Newborn Screening and Followup for Hemoglobinopathies

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Disclosures

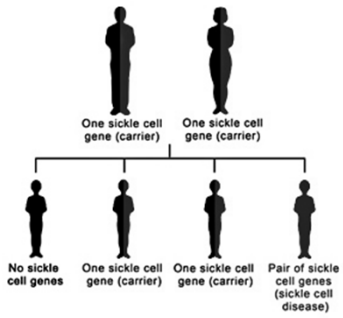
- I have no relevant financial relationships.
  - My husband is employed at Pfizer Inc. as a quality scientist.
- I will discuss off-label use of hydroxyurea.

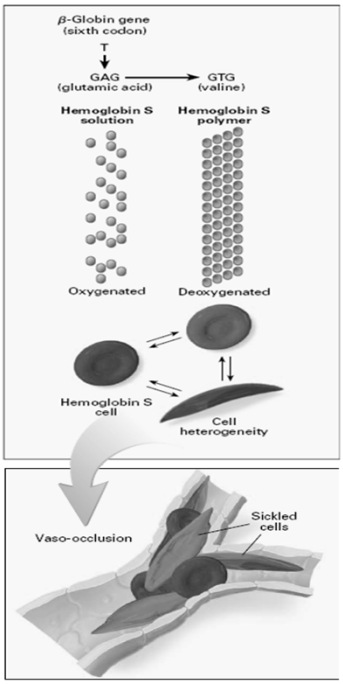
Objectives

- To review the rationale for newborn screening for sickle cell disease (SCD).
- To discuss the followup process for abnormal hemoglobinopathy screens in Missouri Region 3
- To discuss ongoing care and services provided through the newborn screening program and Sickle Cell Disease Program at St. Louis Children's Hospital.

Inheritance of hemoglobinopathies

- Autosomal recessive
- Point mutation in beta globin gene causes Hemoglobin S
- Sickle Cell Anemia = 2 Hb S mutations
- Sickle Cell Disease = Hb S + another abnormal hemoglobin trait
- Combinations of various traits lead to a wide range of disease severity



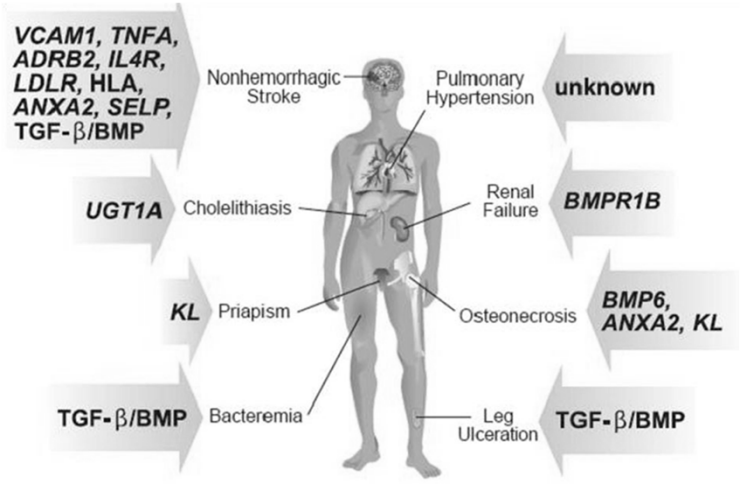


SCD Pathophysiology: Vaso-Occlusion and Viscosity

Figure 1. Pathophysiology of Sickle Cell Disease.
In hemoglobin S, a substitution of T for A in the sixth codon of the β-globin gene leads to the replacement of a glutamic acid residue by a valine residue. On deoxygenation, hemoglobin S polymers form, causing cell sickling and damage to the membrane. Some sickle cells adhere to endothelial cells, leading to vaso-occlusion.

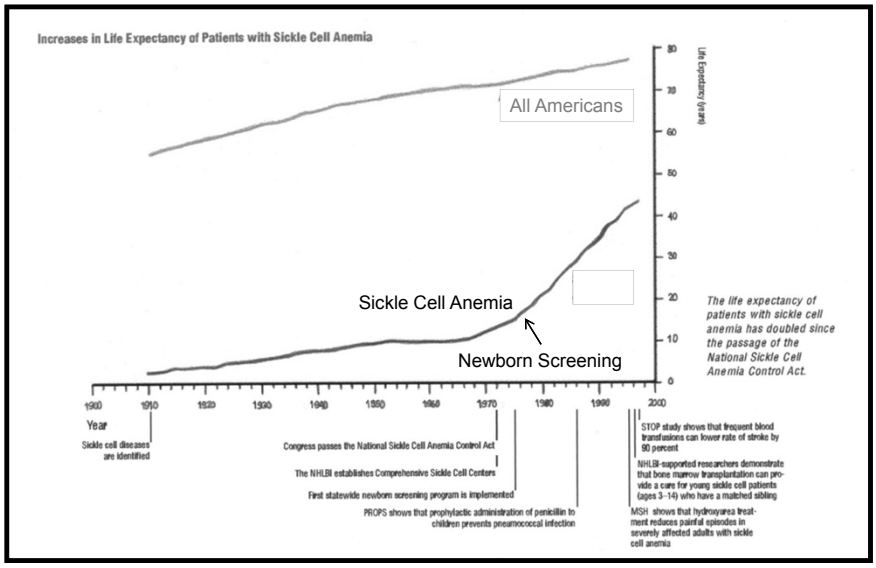
Steinberg 1999

SCD affects every organ system



15 JUNE 2008 I VOLUME 111, NUMBER 12 blood

Survival of people with SCD since 1910



NHLBI 2002

Why do newborn screening?

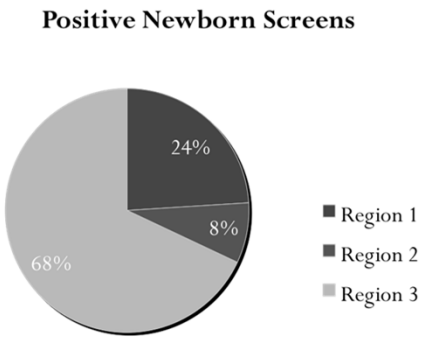
- Newborn screening for hemoglobinopathies is mandated in all 50 states
- Goals:
  - Identify infants with SCA/SCD, initiate penicillin prophylaxis to prevent death from pneumococcal infections
  - Identify infants with other hemoglobinopathies, initiate appropriate care
  - Identify families in need of genetic counseling to inform them of risks for future children with hemoglobinopathies

Penicillin Prophylaxis in Sickle Cell Disease Study (PROPS)

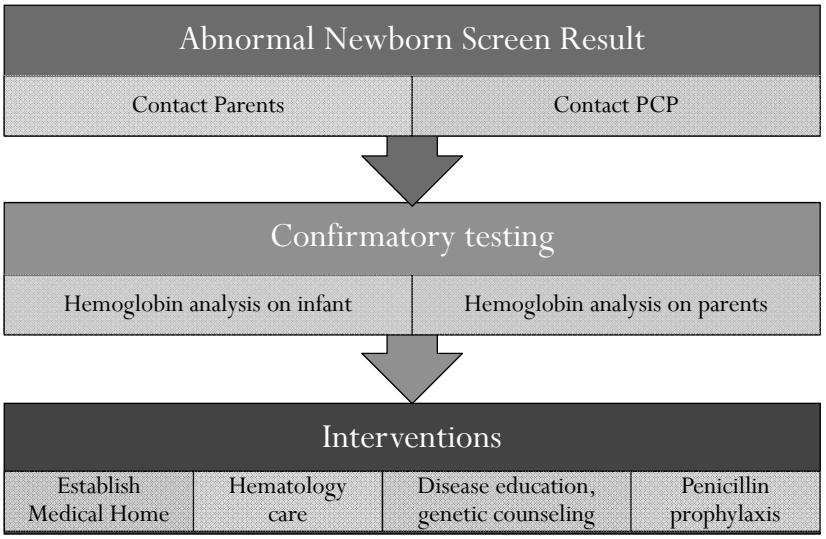
- Randomized, double blinded study of prophylactic penicillin in children with SCA under 3 yrs old (Gaston 1986)
- Terminated early due to 84% reduction in infections
- This study provided the rationale for universal NBS for SCD

	Participants	Sepsis events/ 100 patient years	Deaths
Penicillin	105	2	0
Placebo	110	12	3

Missouri NBS Regions



Newborn Screening Followup Steps



MO Region 3 Followup Process

Area pediatric hematology programs:
St. Louis Children's Hospital
Cardinal Glennon Hospital
Mercy Hospital

Missouri Region 3 NBS results

NBS Result	2010	2011	2012 to date
FS	11	14	9
FSC	11	4	4
FSA	1		4
Other*	8	1	2
Total	31	19	19

*Other includes Hb C disease, Hb C-β^+ thalassemia, Hb SE, β-thalassemia intermedia

Confirmatory Testing

- Hemoglobin analysis on infant
- Genetic testing at Children's Hospital of Oakland:
  - useful if unknown hemoglobin is present
  - or if infant has been transfused
- Hemoglobin analysis on both parents is ideal
- Allows more accurate diagnosis of infant
  - Hb SS vs Hb S-β^0 thal
- Also facilitates genetic counseling of parents

Interventions for positive NBS

Establish Care

- Primary care medical home
- Penicillin for all infants with SCD by age 2 months
  - Not needed for non-SCD diagnoses
- Hematology care
- Disease education and genetic counseling

Report Care

- NBS program coordinator obtains confirmatory test results, penicillin start date if applicable, and hematology center
- Information transmitted to MO Dept of Health via MOHSAIC electronic system

Why is primary care important?

- Children have health needs besides SCD
- Children and families need preventive care and anticipatory guidance
- AAP statement on SCD
  - aappolicy.aappublications.org/cgi/reprint/pediatrics;109/3/526.pdf

Why is SCD Center care important?

- Access to new treatments
- Experience in acute SCD complications
- Specific screening tests available at SCD center
- SCD-specific education and support
- Lower mortality if treated by pediatric hematologist (Adamkiewicz 2003)

SCD Program at SLCH/Wash U

- SCD care spans from infancy through adulthood
- Personnel include physicians, nurse practitioners, nurse coordinators, sickle cell coaches, and social worker
- Funding through:
  - MO newborn screening grant
  - HRSA funding through Dr. Allison King
    - MONET SCD: Missouri Network for Education and Testing for SCD
    - NICHQ participation

SCD Program at SLCH/Wash U

- ~450 children and young adults with SCD
  - Mostly in St. Louis region, some in IL, southeastern MO
- Care organized by age groups
  - Infants through kindergarten
  - School-aged children
  - Teens and young adults
- Transition to adult care at age 19-20 years
- Database with detailed information on disease and complications for each patient allows monitoring of required testing and followup

SCD care for infants

- Begin penicillin prophylaxis by 2 months of age
- Clinic visits every 3 months until age 2 yrs
- Establish medical home with primary care provider
- Family SCD education
  - Written materials
  - Parent Education Program DVD

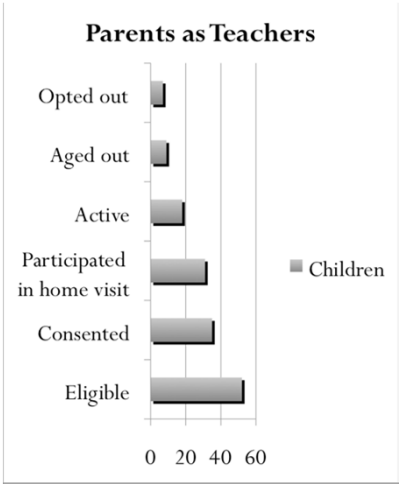
Image from www.nhlbi.nih.gov

SCD education for infants' families

- Fever management
  - ANY fever over 101 deg F may represent serious, invasive bacterial infection
  - Invasive pneumococcal disease decreased but not eliminated by pneumococcal conjugate vaccines (McCavit 2010)
- Splenic sequestration
  - Teach spleen palpation
  - Parent education program decreases mortality (Emond 1985)
- Pain management
- Genetic counseling for parents

Early childhood intervention in SCD

- In-home early childhood assessments and interventions offered through Parents as Teachers research protocol
- Dr. Allison King/Catherine Hoyt, OTD, OTR/L
- Goal: improve early verbal skills and parent-child interactions, hopefully leading to improvements in later educational progress



Parents as Teachers for SCD

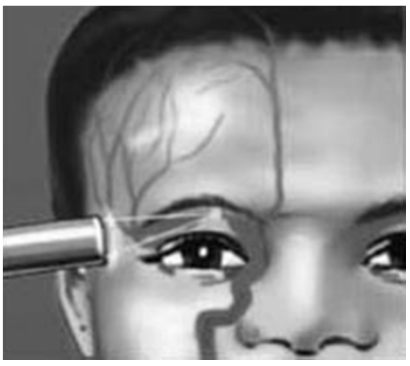
- Education on child development and parenting
- Reinforcement of SCD education from clinic appts
- 6 children referred to First Steps
  - 3 receiving services
- Significant family needs identified (beds, clothing) and assistance provided

SCD care for school-aged children

- SCD pain management: individualized Pain Action Plan
- SCD pain prevention: consideration of hydroxyurea therapy

- Children with SCD are at high risk for overt strokes (clinically apparent) and silent strokes (not clinically evident)
- Focus on school attendance and attainment
  - Neurocognitive testing for those with strokes or school problems
  - Individualized Education Plan
  - 504 Plan

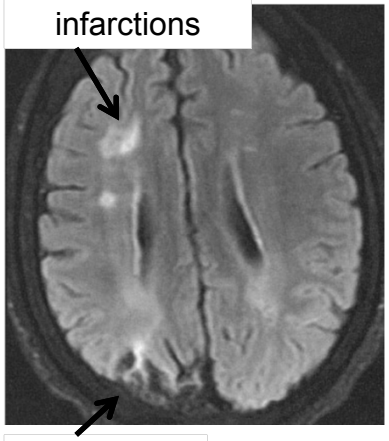
Trancranial Doppler Ultrasound



- Ultrasound measurement of blood flow velocity in internal carotid and middle cerebral arteries
- Children with Hb SS or Hb S-beta 0 thalassemia screened annually from 2 to 16 yrs
- If TCD velocities above threshold, stroke risk is elevated and chronic transfusions are indicated (Adams 1992; Adams 1998)

Silent and overt strokes in SCD

- Strokes cause cognitive and physical problems
- Silent Infarct Transfusion study aimed at determining whether chronic blood transfusion therapy prevents progression of silent strokes
- Chronic transfusion therapy is the standard of care for overt strokes



DeBaun 2006

SCD in adolescents/young adults

- Adolescents and young adults with SCD have
  - more acute pain
  - chronic pain
  - more hospitalizations
  - longer LOS
  - Increasing prevalence of irreversible organ damage
  - increased risk of death (Quinn et al, *Blood*, 2009)
- National push for better adolescent/young adult SCD care

Fig. 1. The number of hospital discharges and total hospital days per each year of age for children with vaso-occlusive crises in sickle cell disease.

Panepinto et al, *Pediatr Blood Cancer*, 2005

Adolescence: psychosocial factors

- Usual teen struggles with independence
- Realization that SCD is chronic and lifelong
- School attainment may be low
  - Due to cognitive deficits and/or school absences
  - Readiness for higher education/work can be compromised
- May have poor access to healthcare
  - Insurance status
- Not enough adult SCD providers
  - Primary care physicians, hematologists, SCD centers

Adolescence: what can we do?

- Start early! Age 12-14 years
- Build sense of responsibility for care
- Structured transition process from pediatrics to adult care

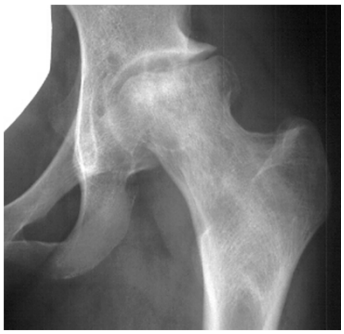
Image from "Health Smart: Teens with Sickle Cell Disease Moving from Pediatric Care to Adult Care" www.stjude.org

Adolescent SCD Clinic at SLCH

- Monthly multidisciplinary clinic
  - Hematologist/PNP, adolescent medicine, psychologist, SW, recreational therapist
- Visit focuses on the teen
  - Teen sees providers, then parents are invited to join for summary
- Goals
  - to address hematological, mental health, contraceptive needs and preventive care
  - encourage independence in healthcare

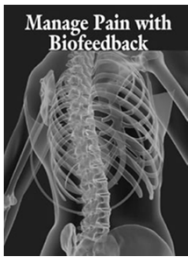
Adolescent SCD Clinic: Hematology

- Disease self-management
- Medication compliance
- Education and screening
  - Proteinuria
  - Priapism
  - Retinopathy
  - Avascular necrosis
  - Iron overload
  - Hydroxyurea?
  - Inheritance of SCD
  - Genetic counseling for teen



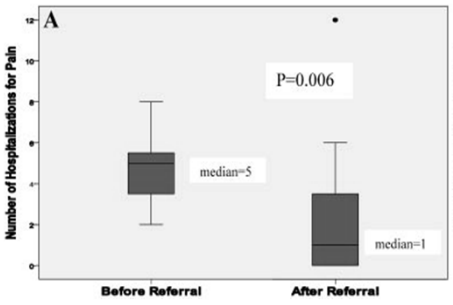
Adolescent SCD Clinic: Psychology

- Relationship between mood, anxiety, and pain
- Non-pharmacological pain management
- Facilitates teen group discussion about "Ten Commandments of Sickle Cell Disease"



Adolescent SCD Clinic

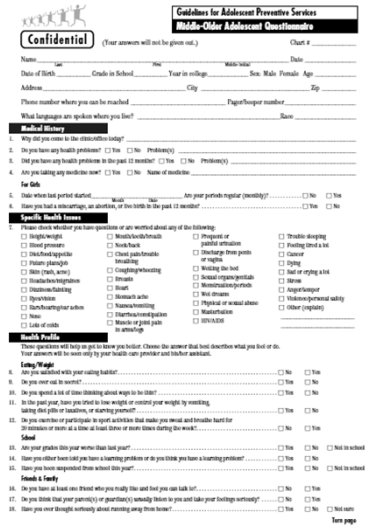
- Multidisciplinary approach to SCD pain decreases hospitalizations
  - Chronic and acute pain
  - Disease-modifying therapy
- Non-pharmacological pain management techniques
- Treat depression and anxiety
- Frequent followup



Brandow et al, Pediatr Blood Cancer;2011:56:789-93.

Adolescent SCD Clinic

- Adolescent medicine component
- Uses a standardized screening tool for adolescent concerns
  - GAPS assessment
- Top concerns: STD testing/education, contraception, mental health
- Management of antidepressant therapy and referral to counseling/psychiatry if needed



Confidential (Your answers will not be given out.)

Guidelines for Adolescent Preventive Services

Middle-Older Adolescent Questionnaire

Chart #

Name Last First Middle Initial Date

Date of Birth Grade in School Year in college Sex: Male Female Age

Address City Zip

Phone number where you can be reached Pager/beeper number

What languages are spoken where you live? Race

Medical History

1. Why did you come to the clinic/office today?
2. Do you have any health problems? ☐ Yes ☐ No Problem(s)
3. Did you have any health problems in the past 12 months? ☐ Yes ☐ No Problem(s)
4. Are you taking any medicine now? ☐ Yes ☐ No Name of medicine

For Girls

5. Date when last period started Month Date Are your periods regular (monthly)? ☐ No ☐ Yes
6. Have you had a miscarriage, an abortion, or live birth in the past 12 months? ☐ Yes ☐ No

Specific Health Issues

7. Please check whether you have questions or are worried about any of the following:

☐ Height/weight ☐ Mouth/tooth/breath ☐ Frequent or painful urination ☐ Trouble sleeping
☐ Blood pressure ☐ Neck/back ☐ Discharge from penis or vagina ☐ Feeling tired a lot
☐ Diet/food/appetite ☐ Chest pain/trouble breathing ☐ Cancer
☐ Future plans/job ☐ Coughing/wheezing ☐ Waking the bed ☐ Dying
☐ Skin (rash, acne) ☐ Bruises ☐ Sexual organs/genitals ☐ Sad or crying a lot
☐ Headaches/migraines ☐ Heart ☐ Menstruation/periods ☐ Stress
☐ Dizziness/fainting ☐ Stomach ache ☐ Wet dreams ☐ Anger/temper
☐ Eyes/vision ☐ Nausea/vomiting ☐ Physical or sexual abuse ☐ Violence/personal safety
☐ Hurts/hearing/ear aches ☐ Diarrhea/constipation ☐ Masturbation ☐ Other (explain)
☐ None ☐ Muscle or joint pain in arms/legs ☐ HIV/AIDS
☐ Lots of colds

Health Profile

These questions will help us get to know you better. Choose the answer that best describes what you feel or do. Your answers will be seen only by your health care provider and his/her assistant.

Eating/Weight

8. Are you satisfied with your eating habits? ☐ No ☐ Yes
9. Do you ever eat in secret? ☐ Yes ☐ No
10. Do you spend a lot of time thinking about ways to be thin? ☐ Yes ☐ No
11. In the past year, have you tried to lose weight or control your weight by vomiting, taking diet pills or laxatives, or starving yourself? ☐ Yes ☐ No
12. Do you exercise or participate in sport activities that make you sweat and breathe hard for 20 minutes or more at a time at least three or more times during the week? ☐ No ☐ Yes

School

13. Are your grades this year worse than last year? ☐ Yes ☐ No ☐ Not in school
14. Have you either been told you have a learning problem or do you think you have a learning problem? ☐ Yes ☐ No
15. Have you been suspended from school this year? ☐ Yes ☐ No ☐ Not in school

Friends & Family

16. Do you have at least one friend who you really like and feel you can talk to? ☐ No ☐ Yes
17. Do you think that your parent(s) or guardian(s) usually listen to you and take your feelings seriously? ☐ No ☐ Yes
18. Have you ever thought seriously about running away from home? ☐ Yes ☐ No ☐ Not sure

Turn page

Adolescent SCD Clinic

- Social Work component:
- Educational assessment and intervention with IEP/504 plan process
- Insurance assessment
- Family needs assessment
- Additional resources:
  - Adolescent autonomy checklist: tool to identify life skills that teens need to work on prior to transition

Partnership with adult providers

- Adult SCD nurse practitioner and medical assistant come to adolescent clinic to meet teens
- Tour of adult clinic facility
- Monthly joint peds/adult meetings to discuss upcoming transitioning patients, clinical issues
- Adult Medical Home project: facilitates adults' referrals to FQHC for primary care
  - funded through HRSA

Adolescent SCD Clinic attendance

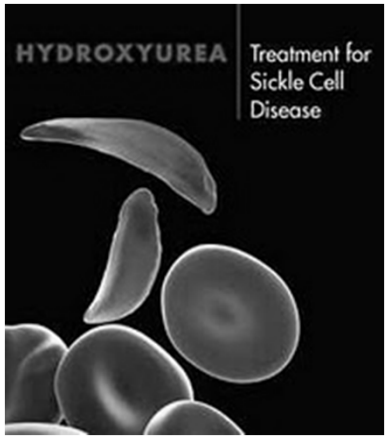
Date	Scheduled	Attended
Apr 18	4	3
May 16	3	2
June 20	5	3
July 18	4	1
Aug 15	7	6*
Sept 19	6	5*

*Reminder phone calls initiated

Image from St. Louis American

Disease Modifying Therapy

- Hydroxyurea increases Hb F, improves anemia
- Reduces hospitalizations for pain, acute chest syndrome in all ages
- Improved growth in kids
- Reduces mortality over 15-20 yrs in adults
- Minimal side effects
- NHLBI recommendation to get more patients on hydroxyurea therapy



Hydroxyurea barriers

- Patient and family-specific barriers
  - Concerns about perceived side effects (hair loss, cancer in other dz)
  - Disinterest in daily medication or frequent clinic visits
  - Hope that SCD will get better without intervention
- Provider-specific barriers
  - Worries about side effects, including as-yet unidentified side effects
  - Concerns about compliance based on family's past history
- System-specific barriers
  - Lack of patient access to SCD center
  - Insurance barriers
- Reviewed by Brandow and Panepinto, *Exp Rev Hematol* 2010

SCD community partnerships

- Community organization: Sickle Cell Disease Association
- Monthly support group
- Hemoglobinopathy trait testing/counseling
- Sickle Cell Stroll community event, sponsored by Wash U and MONET SCD

Conclusions

- SCD requires coordinated care from newborn screening through adulthood
- Early childhood evaluations complement SCD center care
- Multidisciplinary approach improves access to care and readiness for self-management in adolescent population
- Partnership between medical center and community organization provides additional services and support to families

SLCH SCD Program

- Monica Hulbert, MD, Director
- Elliot Gellman, MD
- David Wilson, MD, PhD
- Debbie Woods, CPNP
- Alison Towerman, CPNP
- Kim Ferguson, LCSW
- Ta'Lisa Davis, RN
- Tammy Taylor, RN
- Tinishia Greene, NBS coordinator
- Kelley Chadwick-Mansker, RRT

MONET-SCD

- Allison King, MD, MPH
- Terianne Lindsey, CPNP
- Regina Abel, PhD
- Suzanne Bell, MS
- Catherine Hoyt, OTD, OTR/L
- Mackenzie Ray, MPH
- Ashley Housten, MPA

MO Newborn Screening

Nancy Althouse-Hill