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ORIGINAL RESEARCH

Who Counsels Parents of Newborns Who Are Carriers of Sickle Cell Anemia or Cystic Fibrosis?

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Abstract Our objective was to describe: 1) physicians' knowledge of whether genetic counseling is provided to parents of newborns with sickle cell trait (SCT) or who are cystic fibrosis carriers (CFC), and 2) the prevalence of genetic counseling provided by primary care physicians. We conducted a cross-sectional descriptive survey of 600 randomly-sampled Michigan-based pediatricians and family physicians, assessing physician knowledge of where and whether genetic counseling is received by parents whose newborns are carriers. Chi-squared testing determined associations between genetic counseling location and physician demographic characteristics. Our response rate was 62 %: 298 (84 %) provided infant well care (183 pediatricians, 115 family physicians). Most respondents were non-Hispanic White (65 %). Virtually all physicians believed parents whose newborns are carriers of either SCT or CFC should receive some genetic counseling (from the physician and/or another source), yet 20 % reported that parents of newborns with SCT did not receive counseling. Parents of infants with CFC received more counseling overall (92 % vs. 80 %; $p<0.01$) and were counseled more frequently by genetic counselors or specialty centers than parents of newborns with SCT (85 % vs. 60 %; $p<0.01$). Although physicians agreed that parents whose newborns are carriers should receive genetic counseling, fewer parents of newborns with SCT than with CFC received counseling from any source. This finding strongly suggests the need for further education and investigation of this apparent health disparity.

Keywords Newborn screening · Genetic counseling · Sickle cell trait · Cystic fibrosis

Abbreviations

SCD	Sickle cell disease
CF	Cystic fibrosis
SCT	Sickle cell trait
CFC	Cystic fibrosis carrier
NCAA	National Collegiate Athletic Association
PCP	Primary care physician

Introduction

Sickle cell anemia/disease (SCD) and cystic fibrosis (CF) are the most common life-shortening, childhood-onset inherited disorders in the United States (Centers for Disease Control and Prevention 2004). All 50 states screen newborns for both conditions, although cystic fibrosis

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screening is a new addition for most (National Newborn Screening and Genetics Resource Center 2010). The state of Michigan initiated newborn screening for CF in 2007, while newborn screening for SCD began 20 years earlier in 1987 (Kleyn et al. 2011; Kleyn et al. 2009a). Unlike most other newborn screening tests, tests for sickle cell anemia and cystic fibrosis also detect infants who are carriers of sickle cell disease (sickle cell trait, SCT) or cystic fibrosis (cystic fibrosis carriers, CFC).

For the parents whose newborns are carriers of either SCT or CF, genetic counseling is helpful to assess the parents' risk of having affected children or children who are carriers in future pregnancies. The risk of having an affected child can be as high as 25 % if both parents are carriers. For the newborn, the health implications of being a carrier of one of these diseases are very different. CF carriers have no increased personal health risk, while health risks do exist for persons with SCT. Individuals with SCT risk developing hematuria and a decreased ability to concentrate urine beginning in adolescence and worsening with age (Le Gallais et al. 1996; Mitchell 2007). Research also supports an increased risk of sudden death or serious illness under conditions of severe hypoxia, extreme physical exertion or significant dehydration (American College of Medical Genetics 2006; Kark et al. 1987; Le Gallais et al. 1996; Mitchell 2007).

The results received by the primary care physician are also different for the two newborn screening tests. In nearly all cases, SCT is identified on the initial newborn screen without the need for further testing. In contrast, the positive result on the initial newborn screening test for CF does not differentiate between those with the disease and carriers. Further testing (usually a sweat test) is required to separate CF carriers from children who actually have the disease. However, the sweat test can be ordered and interpreted by a primary care physician without referral to a specialist.

Purpose of the Present Study

Guidelines from the American Academy of Pediatrics and the American College of Medical Genetics recommend that parents whose newborns are carriers of SCT receive genetic counseling. Consultation with a CF specialist is recommended for all those whose newborn screens are positive for CF (American College of Medical Genetics 2006; American College of Medical Genetics 2010; National Heart Lung and Blood Institute; National Institutes of Health 2002). Since genetic counseling requires more time than is generally available during a routine newborn visit in the primary care physician's office, we were interested in whether physicians provided counseling in their office and/or knew that parents had received counseling elsewhere. We were also interested in determining whether there were any differences between the two carrier states in physician provision and/or knowledge of parental counseling. Our prior work demonstrated that, despite the recommendations, primary care physicians who provide well care for newborns are significantly less likely to endorse a need for genetic counseling for parents of infants with SCT than for parents of infants with CFC (Kemper et al. 2006).

Methods

Sampling Frame

For this cross-sectional descriptive study, we requested the names and office addresses of all the self-identified pediatricians and family physicians in the state of Michigan from the American Medical Association's (AMA) Physician Masterfile. According to the AMA (2012), "the Physician Masterfile includes current and historical data for more than one million residents and physicians and approximately 82,000 students in the United States," regardless of AMA membership. We requested that the list include only allopathic and osteopathic physicians, practicing office-based, direct patient care, and whose board certification and self-reported primary specialty were either pediatrics or family medicine and exclude those who reported a secondary specialty or sub-board, resident physicians, physicians practicing at a military, prison, or federal facility, and physicians 70 years of age or older. We used a random number table to select a sample of 300 pediatricians and 300 family physicians from this list. While the incidence of cystic fibrosis is evenly distributed throughout the state, the incidence of sickle cell anemia is correlated with the proportion of African Americans living in a given area. To ensure an adequate representation of physicians who had patients with SCD, SCT, CF, and CFC in their practices, we allocated half of our surveys to the six counties with the highest populations of African Americans.

Development of Survey Instrument and Survey Contents

We modified questions from our prior study about sickle cell anemia and cystic fibrosis,(Kemper et al. 2006) adding questions about the provision and location of genetic counseling for parents of newborns with SCT and CFC. The two-page survey was tested for acceptance and feasibility in a population of office-based pediatricians and family physicians who delivered primary care to infants.

The fielded survey consisted of 28 questions covering the following areas:

- Physician experience in providing well care for children with SCT, CFC, SCD, or CF.
- Physician beliefs concerning whether and when parents of newborns with SCT or CFC should be informed of their child's carrier status ("never," "in the newborn period," or "sometime after the newborn period").
- Physician knowledge of whether parents of newborns in their practice with SCT or CFC received genetic counseling ["Do the parents of sickle cell carrier (cystic fibrosis carrier) newborns in your practice usually receive genetic counseling?"].
- If the respondent physician answered yes to the previous question, they were asked to list all locations where parents received counseling (in the primary care physician's office, medical geneticist/genetic counselor office, specialty center, or other locations).
- Physicians who responded that parents of newborn carriers in their practice did not receive counseling were asked their reason(s) why counseling was not given. Response options were the following: "No genetic counselors available," "I do not recommend it, "Parents do not want it," or "Other."
- Demographic questions included physician age, race, years in practice, practice location (urban, suburban, rural), and approximate racial/ethnic composition of patient population.

Survey Administration

The initial mailing in November of 2008 contained the survey, a cover letter describing the study that served as the consent document, a small monetary incentive, and a stamped, self-addressed business reply envelope for return of the survey. Surveys were identified by number only. Respondents were asked not to put their names on the surveys to assure anonymity. Non-respondents received two additional mailings at three-week intervals containing a cover letter, the survey and a reply envelope. The completed and returned survey was viewed as the physician's consent to participate in the study. The University of Michigan Medical School Institutional Review Board approved the study.

Data Analyses

Surveys from physicians who did not provide care to children less than 1 year of age were excluded. Descriptive statistics were calculated for all survey items. Outcome variables were physician report as to whether parents received genetic counseling (yes/no); location(s) of all sources of counseling or reasons parents do not receive counseling. Predictor variables were respondent demographic and practice characteristics. Using chi-square testing, we determined bivariate associations between outcome and predictor variables. We also used chi-square testing to determine whether there were significant differences in outcome variables between the two carrier states.

Respondents used U.S. Census categories to identify their race(s). We categorized race as White (only White selected), African American (only African American selected), Other (single racial category that was neither White nor African American), and Multi-racial (more than one racial category). Due to small numbers, we did not analyze Hispanics separately. We considered a p-value of<0.05 as statistically significant. All analyses were conducted in SAS (version 9.1).

Results

Of the 600 surveys mailed, 28 were undeliverable. We received 356 completed surveys (response rate 62 %). The response rate differed by specialty: 70 % of pediatricians and 56 % of family physicians returned a completed survey. We then excluded the surveys of those who did not provide care to infants younger than one-year of age. We were left with 298 surveys (84 % of responders): 183 pediatricians and 115 family physicians. We report the results of those 298 surveys herein.

Respondents had been in practice an average of 15 years, with less than 20 % of the responding physicians practicing more than 25 years. Average physician age was 46.5. Most were White and only 8 % had a patient panel that was mostly African American (Table 1). Pediatricians reported significantly greater experience than family physicians in providing well care for both children with SCD and CF and carriers of either disease. Regardless of specialty, physicians reported greater experience with well care for children with SCD than for children with CF (Table 1). We asked respondents to answer about the genetic counseling received by parents of newborn carriers in their practice, rather than just their own panel of patients, so we included the responses of physicians who reported no personal experience providing well care for affected children or children who are carriers.

More than 95 % of physicians stated that parents whose newborns are carriers of either condition should be informed of their child's status in the newborn period and receive genetic counseling at that time. However, carrier state-specific differences were noted in whether counseling actually occurred and where counseling was provided.

Receipt and Location of Genetic Counseling (Table 2)

Most physicians reported that parents whose newborns are carriers of either SCT or CFC received genetic counseling. However, the proportion differed significantly by carrier state: 92 % of physicians provided and/or had knowledge

Table 1 Demographic characteristics (n=298)

	All respondents % (*n*)	Pediatricians (*n*=183) % (*n*)	Family physicians (*n*=115) % (*n*)
Mean years in practice (range)	15 years (1–42)	15.4 years (1–40)	14.7 years (1–42)
Mean MD age (range)	46.5 years (29–69)	46.7 years (29–69)	46.2 years (30–68)
MD race			
White only	65 (188)	73 (84)	57 (104)
Black only	6 (16)	5 (6)	5 (10)
Other	29 (84)	27 (49)	13 (15)
Multiracial	7 (20)	7 (13)	6 (7)
Practice location			
Urban	20 (59)	22 (39)	18 (20)
Suburban	59 (170)	64 (113)	50 (57)
Rural	21 (62)	14 (25)	32 (37)
Practice demographics			
> 50 % White	75 (223)	72 (132)	79 (91)
> 50 % AA[a]	8 (23)	7 (8)	8 (15)
SCD[b] well care experience			
None	30 (89)	18 (32)*	50 (57)*
Extensive (≥ 4 children)	13 (37)	19 (35)*	1 (2)*
CF[c] well care experience			
None	39 (115)	24 (43)*	63 (72)*
Extensive (≥ 4 children)	13 (38)	19 (35)*	2 (3)*

[a] *AA* African American

[b] *SCD* Sickle cell disease

[c] *CF* Cystic Fibrosis

*$p<0.001$ between pediatricians and family physicians

of the receipt of genetic counseling for parents in their practice whose newborns were CFC carriers, while 80 % of physicians provided and/or had knowledge of the receipt of genetic counseling for parents in their practice whose newborns were SCT carriers.

Differences were also seen in counseling location. A greater proportion of responding physicians provided counseling in their offices (office-based counseling) to parents whose infants were SCT carriers compared to parents whose infants were CFC carriers (41 % vs. 20 %; $p<0.01$). Primary care physician (PCP) office counseling only, without additional counseling elsewhere, was reported by 20 % of responding physicians for parents whose newborns were SCT carriers. Only 7 % of physicians reported providing office-based counseling only for parents whose newborns were CFC carriers ($p<0.01$). Physician demographic characteristics (physician specialty, age, race, and years in practice) were not associated with office-based counseling for either carrier state.

Lack of Counseling (Table 2)

A minority of physicians reported that parents whose newborns were carriers in their practice were not counseled at all—not in their office or in any other location. A difference between SCT and CFC was again apparent. While

Table 2 Location of counseling by carrier type

	None % (n)	PCP office counseling only % (n)	Genetic counselor office % (n)	Specialty center referral % (n)	PCP office counseling +/− other sites[a] % (n)
SCT* (*n*=246)	20 (48)	20 (50)	52 (103)	32 (63)	35 (81)
CFC* (*n*=206)	8 (16)	7 (14)	66 (122)	49 (91)	18 (37)

[a] Any parental counseling received in the primary care physician office whether or not additional counseling was provided by a genetic counselor and/or specialty center

*$p<0.01$ between SCT and CFC for all 5 columns

Percent adds to>100 % because participants could select more than one option

20 % of physicians stated that parents whose newborns were SCT carriers did not receive counseling, only 8 % of physicians reported that parents whose newborns were CFC carriers were not counseled. Physicians' top reasons for lack of counseling were: a dearth of available genetic counselors, parental preferences not to be counseled, and that they (the physician) do not recommend counseling, in that order (Tables 3). Physicians' ranking of reasons for lack of parental counseling were similar in response to both SCT and CFC genetic counseling. However, the proportions of physicians endorsing each reason were greater for SCT than for CFC. We were unable to analyze these data further due to small numbers.

Practice Location and Experience

PCP office counseling was reported by a greater proportion of physicians in suburban or urban practices than by rural physicians for parents whose newborns were carriers of either CFC or SCT. In all practice locations, PCP office counseling was more commonly reported for parents whose newborns were carriers of SCT than for parents whose newborns were carriers of CF (Table 4).

Physicians experienced in providing well care to children with SCD (caring for four or more children) were significantly more likely to counsel parents whose newborns were SCT carriers in their office than physicians lacking any SCD well care experience, whether or not additional counseling was provided elsewhere (63 % vs. 32 %; $p=0.02$). The association of greater CF well care experience with increased PCP office counseling of parents whose newborns were CFC carriers was not significant, likely due to the small numbers of physicians who provide any in-office counseling to parents whose newborns were CFC carriers.

Non-response

Approximately 18 % of physicians did not respond to questions concerning counseling of parents whose newborns were SCT carriers in their practice, and 31 % did not answer the counseling questions regarding parents whose newborns were CFC carriers. Non-response was not associated with physician age, years in practice, or practice location. However, nearly all (>94 %) of these non-responding physicians also reported that they had not received a positive newborn screening test for either SCT (for SCT non-responders) or CFC (for CFC non-responders) in their practice in the 12 months preceding the survey.

Discussion

In contrast to our prior study, nearly every responding physician (>95 %) believed that parents whose newborns are carriers of either condition should be informed of their child's status in the newborn period and receive genetic counseling at that time. While the good news is that 80 % or more of physicians report that in their practices, parents whose newborns are carriers are receiving some form of genetic counseling, the bad news is that 20 % of physicians report that parents whose newborns are SCT carriers receive no counseling whatsoever. We also found carrier-related differences in the locations where counseling is provided. Primary care physicians were more likely to counsel parents whose newborns are SCT carriers in their office than parents whose newborns are CFC carriers.

Our findings raise some questions and concerns. Newborns with SCT are at risk for rare, but serious health problems that can begin in late childhood and early adolescence. SCT is associated with painless hematuria, renal papillary necrosis, and a rare form of renal medullary cancer. Hyposthenuria, the inability to produce a concentrated urine, increases with age, and adds to the risk for exertional heat illness, rhabdomyolisis, and sudden death with prolonged exposure to significant heat and dehydration (Tsaras et al. 2009). Between 2000–2009, seven student-athletes with SCT died suddenly. These deaths led the National Collegiate Athletic Association (NCAA) and the National Athletic Trainers Association (NATA) to issue guidelines in 2010 for college sports programs that recommend sickle cell testing for all athletes and modifications to conditioning programs for athletes with SCT (National Collegiate Athletic Association 2010). Even though most children with SCT remain healthy, all are at risk for these complications under specific conditions. Parents should be aware of the potential risks and the situations under which they may occur.

It is not known what information is given to parents when pediatricians and family physicians provide genetic

Table 3 Physicians' reasons for not providing counseling or referrals to parents of newborn carriers

Reason	SCT ($n=48$) % (n)	CFC ($n=16$) % (n)
No counselor available	42 (20)	81 (13)
Parents do not want counseling	31 (15)	13 (2)
Physician does not recommend counseling	21 (10)	13 (2)
Other/no reason	15 (7)	13 (2)

Percent adds to >100 % because participants could select more than one option.

Table 4 Physician practice location and provision of counseling by PCP

	Any PCP office counseling SCT (n=81) % (n)	Any PCP office counseling**CFC (n=37) % (n)
Urban	30* (23)	35** (13)
Suburban	58* (45)	62** (23)
Rural	12* (9)	3** (1)

Counseling given by primary care physician with or without referral to genetic counselor or specialty center

*p=0.02 between practice location and SCT status

**p<0.01 between practice location and CFC

counseling. Primary care physicians may provide parents with written information from reputable sources such as the National Institutes of Health and the Sickle Cell Disease Association of America to parents of newborns with SCT. However, these pamphlets and brochures are intended to supplement, not substitute for genetic counseling. Additionally, most primary care physicians lack formal training in genetic counseling, although they may be aware of the inheritance patterns and some of the health risks to the child.

Genetic counseling provided by a genetic counselor includes, but is not limited to, explanations of inheritance patterns as well as health implications of the carrier state (if any). The risks to carrier individuals are described in detail along with behaviors and/or interventions that can minimize risk. The counselor/geneticist will calculate the parents' risk for having a future affected child or carrier and facilitate any desired testing for parents and family members. While pediatricians and family physicians may convey some of this information to parents, it is highly unlikely that all of this information will be discussed. How much information is needed in the newborn period, and whether PCP counseling is adequate to meet parental needs has not previously been examined and was not the focus of this study.

The differences we found in reported counseling prevalence for CFC and SCT are likely due, at least in part, to the a statewide newborn screening requirement for CF in Michigan, initiated a year prior to our study. Similar to most states, Michigan uses immunoreative trypsinogen (IRT) testing as the initial newborn screen for CF. An algorithm for follow-up is included in a letter to the physician of any infant with a positive test result. Confirmatory DNA and sweat testing are needed to differentiate children with CF from normal children with false positive results and carriers. The algorithm recommends referral to an approved CF specialty center for the necessary testing and genetic counseling, but the referral is not mandatory. The contact information for the center closest to the physician and family is included. Nevertheless, physicians are free to order the sweat test independently without referral to the CF center.

All newborns born in Michigan have been screened for sickle cell anemia since 1987 (Kleyn et al. 2009b). Newborn carriers of SCT are identified on the initial screening—further confirmatory testing is usually unnecessary. The SCT carrier outreach program receives the names and contact information of newborns identified as carriers of SCT. Parents receive a letter from the this program informing them of their infant's carrier status and offering them further information and counseling, either in person or by phone from the outreach program. The contact information of the closest sickle cell center is also included. The infant's physician of record (if known) also receives a letter confirming the newborn's carrier status and informing the physician of the services available from the outreach program for the infant's parents.

The SCT and CFC follow-up programs are fairly similar with regard to the initial physician contact. In both cases, the infant's physician is notified about the carrier status (or likely carrier status) of the infant and is informed of resources available for further counseling of the parents. Despite the similarity in initial physician contact and information, parents whose newborns were SCT carriers were much less likely to receive any counseling; 20 % of physicians stated that in their practice, parents whose newborns were SCT carriers were not counseled at all. We speculate that the inclusion of a follow-up algorithm for CF may have been a significant contributor to the higher prevalence of genetic counseling for parents of newborn CFC carriers, as 85 % of physicians responded that parents whose newborns were CFC carriers received some counseling from a genetic counselor/medical geneticist or specialty center, while only 60 % of physicians reported that parents whose newborns were SCT carriers received counseling from a genetic counselor/medical geneticist or specialty center.

In this study, participants were asked whether or not parents in their practice whose newborns had positive screens for CFC or SCT received genetic counseling. Those respondents who stated that the parents did receive genetic counseling were asked to list all the places where parental counseling occurred, so it is likely that a portion of parents of newborns with SCT received counseling from the outreach program without the physician's knowledge. Our results suggest that the state's sickle cell carrier outreach

program may not be publicized as well to physicians, may be understaffed, or some combination of the two.

Physicians need to be aware if and when parents whose newborns are SCT carriers have received counseling. If the foundational information has been given, intermittent discussion and counseling as the child grows to adulthood may be an effective way to communicate additional information since the potential risks of SCT increase with age. Pediatricians and family physicians should also be prepared to properly counsel the parents about the risks of future pregnancies. Knowing what prior counseling the parents have received is part of that preparation.

Study Limitations

Because our data came from physicians' self-reported behavior, we do not know what physicians actually do with regard to genetic counseling of parents, nor do we know the content of any office-based counseling they say they provide. Physicians may also have over-reported counseling given to parents of newborns with CFC due to social desirability bias with this new program. Although non-response was not significantly associated with any other measured variable except experience with a positive newborn screen, it may have biased our findings in other unknown ways. Additionally, while the methods used for screening and follow-up of newborns with sickle cell and cystic fibrosis or who are carriers of either condition, are similar to those used in many other states, our sample was drawn from a single state, which may limit the generalizability of the findings.

We did not ask physicians about their knowledge of health risks to persons who are cystic fibrosis or sickle cell carriers. As such, we cannot know the extent to which the disparity we found was due to differences in physicians' perceptions of the risks of the two carrier states.

Conclusions and Research Recommendations

Providing timely and accurate genetic counseling for parents of newborns who are carriers of SCT or CFC is an important health service, and one particularly important for parents of newborns with SCT. The presence of sickle cell trait confers potential personal health risks that can manifest in childhood, not present for persons who are carriers of a cystic fibrosis mutation. Although the pediatricians and family physicians in our sample overwhelmingly agreed that parents whose newborns were carriers of either SCT or CFC should receive genetic counseling, their subsequent responses did not support that assertion. When compared to parents whose newborns were carriers of CFC, parents whose newborns were carriers of SCT were less likely to receive counseling from these physicians or were more likely to only receive office-based counseling.

The data we collected does not allow us to determine the reason for this apparent health disparity; however the differences in the information received by the physician between the two screening programs may be at least partially responsible, along with the fact that one requires a confirmatory test and the other does not. In addition, many physicians seemed unaware of the state-supported outreach program for parents of newborns with SCT. Furthermore, an examination of primary care physicians' knowledge of the health risks to the child with SCT should also be conducted, as our results may in part be due to misperceptions about the health significance of having SCT.

While there is consensus that parents whose newborns are carriers of SCT need genetic counseling, we do not know whether in-office counseling by the pediatrician or family physician is adequate to meet parental needs in the newborn period. Research is needed to examine the content and quality of the genetic counseling provided by primary care physicians to parents whose newborns are SCT carriers to fill this knowledge gap. Considering that approximately 8 % of African American infants will be carriers of SCT, there should be ample opportunity to develop and test various methods of providing the necessary information to determine which counseling method is most effective and how much information should be provided in the newborn period, rather than when the child is older. All of this is complicated by the fact that it is likely the physician who sees the newborn child will not be the same one who will see the same child as an adolescent. Given the number of conditions for which newborns are now screened, new and alternative methods of providing genetic information to parents will soon be needed. The lessons learned in creating and testing new models of counseling parents whose infants are carriers of SCT can also serve as a prototype for providing genetic counseling to parents of newborns with other conditions.

References

American College of Medical Genetics (2006). Newborn Screening ACT Sheet: Sickle Cell Carrier (Trait) (Hb AS).

American College of Medical Genetics. (2010). Newborn screening ACT sheet: [Elevated IRT +/− DNA] Cystic Fibrosis.

American Medical Association. (2012). Physician data resources: Physician masterfile. http://www.ama-assn.org/ama/pub/about-ama/physician-data-resources/physician-masterfile.page. Accessed March 13 2012.

Centers for Disease Control and Prevention. (2004). Newborn screening for cystic fibrosis:evaluation of benefits and risks and recommendations for state newborn screening programs. *MMWR, 53*(RR-13), 1–44.

Kark, J. A., Posey, D. M., Schumacher, H. R., & Ruehle, C. J. (1987). Sickle-cell trait as a risk factor for sudden death in physical

training. *N Engl J Med, 317*(13), 781–787. doi:10.1056/NEJM198709243171301.

Kemper, A. R., Uren, R. L., Moseley, K. L., & Clark, S. J. (2006). Primary care physicians' attitudes regarding follow-up care for children with positive newborn screening results. *Pediatrics, 118*(5), 1836–1841.

Kleyn, M., VanOchten, K., Grigorescu, V., & Young, W. (2009). Sickle cell disease in Michigan. Michigan Newborn Screening Follow-Up Brief. In Newborn Screening Follow-up Program (Ed.), (Vol. 1, pp. 2). Lansing, MI: Michigan Department of Community Health.

Kleyn, M., VanOchten, K., Grigorescu, V., & Young, W. (2009). Sickle cell disease in Michigan in newborn screening follow-up program (Ed.), (Vol. 1). Lansing, MI: Michigan Department of Community Health.

Kleyn, M., Korzeniewski, S., Grigorescu, V., Young, W., Homnick, D., Goldstein-Filbrun, A., et al. (2011). Predictors of insufficient sweat production during confirmatory testing for cystic fibrosis. *Pediatr Pulmonol, 46*(1), 23–30. doi:10.1002/ppul.21318.

Le Gallais, D., Bile, A., Mercier, J., Paschel, M., Tonellot, J. L., & Dauverchain, J. (1996). Exercise-induced death in sickle cell trait: role of aging, training, and deconditioning. *Med Sci Sports Exerc, 28*(5), 541–544.

Mitchell, B. L. (2007). Sickle cell trait and sudden death–bringing it home. *J Natl Med Assoc, 99*(3), 300–305.

National Collegiate Athletic Association. (2010). NCAA football rules committee 2009–2010 Point of Emphasis. http://www.ncaa.org/wps/portal/ncaahome?WCM_GLOBAL_CONTEXT=/ncaa/ncaa/academics+and+athletes/personal+welfare/health+and+safety/football+point+of+emphasis+sickle+cell+trait. Accessed July 28 2010.

National Institutes of Health; National Heart Lung and Blood Institute. (2002). *The Management of Sickle Cell Disease* (4ed.).

National Newborn Screening and Genetics Resource Center. (2010). National newborn screening status report. http://genes-r-us.uthscsa.edu/nbsdisorders.htm. Accessed May 27 2010.

Tsaras, G., Owusu-Ansah, A., Boateng, F. O., & Amoateng-Adjepong, Y. (2009). Complications associated with sickle cell trait: a brief narrative review. *The American Journal of Medicine, 122*(6), 507–512. doi:10.1016/j.amjmed.2008.12.020.