KNOWLEDGE AND HEALTH BELIEFS OF SICKLE CELL DISEASE AND SICKLE CELL TRAIT: THE INFLUENCE ON ACCEPTANCE OF GENETIC SCREENING FOR SICKLE CELL TRAIT

by

Shanna Lea Gustafson

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This thesis was presented

by

Shanna Lea Gustafson

It was defended on

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and approved by

Thesis Advisor:
Elizabeth Gettig, M.S., CGC
Associate Professor of Human Genetics
Co-Director, Genetic Counseling Program
Graduate School of Public Health
University of Pittsburgh

Committee Members:
Lakshmanan Krishnamurti, MD
Associate Professor of Pediatric Medicine
Department of Pediatric Medicine
Program Director; Hemoglobinopathy Program
Children's Hospital of Pittsburgh
University of Pittsburgh Medical Center

James Butler, Dr.P.H.
Assistant Professor
Department of Behavioral and Community Health Sciences
Graduate School of Public Health
University of Pittsburgh

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Shanna L Gustafson, M.S.

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Sickle cell trait carriers are healthy; however, they are at risk to have children with sickle cell disease (SCD), a serious hematologic disorder. Unsuccessful population screening for sickle cell trait (SCT) has resulted in a large population of African American individuals entering childbearing age with no knowledge of their risk. Recent experience with newborn screening follow-up of hemoglobinopathies has shown that interest in genetic screening for SCT is low. This study aims to understand and increase the level of acceptance of genetic screening among the African American population through a program of education and assessment of the current state of SCD cultural health beliefs. This is important for Public Health because SCD is the most common genetic disorder affecting the African American community and education to promote screening must be sensitive to the cultural beliefs of the community.

Utilizing a method of anonymous surveys given to female African American patients within a busy prenatal clinic the effect of education of SCD on the acceptance of genetic screening for SCT has been assessed. The Health Belief Model was used to assess the current state of health beliefs regarding SCD and trait testing through anonymous surveys.

This study revealed that a brief educational intervention regarding SCD in a prenatal setting is effective in significantly increasing knowledge of SCD and acceptance of screening for SCT (p-value < 0.001). African American women of childbearing age have a high perception of

severity of SCD, a low perception of susceptibility to SCD, a high perception of benefit to SCT testing and a low perception of barriers to testing for SCT.

Education within a prenatal setting can be used as a model to increase acceptance of screening for SCT. A high level of knowledge of SCD is associated with a high level of acceptance; however, the Health Belief Model revealed that currently the majority of the participants do not feel that they are personally at risk to have a child with SCD, regardless of SCD knowledge. Future education of SCD must take into account these beliefs in order to effectively motivate interest in SCT testing.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ACKNOWLEDGEMENTS

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1.0 INTRODUCTION

The Children's Hospital of Pittsburgh Comprehensive Sickle Cell Program is contracted by the Commonwealth of Pennsylvania for the notification and follow-up of abnormal hemoglobinopathy newborn screening results for the 32 county area of Western Pennsylvania. Approximately 245,000 African Americans live within this area. Each year over 600 newborns are found to carry a hemoglobinopathy trait and 12-15 are diagnosed with sickle cell disease (SCD). 100% of newborns identified to have SCD have been brought into the comprehensive care center and started on prophylactic penicillin since 1997 (Kladny, Gettig, & Krishnamurti, 2005). However, less than 10% of families notified of a hemoglobinopathy trait identified in their infant have accepted an offer of formal genetic counseling and extended family testing (Kladny, Gettig, & Krishnamurti, 2005).

In genetic screening programs, participation of the target population is the key to success. Historically, population screening programs for the detection of SCD and sickle cell trait (SCT) have been controversial. The National Sickle Cell Anemia Control Act, enacted in 1972 quickly developed public screening programs; however, much of the benefit that may have been accomplished was overshadowed by the limits of hasty planning which did not involve members of the target African American population, poor control, lack of education and improper testing procedure (Scott & Castro, 1979). Mandatory population testing of the African American population and inability to distinguish trait from disease led to the improper labeling of people,

as well as unnecessary fear and discrimination (Scott & Castro, 1979). Eventually the program was abandoned and other screening programs had to be developed.

Newborn screening for hemoglobinopathies has been a more successful form of population screening for SCD and SCT, with the majority of states establishing programs of screening for hemoglobinopathies by the mid 1980's. However, the primary goal of newborn screening for hemoglobinopathies has been to identify infants with SCD who would benefit from immediate care, leaving many of the infants identified as trait carriers to go uninformed. Many of these trait infants are now entering the childbearing ages with no knowledge of their trait status. This is an adult population that would benefit from screening for SCT and genetic counseling concerning the possible risks for their children to be affected with SCD; unfortunately, experience has shown that interest in testing and genetic counseling is low among the at risk African American population.

Knowledge of the disorder as well as cultural views, health beliefs, social and economic barriers may be contributors to the lack of interest and support for SCT testing and genetic counseling among the African American community. This study aims to increase and understand the level of acceptance of genetic testing and genetic screening among the African American population through a program of education and assessment of the current state of SCD cultural health beliefs among the target population.

2.0 SPECIFIC AIMS

2.1 SPECIFIC AIM I

Knowledge of Sickle Cell Disease and Acceptance of Genetic Testing and Counseling:

Specific Aim: To improve the acceptance of genetic testing and genetic counseling for sickle cell trait (SCT) among the African American female community of childbearing age by increasing the knowledge of sickle cell disease (SCD) through individual education sessions.

Hypothesis: The lack of interest in genetic testing for SCT among the African American community may be due to a lack of knowledge of SCD and the risks associated with SCT. Acceptance can be improved by increasing the communities' knowledge of SCT.

Plan: Utilizing anonymous paired surveys, assessment of knowledge of SCD and acceptance of genetic testing and genetic counseling for SCT was performed prior to and following the administration of a brief individual educational session. The effectiveness of the educational session will be analyzed as well as the relationship of knowledge of SCD with acceptance of genetic testing.

2.2 SPECIFIC AIM II

Knowledge of Sickle Cell Disease and the Health Belief Model:

Specific Aim: To determine the current health beliefs of the African American female community of childbearing age regarding SCD and genetic testing for SCT.

Hypothesis: Participants in a voluntary genetic screening program will have a high level of perceived severity of SCD, a high level of perceived susceptibility, a high level of perceived benefit to testing, and a low level of perceived barriers to testing. Identifying the current status of health beliefs will determine areas of education that must be stressed in order to increase interest in genetic testing for SCT.

Plan: Utilizing anonymous surveys among the African American community of childbearing age, the current state of SCD and SCT testing health beliefs will be analyzed. Assessment of knowledge of SCD will also be studied to determine a correlation with health beliefs.

3.0 BACKGROUND AND SIGNIFICANCE

3.1 SICKLE CELL DISEASE

Sickle cell disease (SCD), also known as sickle cell anemia, is an autosomal recessive genetic hematologic disorder that results from mutations in both copies of the β-globin gene, a major subunit of hemoglobin. Individuals with only one mutated β-globin gene and one normal working copy are known as sickle cell trait (SCT) carriers. Sickle cell trait carriers are healthy and will not develop SCD. The characteristic phenotype of SCD includes an altered polymerization of hemoglobin resulting in a “sickled” shape to the red blood cells (Figure 1).

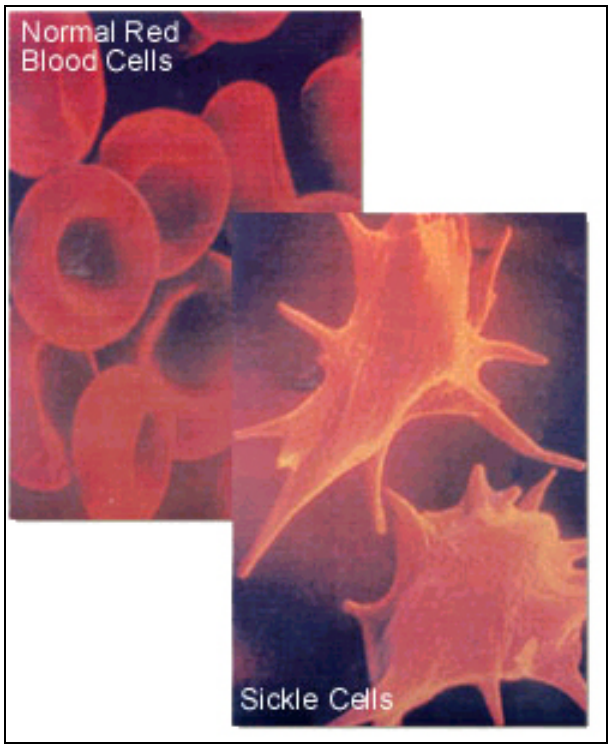

Figure 1: Sickled Red Blood Cells (www.samc.com, 4/2/2006)

Polymerization can result in varied characteristics of hemolysis and vascular occlusion which can lead to tissue ischemia and organ complications. SCD can occur through homozygosity for the sickle (S) β-globin mutations which results in the more severe form of SCD. SCD is also caused by compound heterozygosity of S β-globin mutations with other variant β globin gene mutations (Wilson, Krishnamurti, & Kamat, 2003). Examples of this include, but are not limited to, SC Disease, Sickle-β thalassemia, SE disease and SO^{arab} (Wilson, Krishnamurti, & Kamat, 2003). Variations of SCD can exhibit a range of phenotypes from mild to severe, however the expression of severity is unpredictable based on genotype. Homozygosity of other variant β-globin mutations can also result in other serious hematologic disorders such as

hydrops fatalis or Cooley's anemia. Within this manuscript, the term sickle cell disease (SCD) will encompass all of the variant forms of SCD and the typical presentation.

3.1.1 Incidence of Sickle Cell Disease

Sickle cell disease is the most common single gene disorder among the African American population, with an estimated one in every 375 individuals of African American descent affected. Approximately 1 in every 12 African Americans carry a SCD β-globin mutation (Doris L Wethers, 2000; Lonergan, Cline, & Abbondanzo, 2001). In the United States, approximately 2,000 infants are born each year affected with SCD (Wilson, Krishnamurti, & Kamat, 2003). Hb S is the most common β globin mutation found within individuals of African descent, followed by the Hemoglobin C β globin mutation (Doris L Wethers, 2000). People of Mediterranean, Middle Eastern, Indian, Caribbean and Central and South American descent are also at an increased risk to carry a mutation in their β-globin chains and be affected with a form of SCD or similar hemoglobinopathy (Doris L Wethers, 2000; Karnon et al., 2000; Lonergan, Cline, & Abbondanzo, 2001; Wilson, Krishnamurti, & Kamat, 2003). Figure 2 displays areas of origin in red, which have a high incidence of hemoglobinopathy carriers.

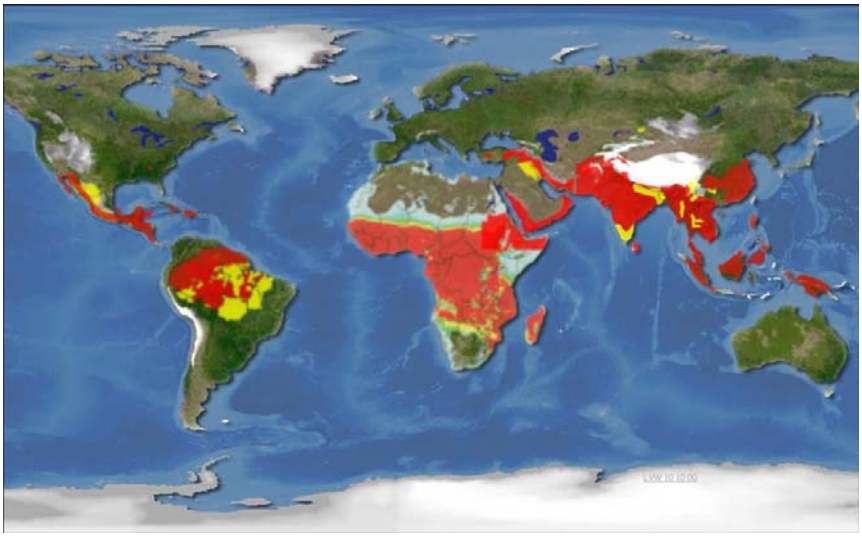

Figure 2: Areas of Increased Hemoglobinopathy Incidence

Individuals who are heterozygous for HbA (adult hemoglobin) and a β-globin variant are carriers for SCD, also known as sickle cell trait (SCT). Carriers for SCD do not typically manifest symptoms of the disorder as they have at least 50% normal hemoglobin; however, they may appear anemic due to the reduced expression of normal β globin subunits (Doris L Wethers, 2000). Awareness of carrier status is important because SCT carriers can pass on their variant gene to their children. Couples where both individuals are carriers of a β-globin variant have a 25% chance with each pregnancy that their child will have SCD, a 50% chance that their child will also be a carrier, and a 25% chance that their child will not be affected or a carrier (Karnon et al., 2000).

3.1.2 Natural History of Sickle Cell Disease

Sickle cell disease was first described in 1910 (Herrik, 1910). Since that time, understanding of the pathophysiology of SCD has increased resulting in effective treatment and reducing morbidity and mortality. Characteristic complications of SCD are the result of the hemoglobin polymerization and sickling shape of the red blood cells. Sickled red blood cells are rigid, sticky and elongated, increasing vasoocclusion as well as a causing a hemolytic state due to the decreased lifespan of these cells. There are many characteristic phenotypes that result due to the polymerization of the sickle hemoglobin. Acute complications include severe pain crisis; strokes; acute chest syndrome; splenic sequestration; and an increased risk of sepsis or other infections as well as many others (Karnon et al., 2000).

The acute-vasoocclusive event or pain crisis is the hallmark feature of SCD, which limits oxygen supply and causes tissue ischemia (Claster & Vichinsky, 2003; Wethers, 2000b; Wilson, Krishnamurti, & Kamat, 2003). Pain crisis are common and unpredictable. Pain crisis is a difficult complication of SCD and clinicians must trust patient self report in order to determine the best standard of treatment (Claster & Vichinsky, 2003; Wethers, 2000a, , 2000b; Wilson, Krishnamurti, & Kamat, 2003). The earliest symptom of vasoocclusion is the “hand-foot syndrome” or dactylitis (Figure 2) which is a swelling of the hands and feet of an infant with sickle cell disease caused by pooling and occlusion of the blood vessels.

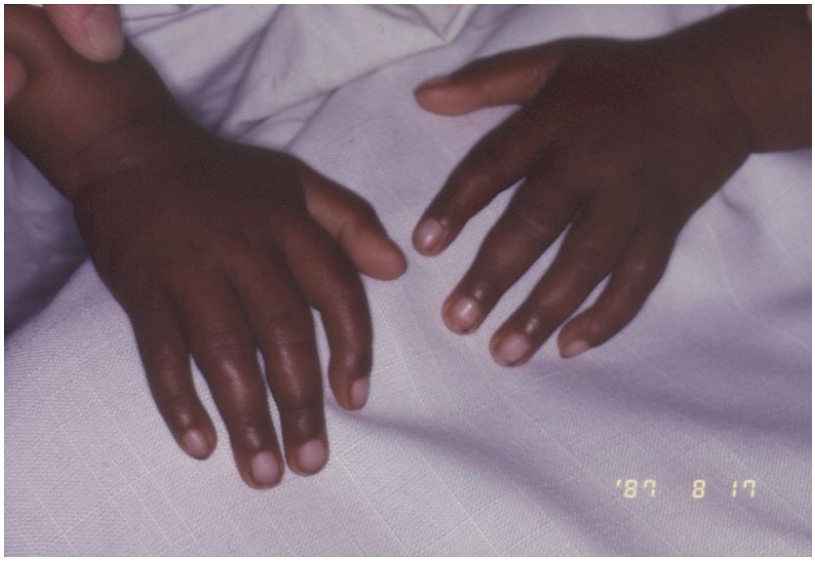

Figure 3: Dactylitis or "Hand-Foot Syndrome".

(http://web.uct.ac.za/depts/ich/teaching/temp/tb_scenarios/case%205/tbs_c05.html, 4/2/2006)

Acute chest syndrome (ACS) is a serious complication of SCD involving the development of infiltrates in the pulmonary system and can include infections (Claster & Vichinsky, 2003; Karnon et al., 2000; Wethers, 2000b; Wilson, Krishnamurti, & Kamat, 2003). ACS can also include symptoms of fever, chest pain, wheezing and cough and may present following or with other acute symptoms. Early treatment of ACS is important because advancement can progress to respiratory failure and death (Claster & Vichinsky, 2003; Wethers, 2000a, , 2000b; Wilson, Krishnamurti, & Kamat, 2003).

Splenic sequestration is characterized by a rapidly enlarged spleen which can lead to a decrease in hemoglobin production and an increased risk for infection (Claster & Vichinsky, 2003; Wethers, 2000a, , 2000b; Wilson, Krishnamurti, & Kamat, 2003). Without treatment, cases can lead to death.

Approximately 10% of all SCD patients will have a stroke at some time in their lives, with the peak incidence occurring between the ages of 4 and 6 (Claster & Vichinsky, 2003; Wethers, 2000a, , 2000b; Wilson, Krishnamurti, & Kamat, 2003). Strokes occur secondary to vasoocclusion within the blood vessels of the brain, limiting oxygen levels and causing hemiparesis, headache, cranial nerve palsy, and dysphagia (Claster & Vichinsky, 2003; Wethers, 2000a, , 2000b; Wilson, Krishnamurti, & Kamat, 2003). Some strokes can be small and go unnoticed, leading to reduced ability to learn and function with no identifiable cause.

Another common complication affecting males with SCD is priapism, or prolonged painful erections due to vasoocclusion (Claster & Vichinsky, 2003; Wethers, 2000a, , 2000b; Wilson, Krishnamurti, & Kamat, 2003). Almost 90% of males with SCD will experience priapism by age 20. Prolonged priapism may result in organ damage and impotence if untreated.

Renal complications can also be manifestations of SCD. Due to the fragility of the kidneys, these organs are prone to damage by the inflexible sickled red blood cells (Claster & Vichinsky, 2003; Wethers, 2000a, , 2000b; Wilson, Krishnamurti, & Kamat, 2003). Children with SCD are also prone to gallstones. Monitoring of these organs is warranted to prevent damage and consider surgery or other treatments (Claster & Vichinsky, 2003; Wethers, 2000a, , 2000b; Wilson, Krishnamurti, & Kamat, 2003).

Although serious health concerns for a child with SCD are numerous, there are also many psychological effects that must be addressed in treatment as well. Adolescence is a particularly difficult time for patients with SCD. Children with SCD often are slow in growth and development (Wethers, 2000a). The social effects of missed school, limitations in activity, and repeated hospitalizations can also cause distress to an adolescent with SCD. These issues along

with reproductive genetic counseling should all be addressed with the patient that is growing up with SCD (Wethers, 2000a).

3.1.3 Treatment of Sickle Cell Disease

Painful vasoocclusive crisis is often the result of bone marrow infarction and can vary in intensity with extreme pain crisis treated with opiates such as morphine and extended hospitalizations, with emphasis on hydration and management of any infections that may precipitate further crisis. Studies have also shown a significant reduction in occurrence of painful crisis in correlation with a high percentage of fetal hemoglobin or Hb F. Treatment with hydroxyurea induces expression of Hb F and a reduction in incidence of crisis (Ballas, 2002; Platt et al., 1994).

Treatment for acute chest syndrome includes pain management as well as oxygenation, hydration, antibiotics and blood transfusions. Splenic sequestration occurs most often in children, with splenic enlargement occurring suddenly requiring transfusion and immediate treatment. In some cases this can be recurrent and surgical splenic removal should be considered due to the risk of fatal complications (Karnon et al., 2000). Patients with SCD are at an increased risk for all types of blood sepsis. Prophylactic penicillin has been shown to significantly reduce the incidence of pneumococcal sepsis among infants with SCD, increasing the importance for early identification and treatment of SCD (Gaston, Verter, Woods, & et, 1986; Karnon et al., 2000). Standard childhood immunizations are recommended for all children, particularly children with SCD due to the high susceptibility to infection. Immunizations include the pneumococcal vaccines; yearly influenza vaccination; as well as meningococcal vaccination for children with

splenic dysfunction (Claster & Vichinsky, 2003; Wethers, 2000b; Wilson, Krishnamurti, & Kamat, 2003).

Approximately 10% of patients with Hb SS will experience a stroke due to vasoocclusion (Karnon et al., 2000). Patients identified at an increased risk for an initial or second stroke are monitored with Transcranial Doppler (TCD) imaging and receive regular blood transfusions in order to reduce the percentage of sickled cells within the blood stream, this type of follow up has shown to decrease the risk for stroke by ten-fold (16% risk to 1.6%) (Adams, McKie, Hsu, Files, 1998; Karnon et al., 2000).

SCD is rarely curable; however, in some cases bone marrow or stem cell transplant has been shown to be successful with minimal recurrence and mortality (Walters et al., 2000). Unfortunately, difficulties may arise in locating sufficient HLA matched donors, limiting the number of candidate patients for this procedure.

3.1.4 Molecular Genetics of Sickle Cell Disease

The healthy adult hemoglobin (HbA) molecule is made of two α globin chains and two β globin chains that bind oxygen in erythrocytes for transport throughout the body. Mutations within the genes which code for the α or β globin protein subunits can result in an imbalance of globins that disrupt the function and oxygen binding ability of red blood cells (Nussbaum, McInnes, & Willard, 2004). Abnormal hemoglobins are designated by the type of mutations present within these globin chains. For example, homozygous sickle cell disease is designated as HbSS, compound heterozygotes formed by one S β-globin chain and one C β-globin chain is distinguished Hemoglobin SC disease (Lonergan, Cline, & Abbondanzo, 2001; Nussbaum, McInnes, & Willard, 2004; Steinberg & Brugnara, 2003). Homozygous HbSS and S β-

thalassemia are considered the most severe forms of SCD (Lonergan, Cline, & Abbondanzo, 2001; Wilson, Krishnamurti, & Kamat, 2003).

Characteristics of SCD are a result of the unique properties of the hemoglobin molecules, leading to vasoocclusion and hemolytic anemia. In Hb S a single point mutation results in a glutamic acid replacing valine (Figure 3).

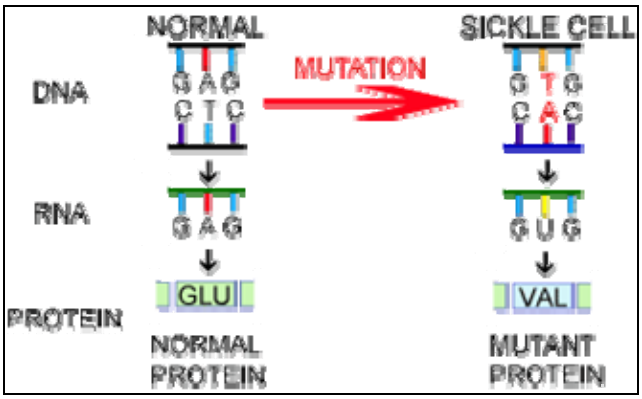

Figure 4: Hemoglobin S Mutation (http://evolution.berkely.edu, 4/2/2006)

This results in binding of Hb S chains and polymerization when deoxygenated, leading to rigid polymerized hemoglobin molecule (Figure 4).

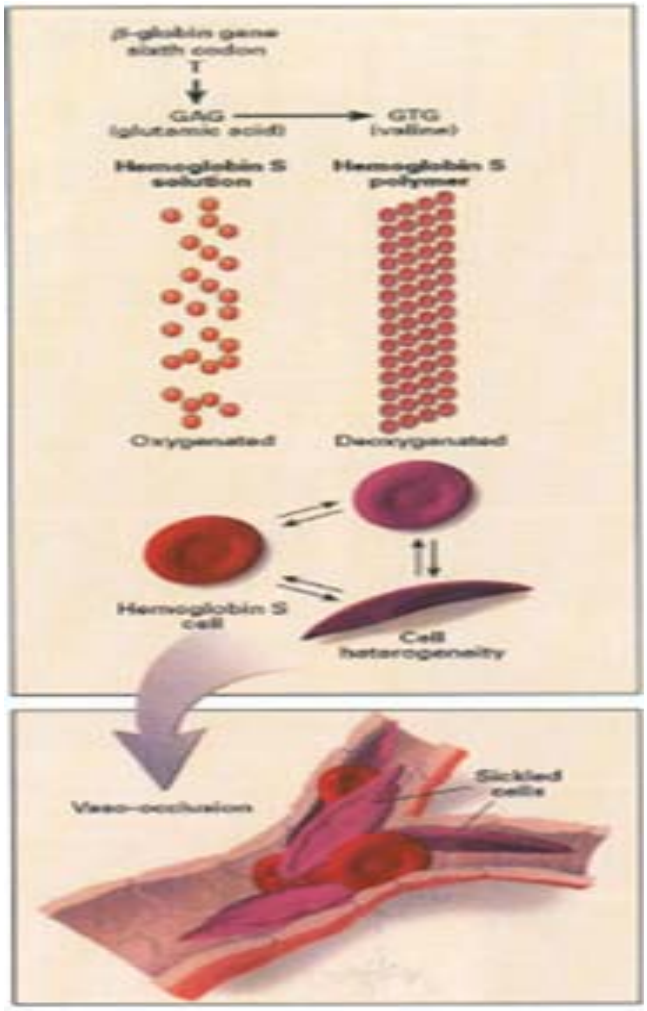

Figure 5: Binding and Polymerization of Hemoglobin S Molecules (Steinberg 1999)

These molecules distort the shape of the red blood cells into a stiff elongated “sickle” shape (Ballas, 2002; Lonergan, Cline, & Abbondanzo, 2001; Nussbaum, McInnes, & Willard, 2004; Steinberg & Brugnara, 2003; Wilson, Krishnamurti, & Kamat, 2003). Polymerization occurrence depends on multiple factors including deoxygenation, increased hemoglobin concentration, dehydration, acidity, temperature, and the presence of other hemoglobins, such as fetal hemoglobin which inhibits polymerization. Polymer formation is reversible with oxygenation; however, polymerization causes an increase in the membrane permeability for sodium, potassium, magnesium and calcium, leading to further dehydration of the red blood cells. Increased hemoglobin density accelerates polymerization further adding to the cycle of red blood cell sickling (Ballas, 2002; Lonergan, Cline, & Abbondanzo, 2001; Nussbaum, McInnes, & Willard, 2004; Steinberg & Brugnara, 2003). These polymerization/depolymerization cycles contribute to the increased hemolysis of SCD decreasing the lifespan of erythrocytes to as few as 20 days, as compared to the 120 day lifespan of healthy red blood cells. The deformed sickled shape of the red blood cells also decreases the red blood cells ability to pass through the blood vessels leading to vascular occlusion. It is also believed that the red blood cells in SCD have an affinity to bind to the vascular endothelium due to surface complexes that bind thrombospondin or other plasma proteins which promote adhesion to vascular endothelium, and reduce the ability for blood vessel relaxation (Ballas, 2002; Lonergan, Cline, & Abbondanzo, 2001; Nussbaum, McInnes, & Willard, 2004; Steinberg & Brugnara, 2003).

Other mutations within the β globin genes, when forming compound heterozygotes with Hb S, can result in features similar to Homozygous Hb SS sickle cell disease. Normal adult hemoglobin is maintained with an equal balance of α globin and β globin chains. Mutations that disrupt this careful balance can lead to a range of hematologic disorders (Doris L Wethers, 2000;

Nussbaum, McInnes, & Willard, 2004). For example, the β^o thalassemia mutation results in a lack of expression of that β globin chain. If this mutation is inherited with the Hb S mutation, only Hb S will be expressed resulting in the SCD phenotype. Other hemoglobin variants that can cause complications when inherited with an Hb S mutation are the Hb C mutation, Hb O-Arab, D^{punjab}, Hb E and β+ thalassemia (Doris L Wethers, 2000; Karnon et al., 2000; Wilson, Krishnamurti, & Kamat, 2003).

3.2 NEWBORN SCREENING FOR SICKLE CELL DISEASE

Newborn screening is used to describe the panel of tests performed on a newborn within the first few hours of life that are traditionally used to detect inherited metabolic disorders. The beginning of newborn screening is marked by the discovery of a blood screening test by Guthrie in the 1960's that could be used to detect phenylketonuria, a metabolic disorder when untreated results in mental retardation. In asymptomatic newborns this test provides the ability to perform dietary intervention and prevent catastrophic health outcomes (Guthrie & Susi, 1963). Since that time numerous screening tests have been developed for newborns, with large differences in testing panels between states. Development of new testing panels have been influenced by government policy, scientific discovery, financial incentives, and political pressures (Therrell, 2001). Infants born in one state may not be screened for the same panel of disorders as an infant born in a neighboring state. Criteria for including a new disorder within a newborn screening panel are shown in Table 1 (Kenneth A Pass, 2000; K. A. Pass et al., 2000).

Table 1: Recommended Criteria for Including a New Disorder within a Newborn Screening Panel

RECOMMENDED CRITERIA FOR INCLUDING A NEW DISORDER WITHIN A NEWBORN SCREENING PANEL (KENNETH A PASS, 2000; K. A. PASS ET AL., 2000)
1) Test should be accurate, specific and sensitive for the disorder and can be integrated in to the current testing protocol
2) Testing of widespread populations is cost effective
3) Disorder of interest should have a high enough incidence within the general population to warrant testing
4) Testing should provide measurable benefit to the newborn such as a substantial benefit to early treatment

Newborn screening for hemoglobinopathies began as a research protocol in the 1960's; however, clinical programs with established follow up were not established until 1975 in New York (Olney, 2000). Until studies were established linking reduction of infant mortality due to sepsis following treatment of prophylactic penicillin, establishment of statewide programs for hemoglobinopathies was slow (Olney, 2000). In 1987, Gaston and colleagues significantly demonstrated an improved prognosis for children with SCD on prophylactic penicillin. In a randomized multi-center trial of prophylactic oral penicillin given to children with SCD, the incidence of infection was reduced by 85% when compared to the placebo group (Gaston, Verter, Woods, & et, 1986). This discovery provided incentive and evidence of the benefits of early diagnosis of sickle cell disease. Following this discovery the National Institute of Health (NIH) consensus development conference recommended the initiation of universal mandatory newborn screening for sickle cell disease (Anonymous, 1987a, , 1987b). As of January, 2006, 49 states and the District of Columbia require universal newborn screening for SCD. According to the National Newborn Screening and Genetics Resource Center, New Hampshire has required screening, but has not yet implemented universal newborn screening for sickle cell disease

(http://genes-r-us.uthscsa.edu/, 4/2/2006). Some controversy existed in early development of hemoglobinopathy newborn screening programs in the establishment of whether screening should be targeted or universal. Targeted screening would perform testing only within populations deemed to be at high risk, while universal screening would test all infants born. State legislation has determined each individual states' protocol; however, deficiencies have been noted in targeted screening such as lack of cost effectiveness, logistics of targeting infants, and ability to miss affected infants due to mixed ancestry (Olney, 2000).

The primary purpose of screening newborns for SCD is the diagnosis of homozygous sickle cell disease for the purpose of beginning oral prophylactic penicillin, and implementing a relationship with a comprehensive sickle cell care team. Comprehensive sickle cell care programs are primarily located in large medical centers, with only 11 comprehensive centers endorsed by the National Institutes of Health (NIH, 2/2/2006). Experience since the implementation of newborn screening programs suggests that rates of morbidity and mortality due to sickle cell disease can be significantly reduced by such programs if they are linked to comprehensive clinical management systems that include parental education. (Davis, 2000; Lee, Phoenix, Jackson, & Brown, 1999; Leikin et al., 1989; Powars, Hiti, Ramicone, Johnson, & Chan, 2002; Quinn, Rogers, & Buchanan, 2004). Although a large portion of children and families affected by sickle cell disease are covered by these established centers, there are many families that do not live within a reasonable distance of a care team and who trust and prefer to be cared for by their regular pediatrician.

Newborn screening for hemoglobinopathies such as SCD also detects heterozygous carriers of SCT. While follow-up of the child identified as heterozygous for a hemoglobinopathy requires no specialized medical care there are several social and genetic counseling implications

of the notification of sickle cell or other hemoglobinopathy trait ("Consensus conference. Newborn screening for sickle cell disease and other hemoglobinopathies", 1987). A newborn detected to have SCT, provides an opportunity to offer testing and genetic counseling to a couple that may be at risk to have a child with SCD in a future pregnancy (Grover, 1989; Laird, Dezateux, & Anionwu, 1996). Information provided should explain that the carrier state is not a disease, that there may be implications for other family members, and that depending on results of family studies, future children may be at risk for a significant hematologic disorder (Whitten, Thomas, & Nishiura, 1981). The implications of sickle cell trait within a family are important information to be shared with the entire family, primarily members that are within or entering the childbearing age.

The ideal age for carrier screening is prior to the initiation of a pregnancy, when mature decisions can be made concerning pursuing testing and utilizing the information obtained from results (D'Souza et al., 2000). This information has the ability to affect family relationships and should be imparted sensitively with care taken of the families needs. Ideally this should be performed in a clinical setting with the assistance of a trained genetic counselor; however, in many states counseling of families is left to the infant's primary care physician or perhaps is not done at all.

3.3 SICKLE CELL TRAIT POPULATION SCREENING

Although screening for sickle cell disease and sickle cell trait is now performed through newborn screening as discussed above, this strategy of follow up for infants identified to be trait carriers is relatively new, leaving a large population of trait carriers unidentified and entering the childbearing age.

Population screening programs for sickle cell trait have been attempted unsuccessfully in the past. The National Sickle Cell Anemia Control Act, enacted in 1972 by the 92nd Congress of the United States, enforced mandatory sickle cell screening laws for the African American population (Grossman, Holtzman, Charney, & Schwartz, 1985; Olney, 2000). These laws were written and passed without caution to avoid stigmatization of individuals found to have SCD as well as those identified to be carriers of SCT (Grossman, Holtzman, Charney, & Schwartz, 1985). These early screening programs have received criticism for insensitivity to issues of race and culture, inadequate education of participants and workers, inaccurate testing procedures, and protection of the participants privacy (Grossman, Holtzman, Charney, & Schwartz, 1985).

Successful recruitment of African Americans for health screening studies has been based upon cultural sensitivity and voluntary involvement of the target population (Paskett, DeGraffinreid, Tatum, & Margitic, 1996). Most health prevention and control research studies have been limited in their ability to access the African American population, resulting in an under representation of this population in health research (Paskett, DeGraffinreid, Tatum, & Margitic, 1996). Planning to incorporate the barriers, beliefs and concerns of African Americans can improve recruitment and participation (Paskett, DeGraffinreid, Tatum, & Margitic, 1996).

Success in recruitment has been reported in many screening programs and research studies for African Americans that have utilized strategies which include multiples characteristics. Table 2 summarizes some of these studies and strategies used for recruitment (K. T. Ashing-Giwa, Padilla, Tejero, & Kim, 2004; Chan, Haynes, O'Donnell, Bachino, & Vernon, 2003; Fouad et al., 2000; Freimuth et al., 2001; B. L. Green et al., 2000; Jones & Broome, 2001; Paskett, DeGraffinreid, Tatum, & Margitic, 1996; Weinrich et al., 1998; Woods, Montgomery, & Herring, 2004).

Table 2: Strategies for Recruitment of African Americans for Health Research and Screening Behaviors

YEAR PUBLISHED	REFERENCE	SUMMARY OF RECRUITMENT STRATEGIES
1996	Paskett, E., C. DeGraffinreid, et al. (1996). "The recruitment of African Americans to cancer prevention and control studies." Preventative Medicine **25**: 547-553	1: Adequately characterize target population 2: Involve members of target population in planning efforts 3: Take the message to the target population 4: Give something back to the community 5: Enhance study credibility by using a community spokesperson 6: Identify and remove barriers to participation 7: Improve staff sensitivity 8: Educate the target population about the importance of prevention and early detection
1996	Voorhees, C. C., F. A. Stillman, et al. (1996). "Heart, body, and soul: impact of church-based smoking cessation interventions on readiness to quit." Prev Med **25**(3): 277-85.	1: Utilize a respected common meeting ground such as a community church
1998	Weinrich, S., D. Holdford, et al. (1998). "Prostate cancer education in African American churches." Public Health Nursing **15**(3): 188-95	1: Utilize a respected common meeting ground such as a community church
2000	Fouad, M. N., E. Partridge, et al. (2000). "Minority recruitment in clinical trials: a conference at Tuskegee, researchers and the community." Annals of Epidemiology **10**(8 Suppl): S35-40.	1: Establish an open dialogue between community members and researchers 2: Establish a respectful partnership with community members from the initial stages of research
2000	Green, B. L., E. E. Partridge, et al. (2000). "African-American attitudes regarding cancer clinical trials and research studies: results from focus group methodology." Ethnicity & Disease **10**(1): 76-86.	1: Active communication with members of target community
2001	Freimuth, V. S., S. C. Quinn, et al. (2001). "African Americans' views on research and the Tuskegee Syphilis Study." Soc Sci Med **52**(5): 797-808	1: Enhance knowledge and understanding of research 2: Improve trust and clarify informed consent procedures 3: Stress importance of research

Table 2 (cont'd): YEAR PUBLISHED	REFERENCE	SUMMARY OF RECRUITMENT STRATEGIES
2001	Jones, F. C. and M. E. Broome (2001). "Focus groups with African American adolescents: enhancing recruitment and retention in intervention studies." Journal of Pediatric Nursing **16**(2): 88-96.	1: Increase knowledge of the disease 2: Clarify expectations of research including time and incentives for participation 3: Utilize study coordinators that can form a trusting relationship with participants 4: Make research interesting for participants
2003	Chan, E., M. Haynes, et al. (2003). "Cultural sensitivity and informed decision making about prostate cancer screening." Journal of Community Health **28**: 393-405.	1: Target education and material towards the cultural differences of the target community
2004	Ashing-Giwa, K. T., G. V. Padilla, et al. (2004). "Breast cancer survivorship in a multiethnic sample: challenges in recruitment and measurement." Cancer **101**(3): 450-65.	1: Utilized telephone calls and recruitment invitations, as well as accommodating preferences of contact of participants. 2: Matched follow up calls with linguistically matched interviewers
2004	Frank, D., J. Swedmark, et al. (2004). "Colon cancer screening in African American women." ABNF Journal **15**(67-70).	1: Target education towards the health beliefs of the target community 2: Faith based education is also useful
2004	Green, P. M. and B. A. Kelly (2004). "Colorectal cancer knowledge, perceptions, and behaviors in African Americans." Cancer Nursing **27**(3): 206-15; quiz 216-7	1: Increase awareness of the disorder 2: Target the health beliefs of the community 3: Educate on the importance of screening
2004	Woods, V., S. Montgomery, et al. (2004). "Recruiting Black/African American men for research on prostate cancer prevention." Cancer **100**(1017-1025).	1: Tailor printed and educational materials to the target culture 2: Utilize targeted locations frequented by the target population 3: Participatory approach 4: Train staff to be sensitive and culturally aware

These strategies include adequate characterization of the target population, involvement of members of the target population in the planning process, taking the message to the target population, providing a return to the community, partnerships with credible community representatives, identification and removal of barriers, staff cultural sensitivity and improving education of the target population about the benefits of early diagnosis and treatment (Chan, Haynes, O'Donnell, Bachino, & Vernon, 2003; Woods, Montgomery, & Herring, 2004).

In regards to sensitive screening programs and promotion, special respect towards cultural beliefs should be incorporated into educational design and intervention. Cultural sensitivity in a respectful, caring, personalized ethnic approach with involvement of the target population in the planning and implementation process are the keys to successful recruitment and participation (K. T. Ashing-Giwa, Padilla, Tejero, & Kim, 2004; Chan, Haynes, O'Donnell, Bachino, & Vernon, 2003; Fouad et al., 2000; Frank, Swedmark, & Grubbs, 2004; Freimuth et al., 2001; B. L. Green et al., 2000; P. M. Green & Kelly, 2004; Jones & Broome, 2001; Lewis & Green, 2000; Paskett, DeGraffinreid, Tatum, & Margitic, 1996; K. O. Plowden, 1999; Voorhees et al., 1996; Weinrich et al., 1998; Woods, Montgomery, & Herring, 2004).

In 1994, the National Institutes of Health (NIH)-Department of Energy (DOE) Working Group on Ethical, Legal and Social Implications (ELSI) of Human Genome Research convened the Task Force on Genetic Testing to make recommendations to ensure the development systems ensuring safety and effectiveness to genetic testing (N. A. Holtzman, 1999; N. A. Holtzman & Watson, 1999). Based on its deliberations and the historical review of the sickle cell, Tay-Sachs, neural tube defects, and Down syndrome screening programs the Task Force on Genetic Testing made the following recommendations regarding the conduct of genetic screening program in order for success (Table 3**)** (N. A. Holtzman, 1999; N. A. Holtzman & Watson, 1999).

Table 3: Recommendations on the Conduct of Genetic Screening Programs

RECOMMENDATIONS BY THE TASK FORCE OF GENETIC TESTING FOR THE CONDUCT OF GENETIC SCREENING PROGRAMS (N. A. HOLTZMAN, 1999; N. A. HOLTZMAN & WATSON, 1999; N. M. D. HOLTZMAN, MPH & WATSON, 1997)
1) Genetic screening programs must be implemented being aware of the sensitivity of the needs of the groups screened and the inclusion of those groups in the planning of screening programs in order to frame the diagnosis and understanding of genetic disease with respect to issues of race, ethnicity, and gender.
2) Patients, physicians, and genetic counselors must understand what these tests actually predict or diagnose in order to ensure that patients make fully informed, autonomous decisions about the test results.
3) Unrelenting vigilance is necessary on the validity of tests and the reliability of the laboratories providing them, both as the tests are developed and as they are used on large numbers of people.
4) It is important to consider how these test results may affect other family members.
5) Confidentiality of the information discovered is vital.
6) The impact of a genetic diagnosis on the patient's health or life insurance status must be carefully considered.
7) The ethical dilemma posed by disease avoidance using pregnancy termination must be addressed sensitively according to the beliefs of the target population.

3.4 TAY-SACHS CARRIER SCREENING

Although the population screening programs for SCD and SCT among the adult African American childbearing population were unsuccessful, the Tay-Sachs carrier screening program among the Ashkenazi Jewish population has given evidence that a targeted genetic carrier screening program can be successful. We plan to utilize the experiences of this effective population screening program to the development of more effective screening program for SCD and SCT.

Genetic carrier screening programs for Tay-Sachs disease among the Ashkenazi Jewish population began in the 1970's alongside the sickle cell screening programs for African Americans; however, Tay-Sachs screening has experienced widespread community acceptance and has successfully reduced the incidence of Tay-Sachs disease by over 90% (M. Kaback et al., 1993; M. M. Kaback, 1977). Tay-Sachs is an autosomal recessive disorder which results in severe neurological damage and mental retardation in those affected. Since 1970 more than 1.4 million individuals worldwide have been voluntarily screened to determine if they are carriers for Tay-Sachs disease (M. M. Kaback, 2000). Lessons learned from the Tay-Sachs disease screening model include a need for educational and counseling components before and after testing within a population screening program. Additional concerns include the privacy and confidentiality of participants, insurability, quality control of testing, and the level of communication between the health community and the target population (M. M. Kaback, 2000).

From the initial planning stages of the Tay-Sachs screening model, community leaders, health professionals, and religious advisors were involved in order to ensure the target populations participation (M. Kaback et al., 1993).

Australian Tay-Sachs screening programs have utilized educational sessions as a method of promoting acceptance of screening among high school students resulting in a high retention of knowledge up to six years later and an increased positive attitude towards genetic testing and genetic counseling (Barlow-Stewart et al., 2003). A study performed by Becker et. al. utilized the Health Beliefs model to assess motivations for voluntary participation in Tay-Sachs carrier screening programs (Becker, Kaback, Rosenstock, & Ruth, 1975). Participants of the program were found to 1) desire future children, 2) belief that they had a high risk of being a carrier, 3) believed that learning of carrier status did not hold extreme consequences, 4) understood that testing in pregnancy is available for at risk pregnancies, 5) feel favorably towards the termination of an affected fetus, and 6) do not believe that the psychosocial affects of carrier testing are severe (Becker, Kaback, Rosenstock, & Ruth, 1975).

3.5 THE HEALTH BELIEF MODEL

The Health Belief Model was first described in the U.S. Public Health Services by a group of psychologists in order to understand the failed acceptance of disease prevention and screening services among various populations (Janz & Becker, 1984). Health screening behavior was determined to be driven by a combination of: 1) the individual's perceived susceptibility to the condition, 2) the individual's perceived seriousness of the condition, 3) the individual's perceived benefit of the specific behavior, and 4) the individual's perceived barriers to the behavior (Champion, 1984).

Use of the Health Belief Model has been successful in assessing and motivating health behavior change among African Americans in regards to cancer screening, genetic information, and utilization of health care resources for sickle cell patients, diabetic health care compliance, and sexual practices over a range of age groups (K. Ashing-Giwa, 1999; C. M. Brown & Segal, 1996; K. M. Brown, 2005, hsc.usf.edu/~kmbrown/Health_Belief_Model_Overview.htm; Byrne, Walsh, & Murphy, 2005; Douglass, Bartolucci, Waterbor, & Sirles, 1995; Doukas, Localio, & Li, 2004; Elliott, Morgan, Day, Mollerup, & Wang, 2001; Farquharson, Noble, Barker, & Behrens, 2004; Foxall, Barron, & Houfek, 1998; Frank, Swedmark, & Grubbs, 2004; Gipsh, Sullivan, & Dietz, 2004; Graham, Liggons, & Hypolite, 2002; P. M. Green & Kelly, 2004; James, Campbell, & Hudson, 2002; Juniper, Oman, Hamm, & Kerby, 2004; Lewis & Green, 2000; Mashegoane, Moalusi, Peltzer, & Ngoepe, 2004; McGarvey et al., 2003; Norman & Brain, 2005; Orr & Langefeld, 1993; K. Plowden & Miller, 2000; K. O. Plowden, 1999; Reese & Smith, 1997; Roden, 2004; Scollan-Koliopoulos, 2004; Sharps, El-Mohandes, Nabil El-Khorazaty, Kiely, & Walker, 2003; Steers, Elliott, Nemiro, Ditman, & Oskamp, 1996; Wiebe & Christensen, 1997).

It has been shown that health beliefs differ between African Americans and Caucasians (Barroso et al., 2000; Foxall, Barron, & Houfek, 1998). African American women who perceive fewer barriers to screening, perceive more benefits to pursuing screening, have an increased perception of susceptibility, and have confidence in the accuracy of screening are more likely to undergo screening for cancer (Frank, Swedmark, & Grubbs, 2004; P. M. Green & Kelly, 2004; James, Campbell, & Hudson, 2002). Increased understanding and knowledge of screening methods and the disease state also increase these factors (Frank, Swedmark, & Grubbs, 2004; P. M. Green & Kelly, 2004; James, Campbell, & Hudson, 2002). The health belief model has been

used in the assessment of utilization of health care facilities by sickle cell patients, suggesting that the health beliefs pose modifiable psychosocial variables that could be used in development of interventions to reduce health care costs (Reese & Smith, 1997).

A prenatal hemoglobinopathy screening program identifying carriers introduced three decisions a carrier mother must make: 1) whether to accept counseling, 2) whether to have her partner tested, and 3) whether to accept prenatal diagnosis (Rowley, Loader, Sutera, Walden, & Kozyra, 1991). Multiple factors affect this decision process, with the health belief model identifying motivators within the carrier mothers perceived belief that their partner is a carrier, knowledge of the disorder, perceived barriers to testing, perceived seriousness of the disorder, and desire to have additional children (Rowley, Loader, Sutera, Walden, & Kozyra, 1991). Yet the health belief model has not been used to assess motivations among the African American childbearing population to pursue sickle cell trait testing in themselves.

4.0 MATERIALS AND METHODS

4.1 PARTICIPANTS

A partnership between Magee Women's Hospital and Children's Hospital of Pittsburgh was formed as part of a community-based educational strategy to raise awareness of SCD and the importance of SCT follow up. African American women, above the age of 18 who were obtaining blood work by the Magee Outpatient Obstetrics and Gynecology Clinic's lab were invited to participate in an anonymous survey and short educational session regarding SCD and SCT. Participants included women who were pregnant as well as women who were receiving gynecological care. Ethnicity was used as inclusion criteria due to the high incidence of SCT among individuals of African American descent. As stated previously, 1 in 12 African Americans are at risk to be carriers. Females were identified as the largest consumer of care within the Obstetrics and Gynecology clinic and the usual parent member in charge of family health care.

4.2 SPECIFIC AIM I: KNOWLEDGE OF SICKLE CELL DISEASE AND ACCEPTANCE OF GENETIC TESTING AND COUNSELING

The initial experimental design was approved by the University of Pittsburgh Institutional Review Board (IRB) as a portion of a larger protocol entitled, "A Community Based Model for Improving the Acceptance of Newborn Screening Follow-Up, Family Testing and Genetic Counseling for Sickle Cell Disease and Trait." This protocol began as a study protocol entitled "Western Pennsylvania Sickle Cell Network: An Integrated System of Care for the Enhancement of Newborn Screening Follow-Up." This protocol was originally approved by the Children's Hospital of Pittsburgh Human Rights Committee in 2002 which has been modified and renewed yearly by the University of Pittsburgh Institutional Review Board. (Replications of IRB Approval letters for protocol #0405149/ 02-138 can be found in Appendix A.)

Initially this study aimed to improve acceptance of genetic testing and genetic counseling for SCT through brief educational sessions and improving knowledge of SCD and trait. An anonymous survey (Appendix B) assessing knowledge of SCD and SCT, acceptance of genetic testing, and demographic information was administered prior to the participant receiving SCD education. A brief five minute educational session was presented by a sickle cell community educator describing the inheritance and etiology of SCD and the importance of understanding SCT. Sessions were administered individually. Educational sessions were accompanied by visual aids and take home brochures. An outline of the brief educational session, including the visual aids and handouts given to participants can be found in Appendix C.

After the brief educational session, an identical anonymous questionnaire was administered to assess a change in knowledge of SCD and any change in acceptance of genetic carrier screening and genetic counseling. This portion of the study and survey questions were

modeled after the study performed by Barlow-Steward et.al. assessing the effect of education on Tay-Sachs carrier screening acceptance (Barlow-Stewart et al., 2003).

Following education and interviews with approximately 80 participants, it was believed that the study could be improved by assessing the psychosocial aspects that influenced acceptance of SCT testing among the African American population. We wanted to be able to better determine which factors must be emphasized within an educational program in order to increase motivation for pursuing genetic testing for SCT.

4.3 SPECIFIC AIM II: KNOWLEDGE OF SICKLE CELL DISEASE AND HEALTH BELIEFS

Modifications to the study protocol were submitted to and approved by the University of Pittsburgh Institutional Review Board under the IRB approval #0405149 to incorporate assessment of the sickle cell disease health beliefs into the survey of the target population in December of 2005 (Appendix A). Knowledge of SCD and demographic information was also included in this survey. Knowledge of SCD was assessed using 8 multiple choice questions modeled after a survey administered to school age children to assess knowledge of SCD (Koontz, Short, Kalinyak, & Noll, 2004). The Health Belief survey was modeled after those used among African American women to assess motivations for participation in cancer screening programs (Barroso et al., 2000; Foxall, Barron, & Houfek, 1998). A 5-point Likert scale response system was used to assess the health beliefs of perceived susceptibility, perceived seriousness, perceived benefit of action, and perceived barriers to action. A score of 1 indicated strongly disagree, or a low level, and 5 indicated strongly agree or a high level, as recommended by

Champion (Champion, 1984; Champion & Scott, 1997). The knowledge and health beliefs survey (Appendix D) was given to participants prior to receiving a brief educational presentation on the inheritance and etiology of SCD and the importance of understanding SCT. The assessment was performed before educating the population in order to avoid influencing the answers and to obtain a representative sample of the current state of knowledge and the health beliefs of the African American female population. Following the brief educational presentation participants were given an educational brochure and contact information of the Children's Hospital of Pittsburgh Sickle Cell Clinics' community educator. An outline of the brief educational session as well as the visual aids and handouts given to participants can be found in Appendix C.

5.0 DATA ANALYSIS

5.1 SPECIFIC AIM I: KNOWLEDGE OF SICKLE CELL DISEASE AND ACCEPTANCE OF GENETIC TESTING AND COUNSELING

Answers to the knowledge of SCD and SCT and acceptance of genetic testing and genetic counseling questions were transformed into dichotomous variables. Correct answers to the knowledge questions were coded as 1, incorrect or unsure answers were coded as 0. A maximum score of 6 was possible for knowledge of SCD. Positive answers with each attitude question towards genetic testing and counseling questions were also coded as 1, negative or unsure answers were coded as zero, with a maximum positive score of 5. Utilizing Stata 7.0 statistical software package the knowledge and acceptance scores prior to and following the educational program were compared using the Wilcoxen paired t-test. Acceptance of SCT testing and genetic counseling and knowledge of SCD were analyzed for correlation to determine if they were significantly related. Linear regression was used to determine which demographic variables significantly predicted the level of acceptance of genetic testing prior to receiving SCD education. Population means were also determined to level of knowledge and acceptance prior to and following receiving SCD education.

5.2 SPECIFIC AIM II: KNOWLEDGE OF SICKLE CELL DISEASE AND HEALTH BELIEFS

Correct answers to the sickle cell knowledge questions were given a score of 1, with a total maximum score of eight possible. A five point Likert-scale was used for assessment of perceived severity, susceptibility, benefits and barriers with 5 indicating a high perception, and 1 indicating a low perception. Stata 7.0 statistical software was used to determine the populations mean perceived severity of SCD, susceptibility to SCD, benefits to SCT testing, and perceived barriers to trait testing. Each health belief was analyzed along with knowledge scores of sickle cell disease to determine correlation. Linear regression was used to determine which demographic characteristics significantly predicted the perceived health beliefs.

6.0 RESULTS

6.1 SPECIFIC AIM I: KNOWLEDGE OF SICKLE CELL DISEASE AND ACCEPTANCE OF GENETIC TESTING AND COUNSELING

The population surveyed for knowledge of SCD and acceptance of genetic counseling and testing were primarily within the ages of 20-25 (34.5%), were high school graduates (32.6%), single (87.5%) with no children (35.9%), and were insured (86.7%) (See Figures 6-10).

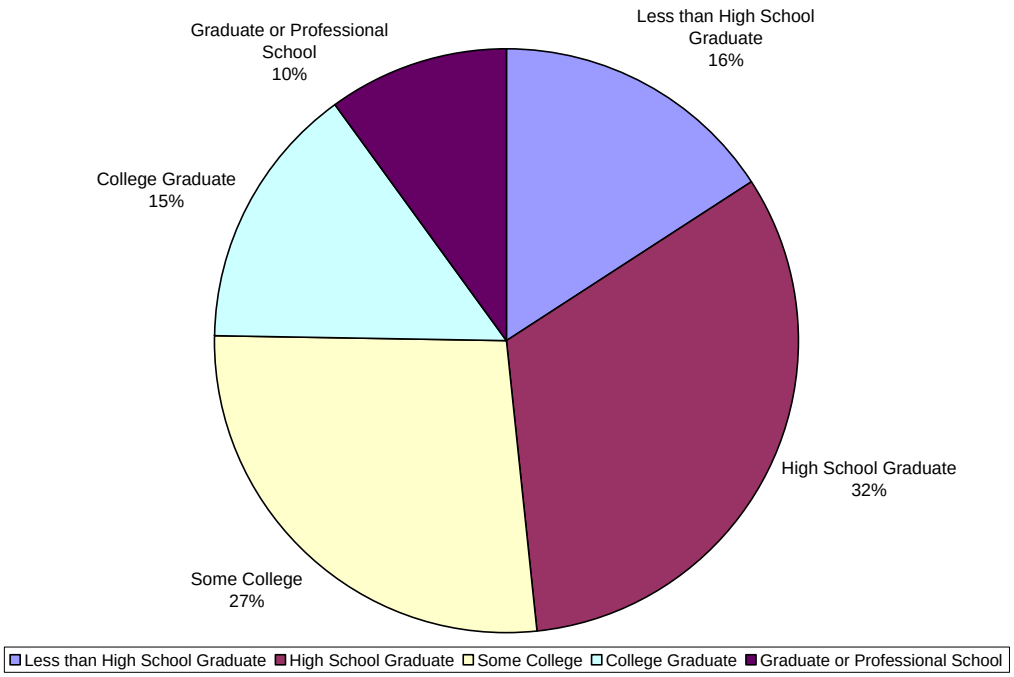

Figure 6: Highest Education Completed of Knowledge and Acceptance Survey Participants

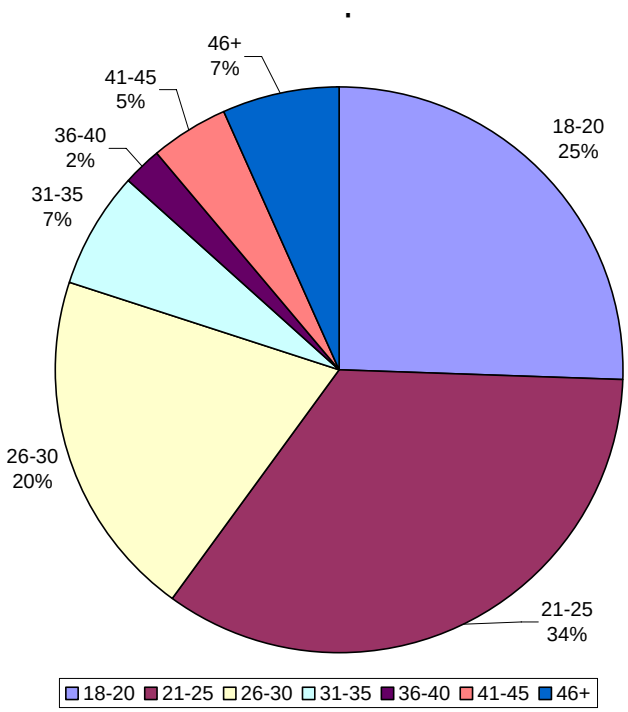

Figure 7: Age Distribution of Knowledge and Acceptance Survey Participants

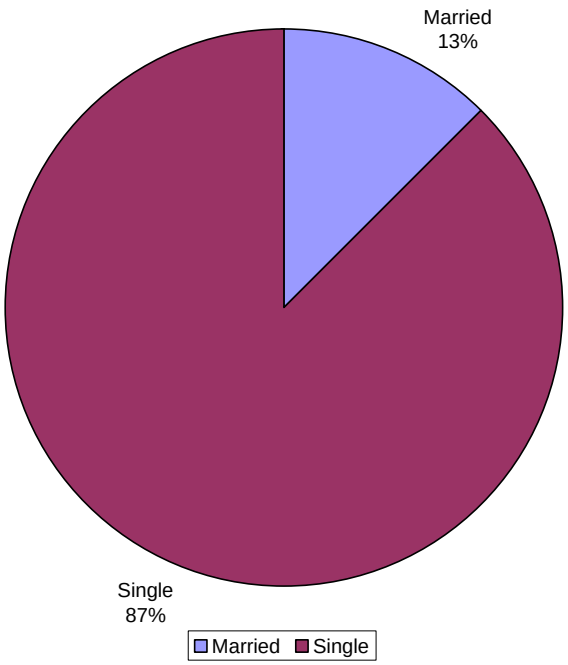

Figure 8: Marital Status of Knowledge and Acceptance Survey Participants

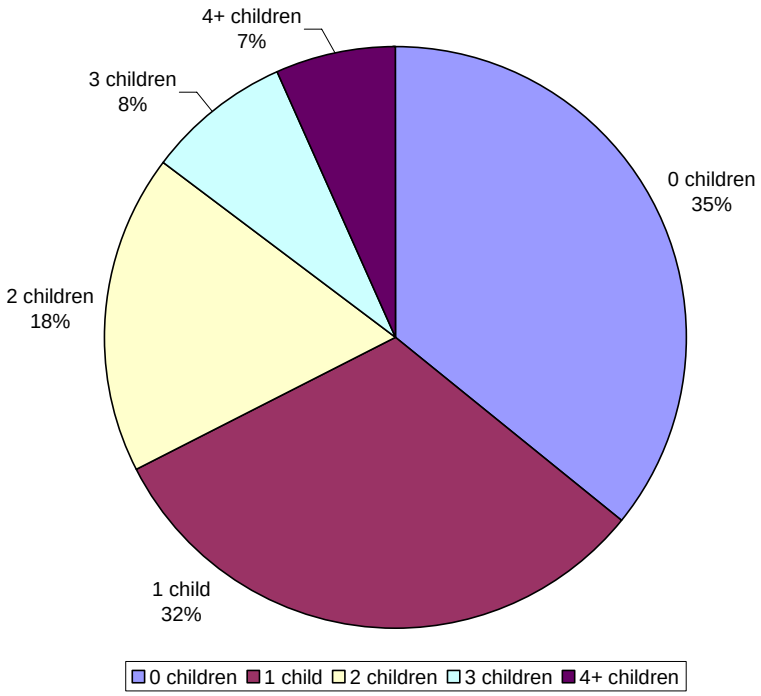

Figure 9: Number of Children of Knowledge and Acceptance Survey Participants

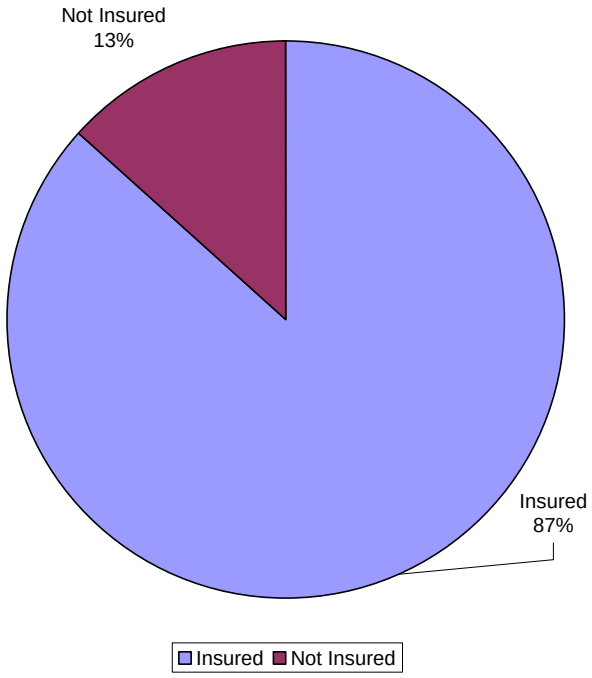

Figure 10: Insurance Status of Knowledge and Acceptance Survey Participants

The mean knowledge score prior to receiving the brief educational programming was 2.62 (± 1.39) (43.66% correct) on a maximum of 6 possible correct answers. Following the education the mean knowledge was 4.65 (± 1.04) (77.5% correct). The level of knowledge following education was significantly greater than knowledge of SCD prior to education, with a p-value < 0.001 (Figure 11).

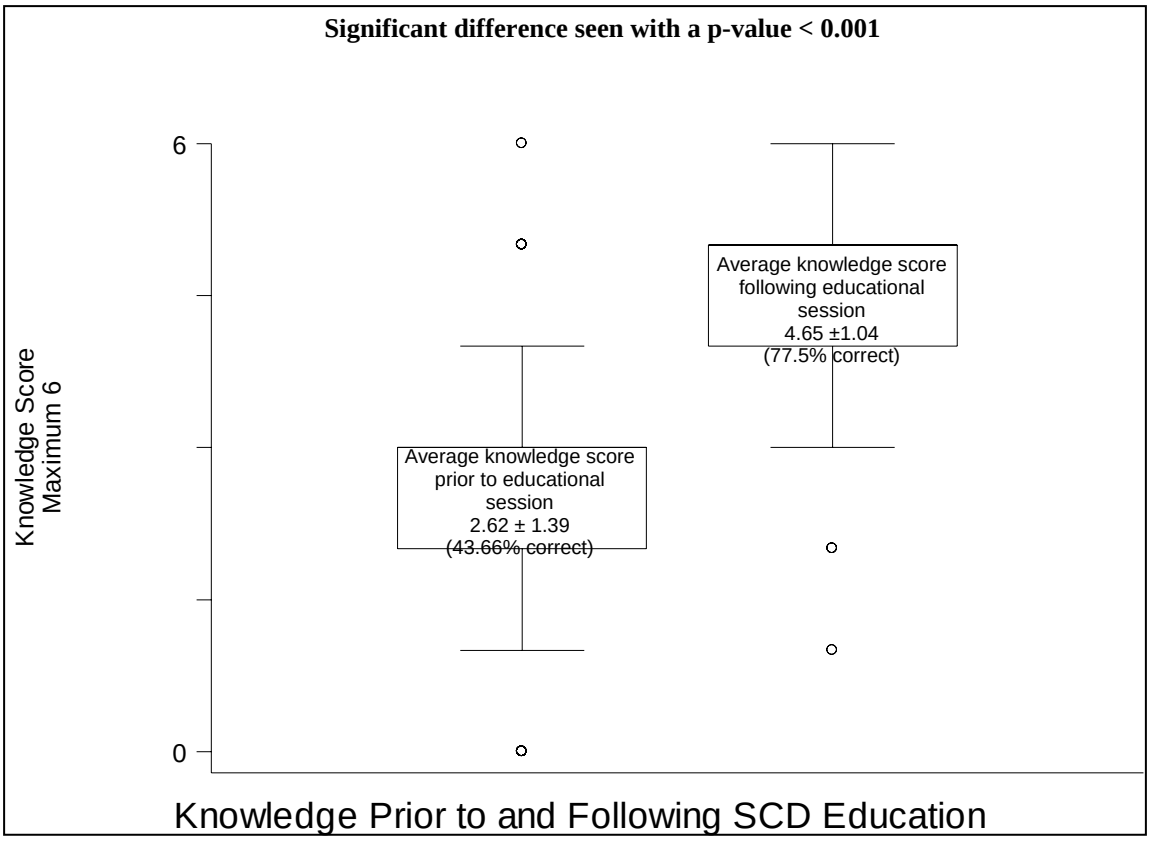

Figure 11: Knowledge of SCD Prior to and Following Brief Educational Session

Acceptance of SCT testing and genetic counseling was scored at a mean of 3.72 (± 1.39) prior to education, and at 4.30 (± 0.87) following education. The acceptance scores were significantly greater following education with a p-value < 0.001 (Figure 12).

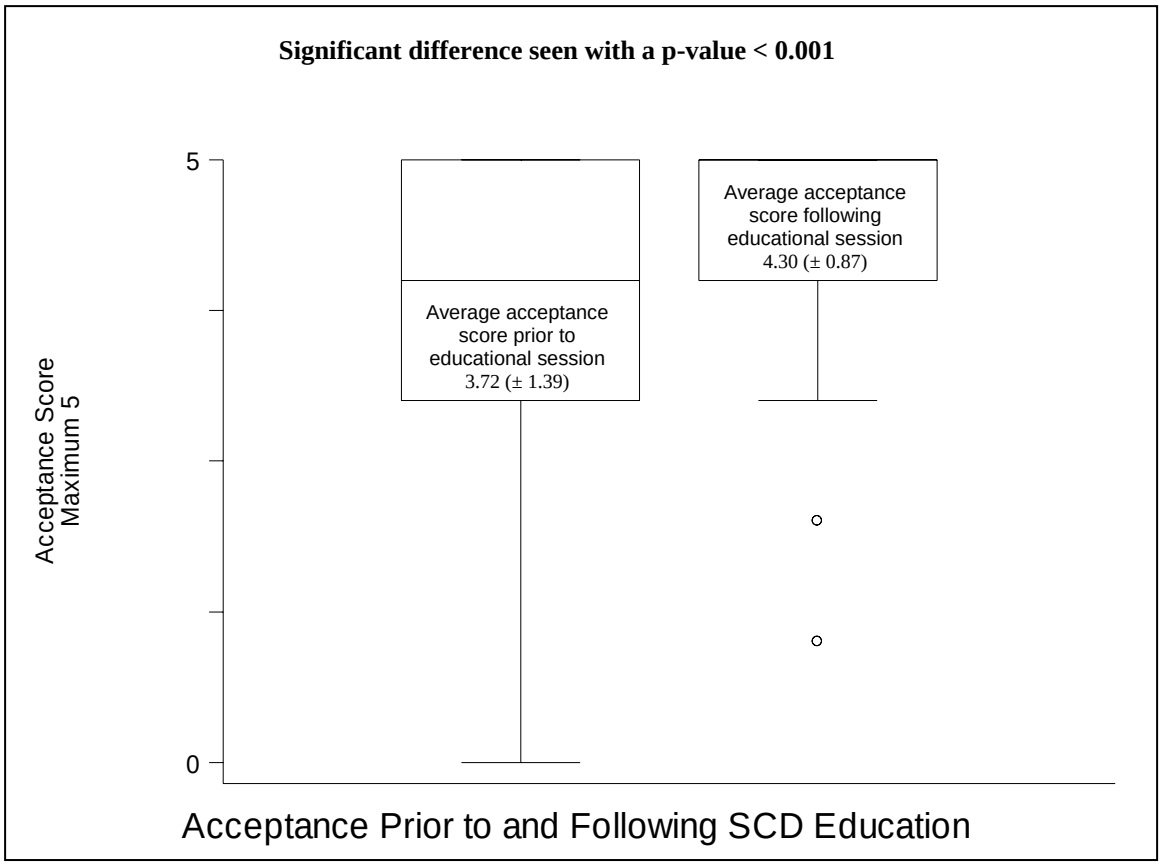

Figure 12: Acceptance of Genetic Testing and Genetic Counseling of SCD and SCT Prior to and Following SCD Education

When analyzed for correlation, an increase in knowledge of SCD was found to be only 25.6% correlated with an increase in acceptance of SCT testing and genetic counseling. Demographic data were analyzed for predictors of acceptance level prior to receiving the educational program. The only significant predictors for a high level of acceptance were insurance status and knowledge of SCD (p-value < 0.05) (Table 4).

Table 4: Linear Regression Analysis of Variables as Predictors of Acceptance Level

VARIABLE ASSESSED	P-VALUE (* INDICATES SIGNIFICANCE)
Knowledge of SCD	0.000 *
Education	0.078
Age	0.071
Marital Status	0.235
Number of Children	0.899
Insurance Status	0.023 *

6.2 SPECIFIC AIM II: KNOWLEDGE OF SICKLE CELL DISEASE AND HEALTH BELIEFS

Forty Five women have been surveyed at this time regarding their perceived health beliefs regarding SCD and SCT testing. The population surveyed for knowledge of SCD and perceived health beliefs averaged in age 20-24 (30%), were high school graduates (40%), and were single (84%), with an average of one child (32%). Forty three percent of participants currently live with their partner (Figures 13-17).

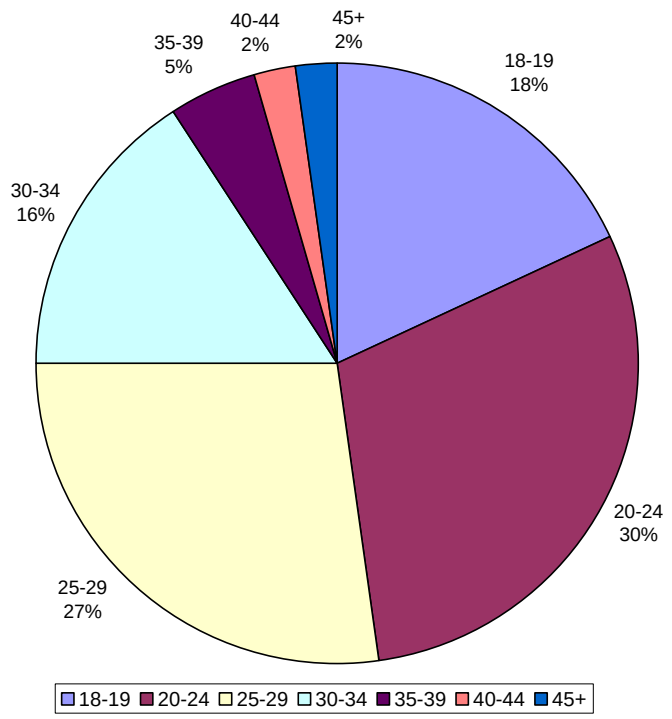

Figure 13: Age Distribution of Health Beliefs Survey Participants

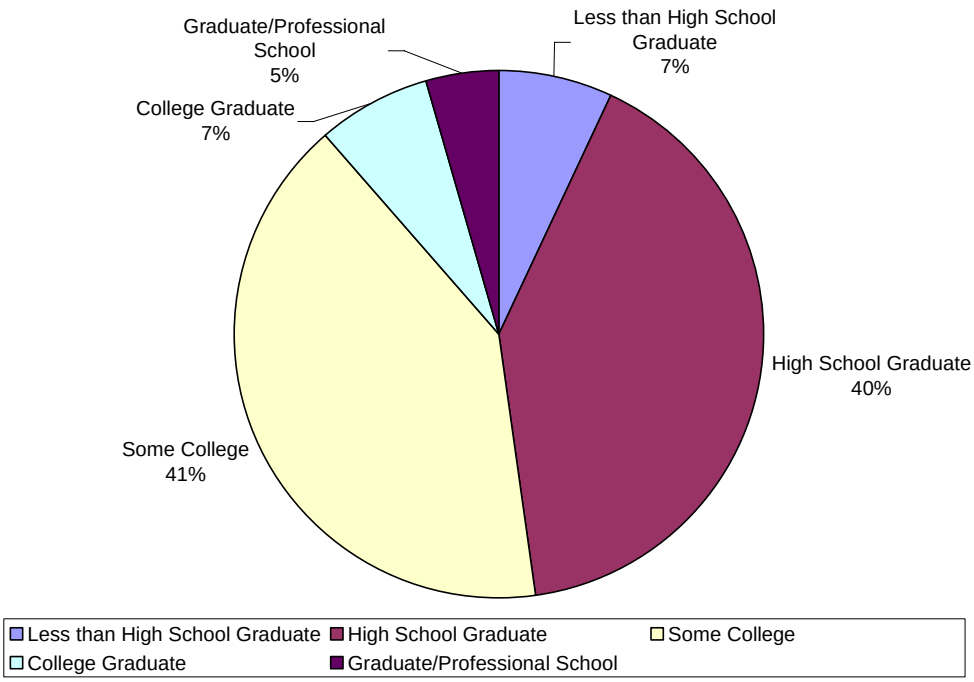

Figure 14: Highest Completed Education of Health Beliefs Survey Participants

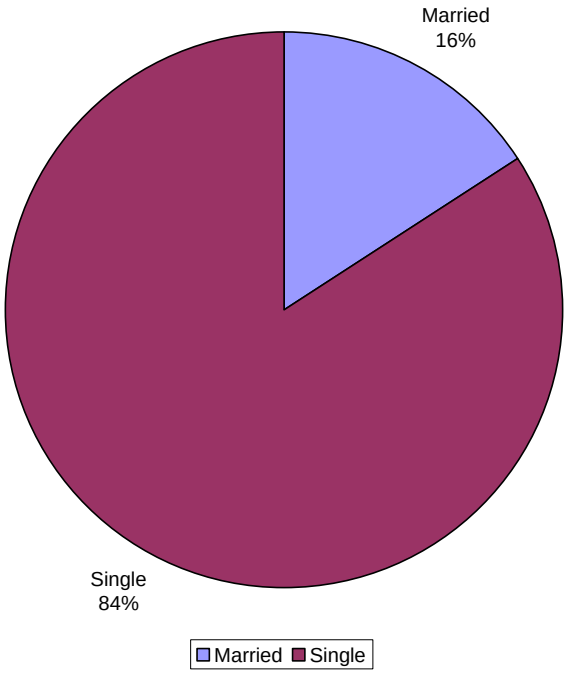

Figure 15: Marital Status of Health Beliefs Survey Participants

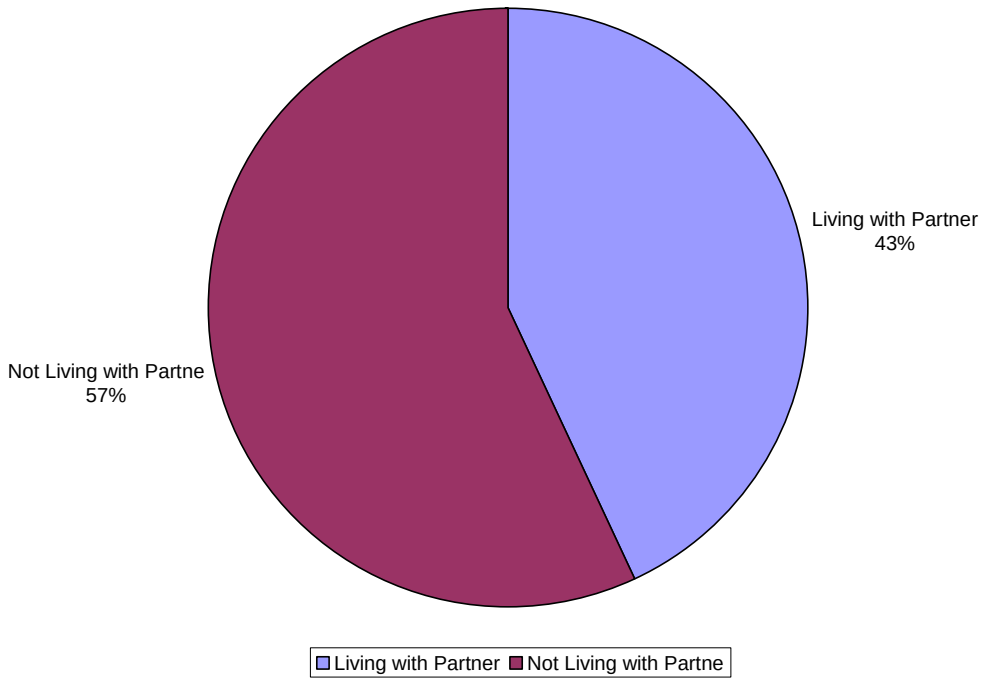

Figure 16: Living Arrangements of Health Beliefs Survey Participants

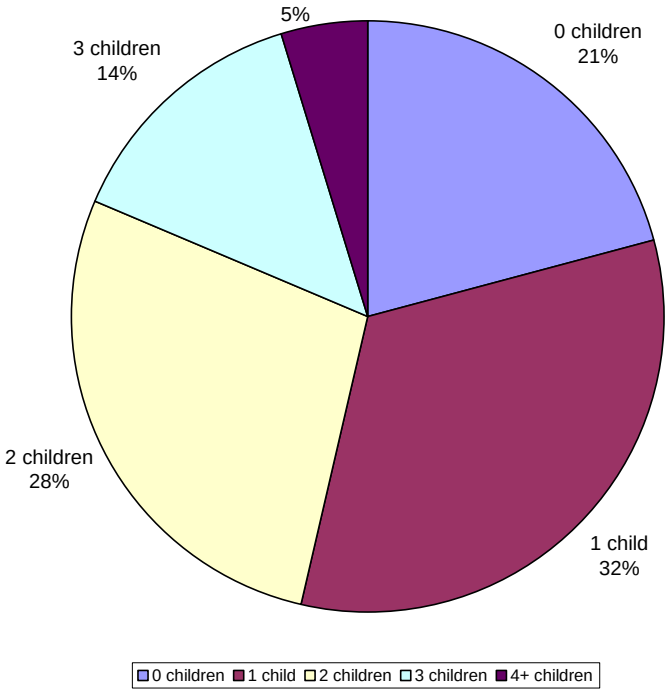

Figure 17: Number of Children of Health Beliefs Survey Participants

The cumulative mean perceived severity prior to education was high at 4.45 (± 0.921) on the 5-point Likert scale. The cumulative perceived susceptibility was moderate at 2.64 (± 0.963) on the 5-point Likert scale. The cumulative perceived benefit to testing was high at 4.03 (± 1.026), and cumulative perceived barriers to testing was low to moderate at 2.31 (± 0.900). The mean knowledge score was moderate at 4.44 (± 1.73) on scale with a maximum score of 8 points (Figure 18, Table 5).

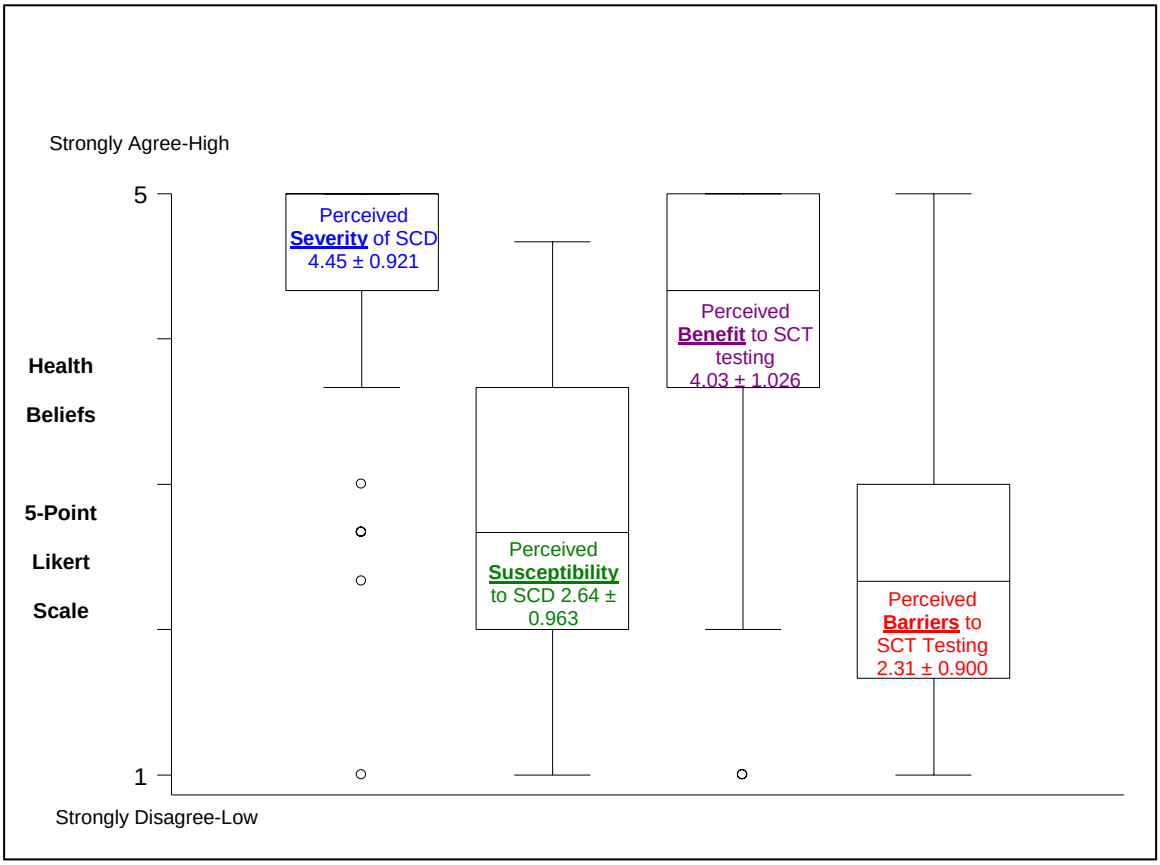

Figure 18: Average Cumulative Health Beliefs of African American Female Participants

Table 5: Summary of Knowledge of SCD and Health Beliefs Survey Results

SUMMARY OF KNOWLEDGE OF SCD AND HEALTH BELIRFS SURVEY RESULTS (* CUMULATIVE INDICATES ALL APPLICABLE ANSWERS HAVE BEEN AVERAGED TO STANDARD LEVEL OF SPECIFIC HEALTH BELIEF)				
Question	**Population Mean**	**Standard Deviation**	**Minimum**	**Maximum**
Knowledge of SCD	4.44 correct	1.73	0 correct	8 correct
Severity (Cumulative) *	4.45	0.92	1	5
Sickle Cell Disease is a serious disease	4.46	0.96	1	5
Having a Child with SCD would be very scary	4.44	1.03	1	5
My life would change if my child had SCD	3.82	1.21	1	5
Susceptibility (Cumulative) *	2.64	0.96	1	5
My children are at risk for SCD	2.06	1.18	1	5
SCD could happen in my family	3.39	1.34	1	5
My partner may be a carrier of sickle cell trait	2.40	1.45	1	5
Benefit (Cumulative) *	4.03	1.02	1	5
It is useful to know if I have sickle cell trait	4.28	1.19	1	5
It is useful to know if my partner has sickle cell trait	4.39	1.19	1	5
Knowing the risk of having a child with SCD would change how I plan my pregnancy	3.48	1.32	1	5
Barriers(Cumulative) *	2.31	0.90	1	5
Testing for sickle cell trait is painful and difficult	1.97	1.13	1	5
My partner would be hard to convince to have testing	2.15	1.38	1	5
I do not want to pay for sickle cell trait testing if it is not paid for by insurance	2.80	1.47	1	5

The Spearman rank correlation function was used to determine correlation between knowledge of SCD score and the health beliefs. A Spearman's rho value of 1 indicates a perfect positive correlation, a rho of -1 indicates a perfect negative correlation, and a rho of zero indicates that the values are completely independent of each other. A weak positive correlation was found between the level of knowledge and the perceived severity of SCD and between the level of knowledge and the perceived benefit to testing with a p-value < 0.05. A statistically significant correlation was not found between the knowledge of SCD and the perceived susceptibility and perceived barriers to testing (Table 6).

Table 6: Spearman Rank Correlation between Knowledge of SCD and Health Beliefs

SPEARMAN RANK CORRELATION BETWEEN KNOWLEDGE OF SCD AND HEALTH BELIEFS (SPEARMAN'S RHO INDICATES THE DEGREE OF RELATION, WITH A RHO OF 1 INDICATING A STRONG POSITIVE CORRELATION, -1 INDICATING A STRONG NEGATIVE CORRELATION, AND A RHO OF 0 INDICATING COMPLETE INDEPENDENCE OF THE VARIABLES)		
Health Belief	**Spearman's Rho**	**p-value * indicates significance (p< 0.05)**
Severity	0.3455	0.0201 *
Susceptibility	0.0210	0.8935
Benefit	0.4459	0.0027 *
Barriers	0.1861	0.2209

Linear regression was used to determine the relationship between the demographic data and the health beliefs. Perceived severity was significantly predicted by knowledge of SCD only, with a p-value < 0.05. Perceived susceptibility to SCD, perceived benefit to testing, and perceived barriers to testing was not significantly predicted by any of the demographic variables available (Table 7).

Table 7: Linear Regression Analysis of Variables and Health Beliefs

LINEAR REGRESSION ANALYSIS OF VARIABLES AND HEALTH BELIEFS		
		p-value *** indicates significance** **(p<0.05)**
Perceived Severity of SCD	**Knowledge of SCD**	0.005 *
	Education	0.486
	Age	0.305
	Living Arrangement	0.492
	Marital Status	0.808
	Number of Children	0.427
Perceived Susceptibility of SCD	**Knowledge of SCD**	0.821
	Education	0.670
	Age	0.112
	Living Arrangement	0.297
	Marital Status	0.304
	Number of Children	0.367
Perceived Benefit of sickle cell trait testing	**Knowledge of SCD**	0.095
	Education	0.864
	Age	0.303
	Living Arrangement	0.811
	Marital Status	0.612
	Number of Children	0.483
Perceived Barriers to sickle cell trait testing	**Knowledge of SCD**	0.108
	Education	0.232
	Age	0.147
	Living Arrangement	0.640
	Marital Status	0.978
	Number of Children	0.262

7.0 DISCUSSION

7.1 SPECIFIC AIM I: KNOWLEDGE OF SICKLE CELL DISEASE AND ACCEPTANCE OF GENETIC TESTING AND GENETIC COUNSELING

Overall this study has shown that a brief educational session is effective in both increasing knowledge of SCD and increasing the level of acceptance of genetic testing and screening for SCT among the African American female community of childbearing age.

A brief individual educational session utilizing visual aids and take home materials given in the prenatal setting was found to significantly increase the level of knowledge of SCD with a p-value < 0.001 among the participants. This is important in establishing evidence that providing education and informational materials regarding SCD and SCT during pregnancy is a good time to access the childbearing population of African American women at risk to have SCT. Although the prenatal visit is very busy with a large amount of information shared, the addition of information regarding SCD and SCT did not show to be an undue burden to the participants.

The brief educational session regarding the etiology and inheritance of SCD and SCT was also shown to significantly increase the level of acceptance of genetic testing and genetic counseling for SCT (p-value < 0.001). Prior to receiving the educational material the acceptance levels of the surveyed population had a large spread, with the average score moderately high on a 5-point scale. Following the educational session the spread minimized, and elevated to a higher

acceptance score, indicating that minimal education on the etiology and inheritance of SCD and SCT can positively affect the acceptance of genetic testing and genetic counseling for SCT.

A correlation study was performed and revealed that an increase in acceptance was correlated with an increase in knowledge of SCD only 25.6% of the time. This was lower than hypothesized but may be limited by the size of the study and the small scale of the assessment tool. With such a small assessment tool, an individual with an initial moderate to high acceptance level can show only limited increase, regardless of the level of increase in their SCD knowledge. For future studies a longer, more in depth assessment tool may be warranted in order to further define the levels of SCD knowledge and the level of acceptance. Unfortunately, a longer more in depth assessment tool may reduce interest in participation. Overall the majority of women invited to participate were receptive when assured that participation did not demand a large time commitment. Common reasons for declining participation were a lack of time and outside distractions such as small children. One proposed method for further study may be to access participants at a different point in care, as part of their visit intake paperwork, or to access women of childbearing age at a different venue such as outside the clinic at hair and nail salons.

Linear regression analyses of the demographic variables assessed in this survey were studied for predictors of a high initial level of acceptance, prior to receiving any SCD and SCT education. It was found that the initial knowledge of SCD as well as having health insurance were the only two significant predictors of a high level of acceptance (p-value < 0.05). This further emphasizes that knowledge of SCD does in fact influence the acceptance of SCT testing, indicating that education of SCD is an effective manner to increase interest in testing.

It is logical that insurance status is also a predictor of the acceptance level for testing. The African American community is commonly associated with lower socioeconomic standards, and

without insurance coverage, additional testing and screening that is not considered emergent may cause additional economic burden, causing a decrease in the acceptance and interest in genetic screening for an uninsured individual. Further research and outreach for SCD and SCT should take this concern into account and consider the benefits of offering testing for SCT at no cost or at a reduced cost, as a way to increase the interest and acceptance in SCT testing.

This project did show that education can increase the acceptance of SCT testing and genetic counseling for SCD and SCT; however, after educating and surveying approximately 80 participants it was decided that it may be of further benefit to understand the predictors of a high acceptance and the motivations, or lack of motivations, that are limiting the interest in SCT testing among the African American childbearing community. From this question the Health Belief Model was developed to study the African American childbearing populations' beliefs regarding SCD and SCT testing.

This study is limited in that the participants were only women who were actively pursuing health care. It is possible that this may be a cause of bias in the data. This is because these women represent a population that may already have a higher understanding and acceptance of health care and testing. Unfortunately, the ability to assess the knowledge and acceptance levels of all African American women of childbearing age in the area is limited by our own ability to access the population. However, one can also argue that as one of the largest prenatal health care facilities for the Pittsburgh area, Magee Women's Hospital facilitates cares for all levels of socioeconomic status, and may be one of the most representative samples of the area's female population of childbearing age. Future research should be conducted among traditionally underserved populations and become creative in areas of outreach and education. Community groups such as women's guilds, churches, youth groups, salons and barbershops

may provide other avenues for reaching a population that may not actively pursue health care and testing.

Another limitation of this study is that we did not assess whether the participants had had prior education on SCD and SCT, or whether the participants had ever been tested for SCT. These are both possible sources of bias in our data. It is possible that those who have had testing and genetic counseling prior to participating would have an increased level of acceptance of testing and counseling.

Although this study does show that women receiving education on SCD during a busy prenatal visit can in fact learn the information, it does not indicate how well this information will be retained in the long run. It would be useful to address the retention of the information given on SCD and SCT following the conclusion of the pregnancy, being this is the time where they will be experiencing newborn screening for hemoglobinopathies. With the Children's Hospital of Pittsburgh Comprehensive Sickle Cell Program contracted to follow-up with all of the families of infants identified to have an abnormal hemoglobinopathy or hemoglobinopathy trait in the Western Pennsylvania area, access is possible to reach a group where an increase in knowledge and understanding of SCD and SCT may be seen among mothers who received prenatal education. Unfortunately this newborn screening follow up program will only reach the small population of mothers where an infant has been identified to have an abnormal screen, losing to follow up the majority of women who received the SCD and SCT education that will not have an infant identified to have an abnormal hemoglobinopathy trait. It is of benefit to assess the knowledge of SCD and SCT among mothers of infants identified to have an abnormal hemoglobinopathy newborn screen prior to their receiving genetic counseling, as this will provide a representation of how aware those truly at risk for an infant to have SCT or SCD are.

7.2 SPECIFIC AIM II: KNOWLEDGE OF SICKLE CELL DISEASE AND HEALTH BELIEFS

The Health Belief Model theorizes that pursuit of a health screening program will occur when an individual believes that the heath concern is serious enough to warrant screening, that they are at risk for the disorder, they believe that there is a benefit to pursuing the screening and that the barriers to pursuing screening are low (K. M. Brown, 2005, hsc.usf.edu/~kmbrown/Health_Belief_Model_Overview.htm; Janz & Becker, 1984). Utilizing the Health Belief Model among a population of 45 African American women of childbearing age determined that the majority of this population believes that SCD is a severe disease, with a perceived severity of 4.45 ± 0.921 on a 5-point Likert scale. Initially it was hypothesized that the reason individuals are not pursuing SCT screening is because they do not believe it to be severe enough to warrant testing. The Health Belief Model indicates that this is not the case.

The women surveyed indicated that they do not believe that they are at an increased risk for SCD, with a perceived susceptibility to SCD of 2.64 ±0.963. Many participants reported that "*Sickle cell disease just doesn't run in my family,"* indicating they believe they were not at risk. Unfortunately, as with many recessive disorders, the family is often unaware of the gene in their family until someone is born with the disease, and so screening of sickle cell trait is still warranted. According to the Health Belief Model, in order to pursue a health screening behavior an individual must think that they are susceptible. This study indicates that the most likely limiting motivator to pursuing SCT screening is that the population does not perceive themselves at sufficient risk. Sickle cell trait carriers are healthy and will not experience any symptoms of SCD. It is understandable that it may be difficult for individuals to believe that they may be at risk to have a child with a severe illness because they themselves are healthy, and no one in their

family has had the same experience. Future studies should address why members of the African American population of childbearing age do not believe that they are at risk for having children with SCD. This information would be useful to effectively target health education interventions towards motivating individuals to pursue genetic testing and genetic counseling for SCT. Focus groups provide a method for utilizing the information obtained in this study to further address the lack of perceived susceptibility among the African American population of childbearing age. Focus groups provide the opportunity for members of the target population to voice their opinions and thoughts on how the health community could sensitively address the beliefs of the community in a culturally appropriate and effective manner. Interviews of members of the African American community of childbearing age who are and who are not actively pursuing health care should probe into the reasons and underlying beliefs that are causing this population to believe that they are not at risk to have SCD in their family. Information obtained from these targeted interviews could then be used to develop the educational materials that will be the most effective in motivating this population to pursue SCT testing and genetic counseling.

A limitation of this study is that it was not assessed whether participants in this study already knew their trait status prior to filling out their health beliefs. If they previously were aware of their own SCT status as well as that of their partner, they would be correct in indicating that their children were not at risk for SCD. This is a limitation and flaw to this survey that future studies should also address. Variance in health beliefs may be seen between individuals who know their trait status and those who do not.

Prior to being educated on the etiology of SCD and the importance of being aware of SCT, the population of African American women surveyed believed that there is a high benefit to testing for SCT, with a perceived benefit to testing of 4.03 ± 1.026 on a 5-point scale. The

Health Beliefs Model reports that in order for an individual to pursue testing, they must believe that the screening behavior has a high benefit. This study indicates that the African American community already believes that screening for SCT is beneficial, prior to being educated on the importance of genetic screening for SCT. This indicates that this area may not need to be emphasized as much in future education, because according to the Health Belief Model, this is not the rate limiting motivator for pursuing SCT screening. Education of the benefits of testing should not be neglected however, because there will always be someone who is at risk who is unaware of the benefits of testing.

The perceived barriers to testing were low with an average of 2.31 ± 0.900, indicating that this is unlikely to be what is causing the lack of interest in genetic testing for SCT, according to the Health Belief Model. Interestingly, one of the questions of barriers inquired on the willingness to pay for SCT screening if it is not covered by insurance. This question returned with the highest barrier score, indicating that insurance coverage of testing may affect the willingness of the at risk population to pursue testing. As discussed previously, the African American population is often largely of a lower socioeconomic status; they may find that paying for additional testing that is not emergent is an unnecessary financial burden. Future studies should take this concern into account and consider different ways to supply testing at little to no cost to the patient who needs financial help.

Spearman rank correlation was utilized to determine if the knowledge level of SCD was related to the health beliefs of this population. The average SCD knowledge score among the population surveyed was moderate, at 4.44 ± 1.73, on a maximum scale of 8 correct answers. Evaluation with Spearman's rank correlation found a significant relationship between the level of SCD knowledge and the perceived severity of SCD ($p\text{-value} < 0.05$). Individuals with an

increased level of knowledge of SCD seem to also have an increased belief that the disorder is severe. This supports the earlier hypothesis that increasing education and knowledge of SCD will increase the motivations towards pursuing SCT testing by exhibiting that improving knowledge increases the belief that the disorder is severe enough to warrant screening. A positive correlation was also exhibited between the level of knowledge of SCD testing and the perceived benefit to testing with a p-value < 0.05. This also supports the hypothesis that increasing knowledge and understanding of SCD will motivate African American women of childbearing age to pursue SCT testing by increasing their perception of the benefit to testing.

No significant correlation was found between the knowledge of SCD and the perception of susceptibility and barriers to testing. As discussed earlier the perception of susceptibility could be influenced by knowledge of SCD; however, it also likely to be strongly influenced by established family myths, and the belief that if they are healthy and their family is healthy they are unlikely to have children at risk for SCD. Family beliefs are often very strong and difficult to influence, even by facts and knowledge because these are the beliefs that individuals learn throughout their whole life and have experienced first hand. Sensitivity and respect of these family beliefs and myths is important to establish in order to connect with patients and successfully educate these families. Future studies must take into account that emotional, strongly embedded family histories and beliefs may be influencing how the at-risk population perceives health information and genetic screening information. Educational material should also acknowledge these myths and stories because these lingering beliefs may clash with the scientific fact. In order to accurately educate at-risk individuals, these stories should be addressed sensitively in education, and not ignored.

Barriers to testing for SCT were not found to be significantly correlated with the level of knowledge of SCD. Although the perceived barriers were low, it is possible that the perceived barriers to testing may be beyond the scope surveyed for in this study. This study addressed the cost of testing and insurance coverage, the participation of partners, and the difficulty of testing; however, other barriers such as limited access to testing, socioeconomic status, not knowing where testing is available and inability to travel to a testing site may also exist as barriers to pursuing testing that have not been addressed. Future studies should address all levels of possible barriers to pursuing testing that were not addressed here.

Demographic variables assessed in this study include the age of the participants, the marital status, whether they lived with their partner, their highest education level achieved, and the number of children they currently had. It was hypothesized that younger participants with fewer children may be more interested in knowing their risks for future children than those participants who had already had many children. Marital status and living situation was also thought to increase an individual's interest in pursuing testing because they would be more likely to have an active partner in their pregnancy. Education was thought to be likely correlated to a higher understanding of SCD and SCT testing as well as a higher socioeconomic status. However linear regression analysis did not find any significant relationship between any of the health beliefs and any of these demographic measures. This study is limited in that it did not directly address socioeconomic status as a possible influential demographic factor. Transportation issues have also been hypothesized as a limitation for individuals to pursue health care and testing for SCT, making this another candidate for future assessment.

7.3 CONCLUSIONS

This study was successful in exhibiting that education of SCD in a prenatal setting can influence the knowledge of SCD and the acceptance of genetic testing for SCT. The feasibility for establishing a successful model of education of SCD within a prenatal setting is high as long as the participation is found between all parties involved. It was found that only minimal education was necessary to improve the knowledge SCD and the acceptance of SCT testing. The majority of the individualized educational sessions were performed in less than 5 minutes.

Characterization of the current state of health beliefs of the African American childbearing population is still in process, as the sample size is a large source of limitation in making final conclusions on the data. According to the data at this point, the health belief that seems to be influencing the lack of interest in pursuing screening for SCT among the population surveyed is the low belief that they are individually at risk for being carriers of SCT. Outreach methods that target these beliefs should be sensitive and respect cultural beliefs. Future proposed use of this data plans to incorporate the results into focus group interviews and education planning sessions with members and leaders of the African American community, in order to improve the public educational materials on SCD and SCT screening. Utilizing input of the target population is an important step in establishing a genetic screening program.

Much was learned throughout the process of developing and implementing this study. First of all, it became clear early on that success of this project would only occur with an open and active partnership of all parties involved. Without the support of Magee Women's Hospital participation would have been very limited. However, as discussed earlier, this may have added some additional limitations and bias into our study by only supplying participants who are already in a heightened state of awareness of the importance of health care and testing. These

participants have actively pursued prenatal care and so may already be more open to health care information and additional testing than the general population of African American women of childbearing age. It was thought though that limiting participants to those individuals who are currently pregnant are also those most likely to benefit from the information prior to dealing with the results of newborn screening. When these participants deliver, a small percentage of them will be identified by the Western Pennsylvania Sickle Cell Comprehensive Sickle Cell Program, and this early experience with information on SCD and SCT may reduce the shock of this contact regarding their newborns hemoglobin status.

As the Western Pennsylvania Sickle Cell Comprehensive Sickle Cell Program continues to educate and access members of the African American community through outreach and newborn screening follow up it is crucial that they consider the implications of the information disseminated. Further development of these materials must take into account the unique beliefs of the community at risk in order to develop a successful partnership. Simple education can be a success, however for maximum success educational materials need to sensitively address the beliefs of the population that are leading to a lack of motivation for testing, particularly the belief that they are not at risk for SCD and SCT.

APPENDIX A

INSTITUTIONAL REVIEW BOARD APPROVAL LETTERS

Children's Hospital of Pittsburgh

Human Rights Committee

3705 Fifth Avenue
Rangos 1303A
Pittsburgh, PA 15213-2583

Ph: (412) 692-5247
(412) 692-5730
Fx: (412) 692-8707

August 28, 2002

Lakshamanan Krishnamurti, M.D.
Children's Hospital of Pittsburgh
Division of Hematology/Oncology

Dear Dr. Krishnamurti:

On July 11, 2002, the Human Rights Committee reviewed your protocol **"Western Pennsylvania Sickle Cell Network: An Integrated System of Care for the Enhancement of Newborn Screening Follow-up (02-138)"** and it was APPROVED by expedited review (category 7) with MINOR contingencies.

As of this date, we have received your satisfactory response to those contingencies. You may use this as your final letter of approval to begin your study.

The HRC would appreciate receiving one copy of any publications or abstracts resulting from this project.

Under our Federalwide Assurance (FWA-600) with DHHS, annual review and approval of all ongoing research protocols is necessary. CHP has instituted an eleven-month cycle for renewals to ensure that there are no periods of lapse. Therefore, you should submit the renewal to the HRC office for consideration by June 30, 2003.

If any untoward results related to this research should occur, they must be reported in a timely manner to the HRC. Any changes in the protocol or the consent document must receive approval from the HRC prior to their implementation.

Sincerely,

Ev Vogeley

Ev Vogeley, M.D., J.D.
Chairman
Human Rights Committee

Children's Hospital of Pittsburgh

Human Rights Committee

3705 Fifth Avenue
Rangos 1303A
Pittsburgh, PA 15213-2583
Ph: (412) 692-5247
(412) 692-5730
Fx: (412) 692-8707

July 3, 2003

Lakshamanan Krishnamurti, M.D.
Children's Hospital of Pittsburgh
3705 Fifth Avenue
Pittsburgh, PA 15213
Division of Hematology/Oncology

Dear Dr. Krishnamurti:

On behalf of the Human Rights Committee, I am providing expedited approval for renewal of the protocol, **"Western Pennsylvania Sickle Cell Network: An Integrated System of Care for the Enhancement of Newborn Screening Follow-up (02-138)".**

I am able to provide expedited approval under 45 CFR 46.110b and 21 CFR 56.110 because the study at this point fits into category 9 of the list of research types that may qualify for expedited review. Category 9 states continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Under our Federalwide Assurance (FWA-600) with DHHS, annual review and approval of all ongoing research protocols is necessary. CHP has instituted an eleven-month cycle for renewal to ensure that there are no periods of lapse. Therefore, before June 30, 2004, you should submit your renewal to the HRC office.

We would appreciate receiving copies of any publications related to this study. All expedited reviews are presented at a convened meeting of the HRC. If any issues arise, I will notify you in writing.

Sincerely,

Ev Vogeley

Ev Vogeley, M.D., J.D.
Chairman
Human Rights Committee

Children's Hospital of Pittsburgh

Human Rights Committee

3705 Fifth Avenue
Rangos 1303A
Pittsburgh, PA 15213

Ph: (412) 692-5247
(412) 692-5730
Fx: (412) 692-8707

April 28, 2003

Lakshamanan Krishnamurti, M.D.
Children's Hospital of Pittsburgh
3705 Fifth Avenue
Pittsburgh, PA 15213
Hematology/Oncology

Re: "Western Pennsylvania Sickle Cell Network: An Integrated System of Care for the Enhancement of Newborn Screening Follow-up (02-138)"

Dear Dr. Krishnamurti:

Members from the Human Rights Committee (HRC) convened on April 24, 2003 to review the revisions to the above-mentioned study. The revisions consist of changes to the consent form(s) to be compliant with HIPAA authorization and were APPROVED.

Under our Federalwide Assurance (FWA-600) with DHHS, annual review and approval of all ongoing research projects is necessary. Therefore, you should submit the renewal to the HRC office for consideration by June 30, 2003.

If any untoward results related to this research should occur, they must be reported to the HRC immediately. Any changes in the project must be approved by the HRC prior to their implementation.

Sincerely,

Ev Vogeley

Ev Vogeley, M.D., J.D.
Chairman
Human Rights Committee

University of Pittsburgh

Institutional Review Board

3500 Fifth Avenue
Ground Level
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)

MEMORANDUM:

TO: Lakshmanan Krishnamurti, M.D.

FROM: Robert Hardesty, M.D., Vice Chair

DATE: July 7, 2004

SUBJECT: IRB #0405149: Western Pennsylvania Sickle Cell Network: An Integrated System of Care for the Enhancement of Newborn Screening Follow-Up

Your renewal with modifications of the above-referenced proposal has received expedited review and approval by the Institutional Review Board under 45 CFR 46.110 (9).

Please include the following information in the upper right-hand corner of all pages of the consent forms.

Approval Date: June 30, 2004
Renewal Date: June 29, 2005
University of Pittsburgh
Institutional Review Board
IRB #0405149

Adverse events which occur during the course of the research study must be reported to the IRB Office. Please call the IRB Adverse Event Coordinator at 412-383-1145 for the current policy and forms.

The protocol and consent forms, along with a brief progress report must be resubmitted at least **one month prior** to the expiration date noted above for annual renewal as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

RH:ky

University of Pittsburgh

Institutional Review Board

3500 Fifth Avenue
Ground Level
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)

MEMORANDUM

TO: Lakshmanan Krishnamurti, MD

FROM: Christopher Ryan, PhD, Vice Chair

DATE: October 27, 2004

SUBJECT: IRB #0405149: A Community Based Model for Improving the Acceptance of Newborn Screening Follow-Up, Family Testing and Genetic Counseling for Sickle Cell Disease and Trait

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The Institutional Review Board reviewed the recent modifications to your protocol and consent form(s) and find them acceptable for expedited review. These changes, noted in your submission of October 6, 2004, are approved.

Please include the following information in the upper right-hand corner of all pages of the consent form:

Approval Date: October 26, 2004
Renewal Date: June 29, 2005
University of Pittsburgh
Institutional Review Board
IRB #0405149

The protocol and consent form(s) together with a brief progress report must be resubmitted at least **one month prior** to the date of renewal listed above for annual review as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh).

If your research proposal involves an investigational drug, please forward a copy of this approval letter along with a copy of the Cover Sheet, protocol, consent form(s) and drug brochure to Investigational Drug Service, PUH Pharmacy.

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

CR:dj

University of Pittsburgh

Institutional Review Board

3500 Fifth Avenue
Ground Level
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)

MEMORANDUM

TO: Lakshmanan Krishnamurti, M.D.

FROM: Christopher Ryan, Ph.D., Vice Chair

DATE: June 29, 2005

SUBJECT: IRB #0405149: A Community Based Model for Improving the Acceptance of Newborn Screening Follow-Up, Family Testing and Genetic Counseling for Sickle Cell Disease and Trait

Your renewal of the above-referenced proposal has received expedited review and approval by the Institutional Review Board under 45 CFR 46.110 (9).

Please include the following information in the upper right-hand corner of all pages of the consent form:

Approval Date: June 29, 2005
Renewal Date: June 28, 2006
University of Pittsburgh
Institutional Review Board
IRB #0405149

Adverse events, which occur during the course of the research study, must be reported to the IRB Office. Please call the IRB Adverse Event Coordinator at 412-383-1504 for the current policy and forms.

The protocol and consent forms, along with a brief progress report must be resubmitted at least **one month prior** to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

CR:ky

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Ground Level
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)

MEMORANDUM

TO: Lakshmanan Krishnamurti, MD

FROM: Christopher Ryan, PhD, Vice Chair

DATE: December 16, 2005

SUBJECT: IRB #0405149: A Community Based Model for Improving the Acceptance of Newborn Screening Follow-Up, Family Testing and Genetic Counseling for Sickle Cell Disease and Trait

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The Institutional Review Board reviewed the recent modifications to your protocol and consent form(s) and find them acceptable for expedited review. These changes, noted in your submission of October 31, 2005, are approved.

Please include the following information in the upper right-hand corner of all pages of the consent form(s), if modifications were made to the consent form(s):

Current Approval Date: June 29, 2005
Modification Approval Date: December 16, 2005
Renewal Date: June 28, 2006
University of Pittsburgh
Institutional Review Board
IRB #0405149

The protocol and consent form(s) together with a brief progress report must be resubmitted at least **one month prior** to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh).

If your research proposal involves an investigational drug, please forward a copy of this approval letter along with a copy of the Cover Sheet, protocol, consent form(s) and drug brochure to Investigational Drug Service, PUH Pharmacy.

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

CR:dj

APPENDIX B

KNOWLEDGE OF SICKLE CELL DISEASE AND ACCEPTANCE OF GENETIC TESTING FOR SICKLE CELL TRAIT SURVEY

SICKLE CELL DISEASE AWARENESS AND BELIEFS REGARDING

CARRIER TESTING

PRE-EDUCATION QUESTIONAIRE: PLEASE CHECK WHETHER YOU AGREE, DISAGREE, OR ARE UNCERTAIN ABOUT THE FOLLOWING STATEMENTS

	AGREE	DISAGREE	UNCERTAIN
Sickle cell disease affects the red blood cells			
Children with sickle cell disease are at risk for infections, Pain, pneumonia and stroke			
African American are at a higher risk of being genetic carriers of sickle cell disease			
Genetic carriers will not develop symptoms of sickle cell disease			
Both parents must be carriers of sickle cell trait in order to have a baby with sickle cell disease			
If only one parent is a carrier of a sickle cell trait, there is no chance of having a baby with sickle cell disease			
I support sickle cell disease carrier testing			
I support sickle cell disease carrier testing for communities			
If both parents are trait carriers , testing in pregnancy should be offered			
I would encourage my partner to be tested for the sickle cell trait if I was found to be a trait carrier			
Having a sickle cell trait would make me less confident about forming relationships			

POST TEST ANALYSIS: PLEASE CHECK WHETHER YOU AGREE, DISAGREE, OR ARE UNCERTAIN ABOUT THE FOLLOWING STATEMENTS

	AGREE	DISAGREE	UNCERTAIN
Sickle cell disease affects the red blood cells			
Children with sickle cell disease are at risk for infections, pain, pneumonia and stroke			
African Americans are at a higher risk for being genetic carriers of sickle cell disease			
Genetic carriers will not develop symptoms of sickle cell disease			
Both parents must be carriers of a sickle cell trait in order to have a baby with sickle cell disease			
If only one parent is a carrier of sickle cell trait, there is no chance of having a baby with sickle cell disease			
I support sickle cell disease carrier testing			
I support sickle cell disease carrier testing for communities			
If both parents are trait carriers, testing in pregnancy should be offered			
I would encourage my partner to be tested for the sickle c ell trait if I was found to be a trait carrier			
Having a sickle cell trait would make me less confident about forming relationships			
I found information on sickle cell disease and sickle cell trait useful			

DEMOGRAPHIC DATA: PLEASE CIRCLE THE ANSWER WHICH BEST APPLIES TO YOU

SEX: FEMALE MALE

AGE (YEARS): 16-20 21-25 26-30 31-35 36-40 41-45 46-50 50+

HIGHEST EDUCATION: LESS THAN HIGH SCHOOL HIGH SCHOOL GRADUATE

SOME COLLEGE COLLEGE GRADUATE GRADUATE/PROFESSIONAL SCHOOL

MARITAL STATUS: MARRIED SINGLE DIVORCED

NUMBER OF CHILDREN: 0 1 2 3 4+

INSURANCE STATUS: INSURED NOT INSURED

APPENDIX C

BRIEF SICKLE CELL DISEASE EDUCATIONAL SESSION OUTLINE

SICKLE CELL DISEASE AND SICKLE CELL TRAIT EDUCATIONAL SESSION OUTLINE

1. Introduction:
    A. Working with Children's Hospital of Pittsburgh and Magee Women's Hospital on developing education on sickle cell disease and sickle cell trait
    B. Ask if patient would mind talking with me for a few minutes
    C. Explain we are talking with women about sickle cell disease and sickle cell trait and hoping to develop more education by finding out what the community already knows and believes about this disease
    D. Ask if they are over age 18
        I. Yes- ask to take the time to fill out anonymous questionnaire before giving education. Reassure it is not a test and that we will go over all of the information together
        II. No- Provide education and handouts.

2. Sickle Cell Disease Education
    A. USE VISUAL AID (FIGURE 19)

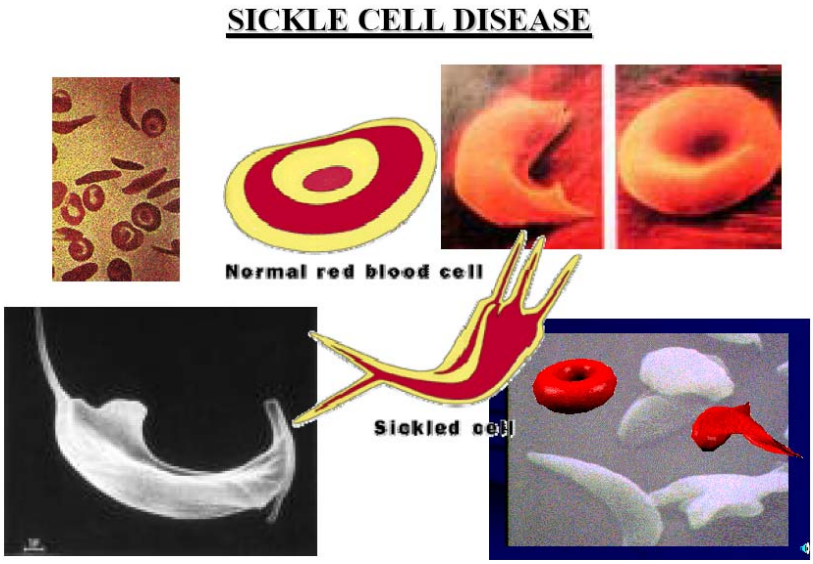


Figure 19: Educational Visual Aid; Sickle Cell Disease

I. Sickle cell disease is a disease that affects the red blood cells
II. Usually our red blood cells are round and soft and squishy and can carry oxygen from our lungs to the parts of our body that need it by squeezing through the small blood vessels in our body.
III. When someone has sickle cell disease their red blood cells can become hard and sickle cell shaped, like a “half-moon” or “banana” shape.
IV. This can cause these red blood cells to get stuck in the blood vessels causing infection, stroke, and severe pain that can result in long hospital visits. Sometimes this can also result in a shorted lifespan.
V. Individuals with sickle cell disease are born with it. It is not contagious and you cannot get sickle cell disease from some one who has it. It is in our genes.
VI. Our genes are the instructions for how our bodies work. We get half of our genes from our mothers and half from our fathers, making for two copies of every gene in our body.
VII. The only way for someone to have sickle cell disease is to have inherited one gene for their red blood cells that is not working from their mother, and one non-working gene from their father. People with sickle cell disease have inherited two genes that are not working properly, causing their red blood cells to change shape.

B. USE VISUAL AID (FIGURE 20)

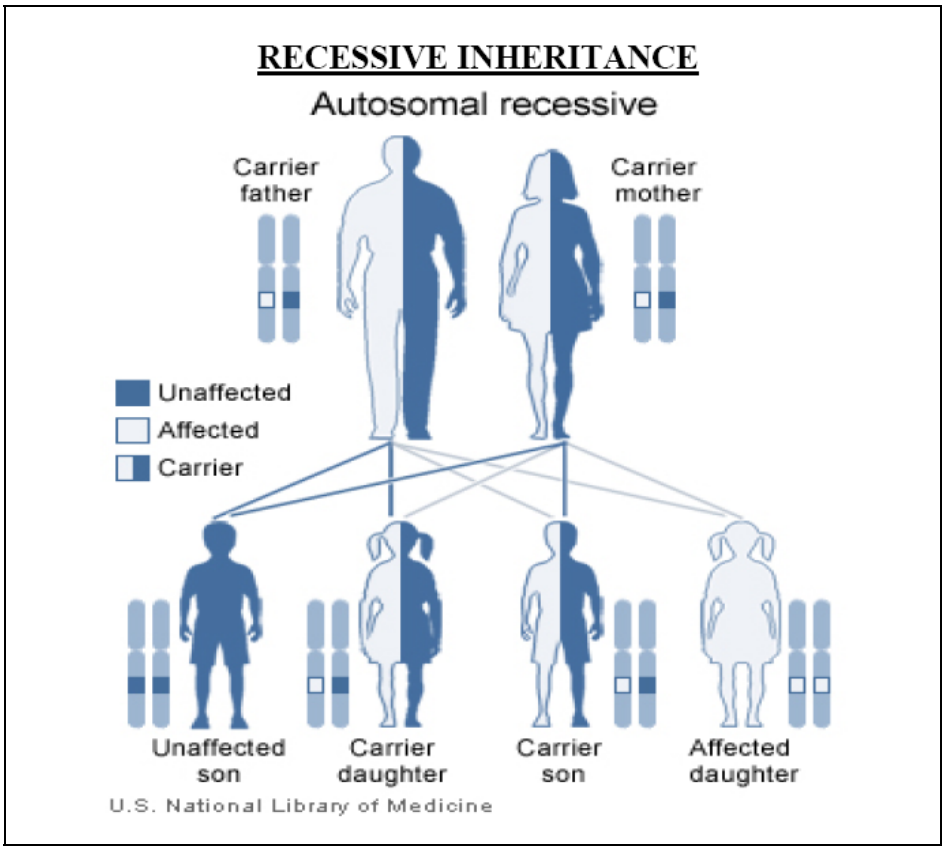


Figure 20: Educational Visual Aid; Inheritance of Sickle Cell Disease

I. People who have one gene for their red blood cell that is not working properly and one that is are called “sickle cell trait carriers”.
II. Sickle cell trait carriers are perfectly healthy; they do not have sickle cell disease and will not ever get sickle cell disease. In fact, without testing they may never even know that they are trait carriers.
III. The reason it is important to be aware of sickle cell trait is because it becomes a concern when it is time to have children. If two people who carry sickle cell trait have children together, their children are at risk to have sickle cell disease.

IV. Couples who are at risk to be carriers should be tested. The only way to know someone is a trait carrier is to have a simple blood test. This information can be used to plan for the possibility of having a sick child and to find out more about testing and other options available in pregnancy.

V. African Americans are at the highest risk to be carriers of sickle cell trait. Because of this, Magee Women's Hospital is now testing all African American women for sickle cell trait at the beginning of their pregnancy.

VI. This is a genetic test that can provide information for other family members and so we are working on providing educational materials for patients concerning this test.

C. QUESTIONS?

D. SEND HOME WITH HANDOUTS REGARDING SICKLE CELL DISEASE AND SICKLE CELL TRAIT TESTING (FIGURES 21-24)

Magee-Womens Hospital
of University of Pittsburgh Medical Center

Planning for Healthy Families:
Early Education on Sickle Cell Disease and Sickle Cell Trait

What is Hemoglobin?

Hemoglobin (Hb) is the special protein within the red blood cells that carries oxygen from the lungs to the rest of the body. Hemoglobin is what makes your blood look red in color.

Your hemoglobin type is passed through family **genes**. The color of your hair, the color of your eyes, how your body works, and your hemoglobin type are all determined by genes. Differences in our genes, called mutations or variants, are what make us unique. We have two genes for our hemoglobin type, one gene for hemoglobin type from our mother and one from our father.

Why should I know what kind of Hemoglobin I have?

Hemoglobin A of adult hemoglobin is the most common hemoglobin gene. There are over 500 different types of hemoglobin. **Sickle cell disease** and other blood disorders are a result of hemoglobin mutations. These variants are more common in people of African American, Mediterranean, Middle Eastern, Indian, Caribbean, South and Central American descent.

IT IS IMPORTANT TO BE AWARE OF HEMOGLOBIN TYPE BECAUSE HAVING A GENE FOR A BLOOD DISORDER SUCH AS SICKLE CELL DISEASE INCREASES THE CHANCE OF HAVING A CHILD WITH THAT DISEASE.

Someone who has one gene for adult hemoglobin and one gene for a variant is said to have sickle cell trait. Carriers lead healthy normal lives. Carriers should be aware of their risk for having children with a blood disorder.

HAVING A TRAIT IS NOT A DISEASE!

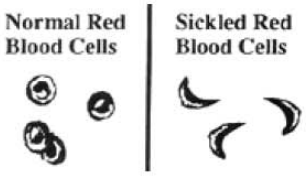
What is a Hemoglobin Electrophoresis?

The best test for sickle cell disease and sickle cell trait is the **hemoglobin electrophoresis**. This test can determine what type of hemoglobin genes you have. This is done by studying a sample of your blood. Our lab will run the test and have results available within two weeks. By looking at your blood we can determine what kind of hemoglobin genes you have.

Figure 21: Educational Handout; Hemoglobin Electrophoresis (page 1)

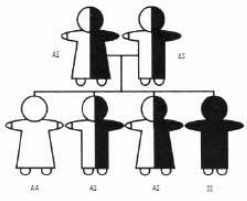
What is Sickle Cell Disease?

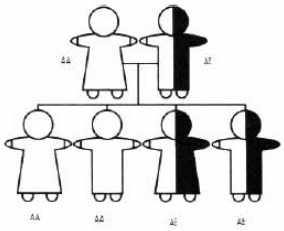
Sickle cell disease is a very serious and painful disease. Children with sickle cell disease can have many infections, pain episodes and suffer from strokes. Sickle cell disease occurs when a person inherits the hemoglobin S gene from each parent (Hb SS). There are other hemoglobin types such as hemoglobin C or hemoglobin E. When these combine with the gene for sickle hemoglobin it can result in different kinds of sickle cell disease (Hb SC, Hb SE, Hb SD, Hb S/beta thalassemia...).



If two people with hemoglobin S trait have a child, there is a 50% (1/2) risk that the child will have hemoglobin S trait. There is a 25% (1/4) chance the child will not have disease or trait. There is a 25% (1/4) chance that the child will have sickle cell disease. These risks are true for **each pregnancy**.

If one parent has sickle cell trait and the other has normal hemoglobin there is no chance of having a child with sickle cell disease. However, there is a 50% chance with **each pregnancy** that the child will have sickle cell trait, as well as a 50% chance child will be unaffected.





What should I do with my results?

We will contact you with your results along with more information about your type of Hemoglobin. This is important information to share with your partner and family. Hemoglobin traits run in families and you may want to suggest testing for family members as well. If you are a carrier for a sickle cell trait it is recommended that your partner be tested.
A genetic counselor can also meet with you. A genetic counselor is a health professional who can discuss the risks to your children and family. They can help you plan ahead for a healthy family and answer any questions you or your partner may have.

Please Call with any Questions or Concerns:

Magee - Women's Hospital
300 Halket St
Pittsburgh, PA 15213
High Risk Pregnancy Clinic
412-641-4459

Children's Hospital of Pittsburgh
Division of Hematology/Onc/BMT
Comprehensive
Hemoglobinopathies Program
412-692-6059

Department of Genetics:
412-641-4168 or
1-800-454-8155

Figure 22: Educational Handout; Hemoglobin Electrophoresis (page 2)

Sickle Cell Trait; It is not a Disease!
It is just as important.

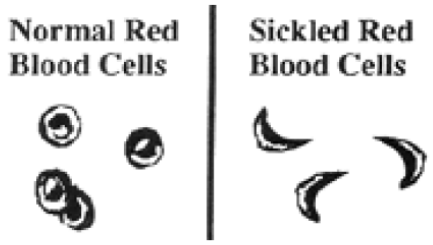
What is a Gene?

Genes are the instructions for how our body should work. We have two copies of every gene in our body. One copy we receive from our mother and one from our father before birth. There is no way to control what genes are passed from parents to children. If a gene has a change in it called a mutation, it can cause that copy of the gene to not work properly.

What is Sickle Cell Disease?

Someone who inherits one non-working red blood cell gene from their mother and one non-working red blood cell gene from their father has Sickle Cell Disease. Sickle Cell Disease is a serious blood disease that affects children from birth. You cannot catch it from someone else who has Sickle Cell Disease.

The non-working gene causes red blood cells to change shape from being round and squishy, to being hard and crescent moon, or sickle shaped.



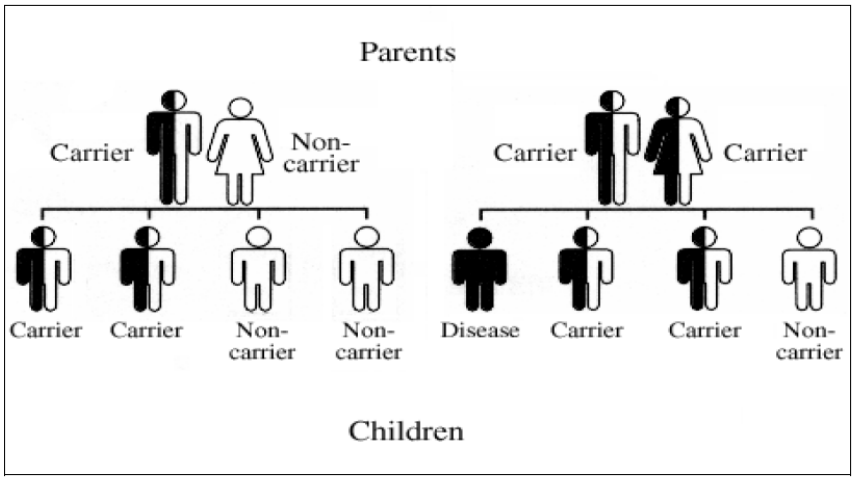
Sickle shaped cells can stick together and cannot carry oxygen very well. This can cause severe pain, infections, many hospital visits and even a shorter life. Sickle Cell Disease is the most common blood disease that is caused by inheriting non-working red blood cell genes; however, there are others. About 50,000 Americans have Sickle Cell Disease. It is important for both parents to be tested in order to know if future pregnancies are at risk.

What is Sickle Cell Trait?

Red blood cells carry oxygen from when we breathe from our lungs to the rest of our body. We have two copies of all of the genes that make up our red blood cells. If someone has one red blood cell gene that is not working correctly, and red blood cell gene that is working correctly they have Sickle Cell Trait, this is also called being a carrier of the sickle cell gene. Sickle Cell Trait is not a disease. If two people who have sickle cell trait have a baby, that child is at risk to receive a non-working red blood cell gene from each parent, which can cause Sickle Cell Disease.

The important reason to be aware of Sickle Cell Trait is to be prepared for the risk of having a child with a serious blood disease. If two people with a Sickle Cell Trait have children, each pregnancy has a 25% or 1 in 4 chance of having a blood disorder. A 50% chance of having a child with trait, and a 25% chance of have a child with two working gene.

Figure 23: Educational Handout; Sickle Cell Trait (page 1)



Who is at risk for Sickle Cell Trait?

Anyone can carry a Sickle Cell Trait; however, some populations are at a higher risk than others are. Sickle Cell Trait is most common in African Americans. One in every 12 African Americans is at risk to have Sickle Cell Trait. People of Mediterranean, Middle Eastern, Indian, Asian and Hispanic descent are also at an increased risk to have Sickle Cell Trait. It is thought that people with Sickle Cell Trait survive a disease called malaria better and so the trait is most common in areas where malaria is common.

How can you tell if someone has Sickle Cell Trait?

People with Sickle Cell Trait are healthy; they do not have a disease. They will not develop Sickle Cell Disease because our genes do not change. You cannot tell of someone has Sickle Cell Trait by looking at them. The only way to tell if someone has Sickle Cell Trait is to be tested. If you would like to be tested, ask your physician or call one of the numbers listed here. Only the most informative test, called a hemoglobin electrophoresis, should be used.

What can I do if I have Sickle Cell Trait?

If you find out that you have Sickle Cell Trait, your partner should be tested. Knowing ahead of time that your future children may be at risk gives you time to prepare and learn more about caring for a child with a serious illness. Genetic Counselors are available to help explain the risks and discuss prenatal testing, and other options. This most important thing you can do is be responsible for the best health care of your child.

Where should I go with more questions?

Doctors, nurses and genetic counselors at Children's Hospital of Pittsburgh are available to answer your questions.

For More information and Testing

- Children's Hospital of Pittsburgh
  Division of Hematology
  412-692-6059
- Magee-Women's Hospital Medical Genetics
  412-641-4168 or
  1-800-454-8155
- Children's Sickle Cell Foundation Inc.
  412-537-8973
  PO Box 5974
  Pittsburgh, PA 15210
- Sickle Cell Society Inc
  (412) 371-0628
  7643 Frankstown Ave
  Pittsburgh, PA 15208

Figure 24: Educational Handout; Sickle Cell Trait (page 2)

APPENDIX D

KNOWLEDGE OF SICKLE CELL DISEASE AND HEALTH BELIEFS REGARDING SICKLE CELL DISEASE AND SICKLE CELL TRAIT SURVEY

Questionnaire for assessment of knowledge and health beliefs of sickle cell disease:

Knowledge Questions: Following are some questions about sickle cell disease. Please read each question very carefully and then circle one answer that is the best. Remember, only one answer for each question.

1) Sickle Cell Disease is caused by
- a. dirty needles
- b. a virus
- c. inheriting genes from parents
- d. bad blood
- e. none of the above

2) How many genes must someone inherit to have Sickle Cell Disease?
- a. zero, it is not caused by genes
- b. one from their mom
- c. two, one from their mom, and one from their dad
- d. three, one from mom, and two from dad
- e. none of the above

3) Sickle Cell Disease can cause
- a. severe debilitating pain
- b. strokes
- c. infections
- d. organ damage
- e. all of the above

4) Sickle Cell Disease occurs most often in
- a. boys
- b. girls
- c. white people
- d. black people
- e. all of the above

5) Sickle Cell Pain can feel worse than
- a. a broken bone
- b. a headache
- c. a gunshot wound
- d. all of the above
- e. none of the above

6) Sickle Cell Disease makes red blood cells
- a. round and soft
- b. hard and sickle shaped
- c. sticky and blue
- d. stiff and round
- e. soft and sickle shaped

7) Sickle Cell Disease is <u>easily</u> cured by
- a. antibiotics
- b. liver transplant
- c. rest
- d. blood transfusions
- e. none of the above

8) How can you tell if someone carries the gene for sickle cell disease?
- a. They look sick
- b. They will eventually have Sickle Cell Disease
- c. With a simple blood test
- d. There is no way of knowing
- e. None of the above

Health Belief Questions:

Please rate your level of agreement with each of the following statements on a 5-point scale where 1 means "**strongly disagree**" and 5 means "**strongly agree**."

Severity

1. Sickle Cell Disease is a serious disease

Strongly Disagree 1 2 3 4 5 Strongly Agree

2. Having a child with sickle cell disease would be very scary

Strongly Disagree 1 2 3 4 5 Strongly Agree

3. My life would change if my child had sickle cell disease

Strongly Disagree 1 2 3 4 5 Strongly Agree

Susceptibility

4. My children are at risk for sickle cell disease

Strongly Disagree 1 2 3 4 5 Strongly Agree

5. Sickle Cell Disease could happen in my family

Strongly Disagree 1 2 3 4 5 Strongly Agree

6. My partner may be a carrier of sickle cell trait

Strongly Disagree 1 2 3 4 5 Strongly Agree

Benefit

7. It is useful to know if I have sickle cell trait

Strongly Disagree 1 2 3 4 5 Strongly Agree

8. It is useful to know if my partner has sickle cell trait

Strongly Disagree 1 2 3 4 5 Strongly Agree

9. Knowing the risk of having a child with sickle cell disease would change how I plan a pregnancy

Strongly Disagree 1 2 3 4 5 Strongly Agree

Barriers

10. Testing for sickle cell trait is painful and difficult

Strongly Disagree 1 2 3 4 5 Strongly Agree

11. My partner would be hard to convince to have testing

Strongly Disagree 1 2 3 4 5 Strongly Agree

12. I would not want to pay for sickle cell trait testing if it is not paid for by insurance

Strongly Disagree 1 2 3 4 5 Strongly Agree

Demographic Questionnaire:

The following questions tell us more about you. Please circle or fill in the answer that best describes you.

1. I am _____ years old

   18-19 20-24 25-29 30-34 35-39 40-44 45+

2. I am _____

   Single Married Divorced

3. I have ____ Children

   0 1 2 3 4 5+

4. I _____ live with my partner

   Do Do Not No Partner

5. The highest level of school I have finished is _____

   Some High School High School Graduate Some College

   College Graduate Graduate/Professional School

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