SICKLE CELL DISORDERS IN MICHIGAN

HISTORY OF SICKLE CELL DISORDERS

Sickle cell disorders (SCD) were first described in the United States in 1910 by James Herrick, a Chicago physician who reported that his patient from Grenada had red blood cells with unusual shape.[1] This report was followed by others which demonstrated that the unusual sickle shape of the red blood cells was related to low oxygen (1927) and that low oxygen conditions change the hemoglobin molecular structure (1940). In 1948, Linus Pauling and his colleagues used protein electrophoresis to show that hemoglobin in patients with SCD differs from that of disease-free individuals, revealing that SCD is caused by a protein abnormality. Hemoglobin from sickle cell patients was sequenced in 1956 and the specific mutation causing abnormal hemoglobin in SCD was discovered.

Treatment of SCD has improved over time, doubling life expectancy since 1970.[2] Pain crises are treated with painkillers and fluids.[3] Blood transfusions can also be used in treatment as they increase the capacity of normal red blood cells. Hydroxyurea has been shown to reduce the frequency of pain crises and other complications of SCD in adults.[4]

Newborn screening (NBS) technology for SCD was made available in the 1970s. However, early diagnosis did not confer health benefits and few states offered universal screening. In 1975, New York became the first state to require NBS for SCD. A 1986 study demonstrated that penicillin prophylaxis markedly reduced the incidence of pneumococcal sepsis among children with sickle cell anemia.[5] This study provided powerful incentive for the widespread implementation of NBS for SCD. When linked to timely diagnostic testing, parental education, family counseling, and comprehensive care, NBS notably reduces morbidity and mortality associated with sickle cell disease in infancy and early childhood.[6] In 1987, the State of Michigan passed Public Act 14, which established statewide screening of all newborns for sickle cell disease and mandated a fee to fund laboratory testing and comprehensive programs for follow-up, medical management, and quality assurance.

NEWBORN SCREENING FOR SICKLE CELL DISORDERS IN MICHIGAN

Bloodspots are collected for all newborns in Michigan between 24-36 hours of life. These bloodspots are sent to the State NBS Laboratory, where high performance liquid chromatography (HPLC) is used to screen for SCD. All specimens with abnormal hemoglobin HPLC results undergo secondary testing using isoelectric focusing. Children with abnormal screening results are referred to the Sickle Cell Disease Association of America-Michigan Chapter (SCDAA-MI) for further testing. The SCDAA-MI sends information about confirmatory results and treatment initiation to the NBS Follow-up Program.

Since screening for SCD began in 1987, 1,565 confirmed cases have been identified in Michigan, resulting in a cumulative detection rate of 1:2,048 newborns screened. In 2010, 61 cases were identified, resulting in a detection rate of 1:1,847 newborns screened (Table 1). Of patients with sickling disorders in the 2010 birth cohort, 54% had sickle cell anemia, 38% had SC disease, and the remaining 8% had sickle β thalassemia. Black infants accounted for 97% of the cases in 2010. Thus, the detection rate in black infants was 1:344 newborns screened, over 5 times the overall detection rate.

A total of 112,680 resident newborns born in 2010 were screened. Eighty-six infants screened positive for SCD and were referred for confirmatory testing and medical management. Sixty-one of the infants were confirmed with a sickling disorder, resulting in a false positive rate (FPR) of 0.02% and a positive predictive value (PPV) of 71%. Of the twenty-five infants who were not confirmed with SCD, 15 did not have disease, 2 expired, 1 moved out of state, and the remaining 7 are pending. Thus, the true FPR is most likely lower, and the true PPV is most likely higher.

Table 1. Sickle Cell Disease Screening, Michigan, 2010

Disorder	Confirmed + (N)		Detection Rate	
	Total	Among Blacks	Total*	Among Blacks*
Sickle cell anemia	33	32	1:3,415	1:634
SC disease	23	22	1:4,899	1:922
Sickle β thalassemia	5	5	1:22,536	1:4,056
Total	*61*	*59*	*1:1,847*	*1:344*

**Out of the number of Michigan resident infants screened, total N=112,680, among Blacks N=20,282*

HEALTHY PEOPLE 2020 OBJECTIVES

Healthy People 2020 contains ten objectives related to hemoglobinopathies. Michigan has developed a plan for using different data sources to track each objective and gather baseline information (Table 2):

1) The NBS Follow-up database contains screening information as well as confirmatory diagnoses and penicillin prophylaxis initiation data from the SCDAA-MI database.

2) The SCDAA-MI provides education to the parents of infants diagnosed with either SCD or trait and to adult patients. Different community activities targeted to increasing awareness about the disease and providing a forum for interaction and recreation are sponsored by SCDAA-MI in collaboration and partnership with different community-based organizations.

3) The Michigan Care Improvement Registry (MCIR) is a web-based system used to track immunizations for Michigan residents. Through linkages between NBS, birth certificate, and immunization records, Michigan is able to obtain immunization data for those with SCD. Additionally, a sickle cell follow-up module in MCIR contains a comprehensive health status assessment that gathers more detailed information about the experiences of those with SCD, currently including 89 cases born 2005-2010.

Table 2. Healthy People 2020 Objectives related to Hemoglobinopathies, Data Sources used for Each Objective, and Baseline Michigan Data

Number	Title	Data Source(s)	Baseline (if available)
BDBS-1	Vaccinations of persons with hemoglobinopathies	Michigan Care Improvement Registry	Of those aged 19-35 months and born 2004-2008, approximately 66% of children with SCD completed the 4:3:1:3:3:1:4 series.
BDBS-2	Patient and family referral for hemoglobinopathies	To be determined	To be determined
BDBS-3	Hemoglobinopathies care in a medical home	Health Status Assessment	Of those born 2005-2010, approximately 33 (35%) have a primary care physician, 2 of which have a hematologist for primary care.
BDBS-4	Screening for complications of hemoglobinopathies	Health Status Assessment	Of those born 2005-2010, approximately 14% had Transcranial Doppler screening in the past 12 months. Of those screened, 17% had abnormal results.
BDBS-5	Disease-modifying therapies for hemoglobinopathies	Health Status Assessment	Of those born 2005-2010, approximately 11% are currently on hydroxyurea therapy. Of those not on hydroxyurea, 70% have discussed it with a health professional in the past year.
BDBS-6	Penicillin prophylaxis for SCD	Health Status Assessment, NBS Follow-up database	Of those born in 2010 and diagnosed with SCD, 46 out of 50 with a known penicillin initiation date (92%) began treatment before 4 months of age.
BDBS-7	Hospitalizations for SCD	Health Status Assessment, Michigan Inpatient Database	Children born 2005-2010 were admitted to the hospital an average of 1.6 times during the previous year. In 2007, there were an estimated 4,570 hospital stays during which sickle cell disease was noted as a diagnosis.
BDBS-8	High school completion among those with hemoglobinopathies	To be determined	To be determined
BDBS-9	Community-based organization campaigns for hemoglobinopathies	SCDAA-MI, NBS Follow-up database	To be determined
BDBS-10	Awareness of hemoglobinopathy carrier status	SCDAA-MI, NBS Follow-up database	To be determined

4) The Michigan Inpatient Database is a database of hospital discharge records. Nearly all hospitals in the state provide their records to the Michigan Health & Hospital Association (MHA). The Michigan Department of Community Health (MDCH) purchases this database from the MHA.

5) The Health Outside Pregnancy (HOPS) survey was developed by the Division of Genomics, Perinatal Health and Chronic Disease Epidemiology (DGPHCDE) to capture more information on the health of women of reproductive age prior to conception, during pregnancy and after. A specific question related to having a hemoglobinopathy like SCD allowed us to learn more about women with this condition.

6) The Behavioral Risk Factor Surveillance System (BRFFS) is a well known statewide survey housed within DGPHCDE. A question related to hemoglobinopathy status (including SCD) was added in 2010 to be able to estimate the statewide prevalence.

CONCLUSIONS AND FUTURE DIRECTIONS

The use of the surveillance process to improve follow-up strategies for those diagnosed through NBS proved to be effective. By using different data sources, the NBS Follow-up Program has been able to collect information not available otherwise and to develop different epidemiological studies that led to a better understanding of the population with SCD. This is still work in progress, and a few other studies are planned. Meanwhile, the surveillance process helped identify other emerging issues, so new hypotheses were generated. Currently, the NBS Follow-up Program is in the process of planning for three special projects:

1) Emergency Department (ED) visits: Substantial numbers of ED visits occur among people with SCD. The most common reason for the ED visits is usually pain symptoms. In order to better understand the use of ED visits and to develop strategies, a workgroup was created. It is formed of participants from Medicaid, MHA, Certificate of Needs (CON), SCDAA-MI and the NBS Follow-up Program.

2) Maternal deaths in women of reproductive age with SCD or trait: This requires manual review of all maternal death charts available at MDCH to identify those with SCD or trait that may have escaped the general review. A data collection form is currently being developed to capture all details needed including the disease complications, behaviors, socioeconomic status and health insurance coverage.

3) Sudden cardiac death in the young population with SCD or trait: Michigan is the first state that developed sudden cardiac death surveillance. Using that model, we would like to explore cardiac deaths among the population of those having SCD or trait. This is a partnership with two other states and is in the planning phase.

None of the above would have been possible without the funding and support from the National Heart, Lung and Blood Institute and the Centers for Disease Control and Prevention that allowed us to develop the Michigan Hemoglobinopathy Surveillance and Quality Improvement Project. This is the foundation for our results and successes.

ABOUT NEWBORN SCREENING FOLLOW-UP IN MICHIGAN

The Michigan Newborn Screening Program screens newborns in the state for 49 disorders, including sickle cell disease. The screening is performed within the Division of Chemistry and Toxicology in the Bureau of Laboratories. The NBS Follow-up Program, located in the Division of Genomics, Perinatal Health and Chronic Disease Epidemiology within the Bureau of Epidemiology, oversees short and long-term follow-up of infants identified through the program. Follow-up begins with referring these infants to one of four NBS-funded medical management centers for diagnosis and treatment. The Follow-up Program maintains short and long-term follow-up databases for monitoring and evaluation. Education, training, and quality assurance measures are also responsibilities of the Follow-up Program.

REFERENCES

1. A Brief History of Sickle Cell Disease. Joint Center for Sickle Cell and Thalassemic Disorders. (accessed June 7, 2011). Available at URL: http://sickle.bwh.harvard.edu/scd_history.html
2. Sickle Cell Research for Treatment and Cure. National Institutes of Health. National Heart, Lung, and Blood Institute. (accessed June 7, 2011). Available at URL: http://www.nhlbi.nih.gov/resources/docs/scd30/scd30.pdf
3. Genetic Disease Profile: Sickle Cell Anemia. (accessed June 7, 2011). Available at URL: http://www.ornl.gov/sci/techresources/Human_Genome/posters/chromosome/sca.shtml
4. Charache et al. Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. N Engl J Med 1995; 332:1317-1322.
5. Gaston et al. Prophylaxis with oral penicillin in children with sickle cell anemia. A randomized trial. N Engl J Med 1986; 314:1593-1599.
6. Vichinsky et al. Newborn screening for sickle cell disease: effect on mortality. Pediatrics 1988; 81:749–755.

Suggested citation: Kleyn M, O'Neill R, Grigorescu V, Young W. Sickle Cell Disease in Michigan. *Michigan Newborn Screening Follow-Up Brief*. Vol. 3, No. 1. Lansing, MI: Michigan Department of Community Health, Newborn Screening Follow-up Program. July 2011.

NEWBORN SCREENING FOLLOW-UP PROGRAM

201 Townsend Street
PO Box 30195
Lansing, MI 48909

Phone: 517-335-9205
Fax: 517-335-9419
E-mail: newbornscreening@michigan.gov

Past and current editions of the NBS Annual Report, NBS Newsletters, and NBS Briefs are available at:

www.michigan.gov/newbornscreening

Michigan Department of Community Health
MDCH
Rick Snyder, Governor
Olga Dazzo, Director