb**			
Kidd	**Jka**	**Jkb**			
MNS	**M**	**N**	**S**	**s**	**U**
Others:	*Please list*_____				

C-10. How difficult is it to obtain phenotypically matched blood for SCD patients?

1. Very Difficult 2. Somewhat difficult 3. Not difficult at all

C-11. Does cost influence your current practices/policies?

0. No
1. Yes → *please describe* _____

_____

C-12. If cost were not an issue, would you alter your current practices/policies?

0. No
1. Yes → *please describe* _____

_____

E. TRANSFUSION PRACTICES: CLINICAL MANAGEMENT

This section of the survey is to be completed by the medical director.
If you are a laboratory supervisor, please skip ahead to Section F on the next page.

The following vignettes represent some clinical scenarios that might arise in managing sickle cell patients. These are not test items. We are simply interested in describing the different ways sickle cell patients are managed at different facilities. We recognize that in real life, you might obtain additional information prior to making a decision. However, please choose the single best response based on 1) the information provided and, 2) how you would manage the patient in your own hospital.

D-1. A 16 y.o. with sickle cell anemia is scheduled for laparoscopic cholecystectomy. The baseline CBC reveals Hct 22% and the Hgb electrophoresis reveals 95% Hb S, 2% Hb A2, and 3% Hb F.

You recommend the following…(Circle one)

1. Perform an exchange transfusion to reduce the Hb S fraction to 30%.
2. Transfuse RBCs to a Hct of 30%.
3. Transfuse RBCs to a Hct of 36%.
4. No transfusion is indicated.

D-2. A 7 y.o. girl with known sickle cell anemia (Hb SS disease) presents to the Emergency Department with a 12-hour history of abdominal pain, nausea, vomiting and lethargy. Physical examination reveals an easily palpable and tender spleen. The CBC shows a WBC count of 29,000/uL with 80% neutrophils and 12% bands, Hct 12%, PLT- 88,000/uL. The physician in charge requests assistance in transfusion recommendations.

You recommend the following…(Circle one)

1. Simple transfusion of packed RBCs
2. Perform an automated exchange transfusion
3. Perform a manual exchange transfusion
4. Transfusion is not indicated

D-3. A 28 y.o. woman with Hb SC disease has acute chest syndrome with progressive hypoxemia. The ICU physician caring has requested transfusion of RBCs for the patient. Review of the CBC reveals WBC 22,000, Hct 28%, platelet count 530,000.

You recommend the following…(Circle one)

1. Simple transfusion of 3 U PRCs
2. Exchange transfusion with target Hct 36%
3. Exchange transfusion with target Hct 28%
4. No transfusion is indicated

D-4. Eight days ago a 29 y.o. African American man with sickle cell anemia (Hb SS) was transfused two (2) units of RBCs for treatment of hypoxia. He was discharged from the hospital 4 days ago and now returns complaining of severe pain of his arms, legs, and back. On physical exam his sclerae are icteric and his abdomen is mildly tender in all quadrants. His Hct upon discharge was 26% and now it is 14%. He was previously known to have anti-C and anti-K antibodies and on this evaluation there is a newly identified anti-S antibody.

You recommend the following…(Circle one)

1. Transfuse 2 units of compatible RBCs
2. Perform therapeutic plasmapheresis
3. Perform an exchange transfusion with compatible RBCs
4. Supportive care and avoid RBC transfusion

SECTION F: Information and Resources

Circle the number on the right which best describes how much you agree or disagree with each statement. **There is clear consensus on…**		**Strongly Agree**	**Agree**	**Disagree**	**Strongly Disagree**
F-4.	**…the selection of blood products for sickle cell patients.**	**1**	**2**	**3**	**4**
F-5.	**…indications for transfusion therapy for sickle cell patients.**	**1**	**2**	**3**	**4**
F-6.	**…phenotypic matching of blood products for sickle cell patients.**	**1**	**2**	**3**	**4**
F-7.	**…the use of chronic transfusion (i.e. hypertransfusion) programs for Sickle Cell patients.**	**1**	**2**	**3**	**4**

APPENDIX B-1: Final Survey Instrument

Circle the number on the right which best describes how much you agree or disagree with each statement.		Strongly Agree	Agree	Disagree	Strongly Disagree
E-1.	**My training has prepared me to manage the transfusion needs sickle cell patients.**	1	2	3	4
E-2.	**Information about the blood bank/transfusion management of sickle cell patients is readily available.**	1	2	3	4
E-3.	**I am familiar with the National Institutes of Health *Management and Therapy of Sickle Cell Disease* publication**	1	2	3	4

E-8. In the past year, I have attended at least one conference on the management of sickle cell patients.

0. No 1. Yes

E-9. How do you obtain current information on the management of sickle cell patients?

_____

_____

E-10 We are very interested in learning more about your chronic tranfusion program. Would you be willing to share your chronic transfusion protocol with us?

1. Yes, a copy of our protocol is enclosed.
2. Yes, I will send a copy.
3. No.
4. Does not apply, we do not have a chronic transfusion program.

E-11. Is there anything else about your care of sickle cell patients that you would like to share?

_____

_____

_____

_____

THIS IS THE END OF THE SURVEY. THANK YOU FOR YOUR TIME!

To thank you for your participating in this survey, we will send you a brief summary of the survey results. If you are interested in receiving a summary, please check the following:

____ Yes, I would like to receive a summary of the survey results.

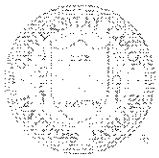
APPENDIX B-1: Final Survey Instrument

Please return this survey in the enclosed, prepaid envelope and mail to:

Araba Afenyi-Annan, MD
Robert Wood Johnson Clinical Scholars Program
University of North Carolina at Chapel Hill
5034 Old Clinic Building, CB# 7105
Chapel Hill, NC 27599-7105

Phone: (919) 966-3798 ***Fax***: (919) 843-9237 ***Email***: nyaniba@med.unc.edu

APPENDIX B-2: Cover Letters



{Date}

Dear {insert name},

Enclosed is a survey questionnaire entitled, "The Blood Bank and Transfusion Medicine Management of Sickle Cell Disease Patients." We invite you to participate in this research sponsored by The Robert Wood Johnson Foundation-Clinical Scholars Program at the University of North Carolina, Chapel Hill, conducted jointly with the researchers in the Division of Hematology/Oncology at the University of Florida, and Cecil G. Sheps Center for Health Services Research, University of North Carolina.

The purpose of this study is to gather information on practices, procedures and policies, knowledge, and approach to care in the transfusion support of sickle cell disease patients. This survey is being sent to all hospital-based blood bank medical directors and laboratory supervisors in North Carolina and Florida (estimated sample size of 600), in an effort to characterize statewide practices and opportunities to improve uniformity of care to this patient population. This survey will take no more than twenty (20) minutes to complete. Your response is important to us, as this will ensure that our data is representative of current practices.

Participation in this study is completely voluntary. By completing and returning the survey, you are providing your inform consent and agree to participate in this study. Your responses will be kept strictly confidential. Any information that would allow identification of an individual or a practice organization will used solely for the purposes of this study, will not be disclosed or released to other persons, or used for any other purposes. All identifying information will be stored in a locked, secure file and will be destroyed at the conclusion of the study (September 1, 2004). Only individuals involved with the study will have access to the collected data.

If you have any questions or comments about this study, please do not hesitate to contact the principle investigator, Dr. Araba Afenyi-Annan by email (nyaniba@med.unc.edu) or by telephone at (919) 966-3798. An addressed, stamped return envelope is enclosed for your convenience. In addition, we would be pleased to provide you a brief summary of the study findings as a thank you for your participation. Please be sure to check the corresponding box on the last page of the survey.

We recognize that there are many demands on your time but hope you will make the effort to contribute to the care of sickle cell disease patients in your state. We appreciate your time and participation.

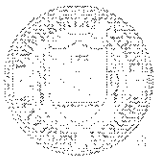
Sincerely,

Araba Afenyi-Annan, MD
University of North Carolina
RWJ-CSP/Pathology and
Laboratory Medicine

Richard Lottenberg, MD
University of Florida
Medicine, Division of
Hematology/Oncology

Thomas R. Konrad, PhD
University of North Carolina
Center for Health Services
Research

APPENDIX B-2: Cover Letters



{Date}

Dear {insert name},

Two weeks ago we mailed you a survey seeking information about your blood bank/transfusion medicine support to sickle cell disease patients. If you have already completed and returned this survey to us, we thank you. If you have not had an opportunity to complete and return the survey, please do so today. We are seeking to fully represent the current practices of hospital blood banks in the state of {insert state}. Your response is essential to us in 1) describing the current delivery of transfusion support for sickle cell patients and 2) guiding efforts to improve the coordination of care for this patient population. Only you can provide this information that will be used to improve the quality of care sickle cell patients receive.

If by chance you have not received the survey, or need another copy, please contact us by phone at (919) 966-3798 or by email (nyaniba@med.unc.edu). We will be pleased to mail you another copy of the survey today. A self-addressed, stamped return envelope will also be enclosed for your convenience. If you also check the appropriate box on the last page of the survey, we will be pleased to send you a brief summary of the study findings as a thank you for your participation in this study.

We want to remind you that any data you provide to us will be will only be used for the purposes of this study and not released to other persons or used for any other purposes. We will make every effort to protect your confidentiality. Only individuals involved with this study are authorized to review collected data. If you have questions or comments about this study, please contact the principle investigator, Dr. Araba Afenyi-Annan, at the above number or email address.

We appreciate your time and hope we may count on your participation.

Sincerely,

Araba Afenyi-Annan, MD
University of North Carolina
RWJ-CSP/Pathology and
Laboratory Medicine

Richard Lottenberg, MD
University of Florida
Medicine, Division of
Hematology/Oncology

Thomas R. Konrad, PhD
University of North Carolina
Center for Health Services
Research

APPENDIX B-2: Cover Letters

{Date}

Dear {insert name},

About a month ago, we wrote to you seeking information about your blood bank/transfusion medicine support to sickle cell disease patients. As of today, we have not yet received your completed questionnaire. You may have sent it back to us already. If so, we thank you.
If not, another copy is enclosed for your convenience.

As you know, hospital blood banks play a critical role in managing the care of sickle cell disease patients. Our group has undertaken this study because we believe that this role has not been adequately explored. By characterizing the current practices of hospital blood banks, we hope to identify opportunities for intervention that will improve the quality of care sickle cell patients receive. We know your time is valuable, but please help us obtain this information by taking time to answer the enclosed questionnaire. We want to assure that we accurately represent all of blood banks in {insert state), especially busy services like yours.

You can make an important contribution to the management of sickle cell patients by returning the enclosed questionnaire today. An addressed stamped envelope is provided for your convenience. We would be happy to provide you a brief summary of the study findings. Please be sure to indicate on the survey that you would like to receive this summary. Your identity will be kept strictly confidential and the information you provide will be used only for the purposes of this study, will not be disclosed or released to other persons, or used for any other purposes. Questions and comments about this study should be directed to the principle investigator, Dr. Araba Afenyi-Annan, at (919) 966-3798 or (nyaniba@med.unc.edu).

Thank you. We appreciate your time and participation.

Sincerely,

Araba Afenyi-Annan, MD
University of North Carolina
RWJ-CSP/Pathology and
Laboratory Medicine

Richard Lottenberg, MD
University of Florida
Medicine, Division of
Hematology/Oncology

Thomas R. Konrad, PhD
University of North Carolina
Center for Health Services
Research

APPENDIX B-3: Administration and Coding Procedures

RWJ SCD SURVEY INSTRUCTIONS

When Sending Surveys:

- Addresses will be entered into an Excel database.
- A mail merge will be performed to enter addresses into letters and addresses labels.
- Packets will be compiled that contain an introductory letter, a survey and a return envelope.
- All surveys to a state will be sent at the same time, i.e. all Florida surveys will be sent on one day and all North Carolina surveys will be sent on one day.

When Surveys are Returned:

- They are logged in using a "1=returned" method in Excel, under the first mailing column.
- After the determined time period, a postcard reminder is sent.
- Surveys returned at this point are still considered part of the first mailing and are logged in as such.
- After the determined time period, a second survey is sent.
- Surveys returned at this point are considered part of the second mailing and are logged in under that category.
- After the determined time period, a third survey is sent.
- Surveys returned at this point are considered part of the third mailing and are logged in under that category.

Process for Returned Surveys

- Date stamp or hand-write date on surveys when they arrive (bottom right-hand corner).

- Enter into the survey tracking system (**"J drive: Tomcat/Araba/Sickle Cell/Tracking???"**). Create a back-up file on disk and copy to the backup tracking system (as **"AAA/rwj/SCD survey /backup of tracking system"**) at least once every two weeks.

- Once entered, each survey should be reviewed for completeness and accuracy. All tracking and initial review of the surveys will be performed by the RWJ Research Coordinator. Any missing information, incorrect responses (i.e. two items circled or marked, range provided instead of specific number, etc.) should be flagged with a **yellow highlighter**. Any notes or comments for investigator review should be marked in **red pencil** to the left of the questionnaire item (margin).

- All surveys with problems should be entered into a separate log, **("J drive:Tomcat/Araba/Sickle cell/problemlist")** listing the ID number, specific issues, etc. prior to coding.

Process for Coding

- Prior to data entry, all surveys must be manually coded.

- All coding will be performed in **blue pencil.**

- All forms will be coded by the Research Assistant (or other assigned person), and checked by the Research Assistant or principle investigator. As each person tracks, codes and reviews each survey, her/his initials and job function (Tracker, Coder, 1st Reviewer, Final Reviewer) will be noted in the bottom left-hand corner of the front page of the survey.

- **For open-ended questions, enter word for word responses in Excel file called "J:\Tomcat/Araba/Sickle Cell/data/openended" on server. Every survey needs to have open-ended responses entered before going to data entry.**

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- When coding open-ended responses, if there are any other marginal comments (i.e. hand-written), please record these in the last field in the open-ended response file under "all other marginal comments", by noting the question number and the comment word for word.
- Newly created variable items (**i.e. A2text**) are indicated in **BOLD**.
- Many questions DO NOT need additional coding. Specific instructions are noted below when an item requires coding. **All other items not specifically mentioned below must to be checked for accuracy and legibility**, but no special coding is necessary. Also check all questions for questions omitted by respondent, two items circled in one question, etc.
- **Missing data is always coded as 'X'.**
- **If don't know is written in, code as 'D', unless otherwise instructed.**
- **If not applicable or NA is written in, code as 'N', unless otherwise instructed.**
- Percentages should NOT be rounded.

DECISION RULES

- Anytime respondent provides a range (e.g. if they answer question saying 27-33%) code the midpoint of the range.
- If a respondent circles or indicates two responses, or makes a note in between 2 responses (indicating they fall between two responses on a continuum), flip a coin to decide (i.e. heads is even number, tails is odd number); then code that choice in the margin.
- Any remaining questions or concerns should be flagged for the principle investigator.

CODING QUESTION BY QUESTION:

Screening Question: Code X for missing. If anything else comes up, flag for Araba.
If "4" selected, make sure next field (screeningtext) is coded "1" and response entered into Excel File word for word.

Screeningtext: Enter **1** if text.
Enter **0** if no text.
Enter response word for word into separate Excel file.
Code X for missing.

A1. Enter 5-digit zip code. Code X for missing. If anything else comes up, flag for Araba.

A2. Enter "1-6" (choose one).
Code X for missing. If anything else comes up, flag for Araba.
If "6" selected, make sure next field (A2text) is coded as "1")

A2text. Enter **1** if text.
Enter **0** if no text.
If text, enter word for word into separate excel file.

A3. Enter "1-5" (choose one).
If "5" selected, make sure next field (A3text) is coded as "1".
Code X for missing.

A4a-e. For each letter, enter "1" for each item selected (all that apply).
Enter "0" for each item not selected.
If "e" selected, make sure next field (A4text) is coded "1".
Code X for missing.

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A4text. Enter **1** if text.
Enter **0** if no text.
If text, enter word for word into separate Excel file.

A5a-e. For each letter, enter "1" for each item selected (all that apply).
Enter "0" for each item not selected.
If "e" selected, make sure next field (A5text) is coded "1".
Code X for missing.

A5text. Enter **1** if text.
Enter **0** if no text.
If text, enter word for word into separate Excel file.

B1. Enter number. If range provided, use midpoint.
If the symbols "<" or ">" are given, enter number indicated after symbol.
Code X for missing.

B2. Enter "0" or "1".
If "1" selected, make sure next field (B2text)) is coded "1".

B2text. Enter **1** if text.
Enter **0** if no text.
If text, enter word for word into separate excel file.

B3a-c. Enter "1" for each letter selected.
Enter "0" for each letter not selected.
Code each item as X if no items are checked to indicate that the question was skipped.

B4. If respondent provides range, code the midpoint of the range.

B5. If respondent provides range, code the midpoint of the range.

B6. Enter "0" or "1".
Code X for missing (i.e. no answer indicated).

B7a-e. Enter "1" for each letter selected.
Enter "0" for each letter not selected.
If "e" selected, make sure next item (B7text) is coded "1".

B7text. Enter **1** if text.
Enter **0** if no text.
If text, enter word for word into separate Excel file.

C1a-b. Code each item as X if no items are checked to indicate that the question was skipped.

C2a-b. Code each item as X if no items are checked to indicate that the question was skipped.

C3. Code X for missing.
If response between 2 values, code as odd number (i.e. question #3, odd number).

C4. Code X for missing.

C5. Enter "0" or "1".
If "1" selected, make sure next item is coded "1".

C5text. Enter **1** if text.
Enter **0** if no text.
If text, enter word for word into separate Excel file.

C6a-g. Enter "1-4" for each letter.
If response is between 2 values, code based on above decision rules.
If "g" selected, make sure next item (C6gtext) is coded "1".

Code X for missing letter.

C6gtext. Enter **1** if text.
Enter **0** if no text.
If text, enter word for word into separate Excel file.

C7. Code X for missing.
If response is between 2 values, code based on above decision rules.

C-8. Code X for missing.
If "3" selected, make sure all C-9 items are each coded as X.

C-9. Code each blood group sequentially as 1 through 6 (Rh=1 → Others=6).
Code each specific antigen as "a" through "e" (as needed).
If additional antigens are written in on any row, please flag for Araba.

C-9_1 For each letter, enter "1" for each item selected ("a through e").
Enter "0" for each item not selected.

C-9_2 For each letter, enter "1" for each item selected ("a through b").
Enter "0" for each item not selected.
Please correct column "b" to "little k" if not already marked as such.

C-9_3 For each letter, enter "1" for each item selected ("a through b").
Enter "0" for each item not selected.

C-9_4 For each letter, enter "1" for each item selected ("a through b").
Enter "0" for each item not selected.

C-9_5 For each letter, enter "1" for each item selected ("a through e").
Enter "0" for each item not selected.

C-9_6 If selected, code as "1".
If not selected, code as "0".

C-9_6text Enter response word for word into Excel file.

C-10. Code X for missing.
If between 2 responses, code based on above decision rules.

C-11. If "1" selected, make sure next item (C-11text) is completed.

C-11text. Enter response word for word into Excel file.

C-12. If "1" selected, make sure next item is completed.
Code X for missing.

SECTION D. If respondent is Laboratory Supervisor, code D-1 through D-4 as S.

D-1. Code X for missing.
If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

D-2. Code X for missing.
If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

D-3. Code X for missing.

If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

D-4. Code X for missing.
If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

SECTION E: PLEASE VERIFY THAT ITEMS E-1 THROUGH E-8 ARE NUMBERED AND CODED SEQUENTIALLY (ACCURATELY). MAKE ANY NEEDED CORRECTIONS TO THE LEFT OF EACH ITEM.

E-1. Code X for missing.
If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

E-2. Code X for missing.
If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

E-3. Code X for missing.
If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

E-4. Code X for missing.
If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

E-5. Code X for missing.
If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

E-6. Code X for missing.
If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

E-7. Code X for missing.
If response between 2 values, code based on decision rules.
Please enter any comments or notes into "all marginal comments" file.

E-8. Code X for missing.

E-9. If text, code as "1".
If no text, code as "0".

E-9text. Enter text word for word.

E-10. Code X for missing.
If "1" selected, verify protocol was enclosed with survey. If protocol was **not sent** with the survey, please flag for follow-up as "not sent" in **red pencil**.
If "2" selected, verify protocol was enclosed with survey. If protocol was **never sent** please flag for follow-up as "never sent" in **red pencil**.

E-11. If text, code as "1". If "1" selected, please make sure next item (E-11text) is completed.
If no text, code as "0".

E-11text. Enter response word for word.

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Request for Summary:	Please track summary requests with survey tracking form. Also, create a new file "J: Tomcat/Araba/SCD/summaryrequest" with the following information: ID Number, Name, Address, Summary request. Enter "1" into Summary request field if item checked off by respondent. Enter "0" if not indicated. Indicate request entered into tracking system and new file by circling item in **red pencil**.

Other decisions to be made by Project Manager only (after discussion with PI)…