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.

SCD affects every organ system
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

<table>
<thead>
<tr>
<th></th>
<th>Participants</th>
<th>Sepsis events/100 patient years</th>
<th>Deaths</th>
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<tbody>
<tr>
<td>Penicillin</td>
<td>105</td>
<td>2</td>
<td>0</td>
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<tr>
<td>Placebo</td>
<td>110</td>
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Missouri NBS Regions

Positive Newborn Screens

- Region 1: 68%
- Region 2: 8%
- Region 3: 24%
Newborn Screening Followup Steps

Abnormal Newborn Screen Result
- Contact Parents
- Contact PCP

Confirmatory testing
- Hemoglobin analysis on infant
- Hemoglobin analysis on parents

Interventions
- Establish Medical Home
- Hematology care
- Disease education, genetic counseling
- Penicillin prophylaxis

MO Region 3 Followup Process

Abnormal result sent from Dept of Health to NBS coordinator
Coordinator contacts PCP and family
PCP and family choose hematology center

Area pediatric hematology programs:
- St. Louis Children’s Hospital
- Cardinal Glennon Hospital
- Mercy Hospital
Missouri Region 3 NBS results

<table>
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<tr>
<th>NBS Result</th>
<th>2010</th>
<th>2011</th>
<th>2012 to date</th>
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<td>FS</td>
<td>11</td>
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<td>FSA</td>
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<tr>
<td>Other*</td>
<td>8</td>
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<tr>
<td>Total</td>
<td>31</td>
<td>19</td>
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*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-β⁰ 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

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

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

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

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

I just turned 14! Can I come to the adolescent clinic??

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

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

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

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<tr>
<td>Sept 19</td>
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*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 dx)
  - 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
<table>
<thead>
<tr>
<th>SLCH SCD Program</th>
<th>MONET-SCD</th>
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<tbody>
<tr>
<td>• Monica Hulbert, MD, Director</td>
<td>• Allison King, MD, MPH</td>
</tr>
<tr>
<td>• Elliot Gellman, MD</td>
<td>• Terianne Lindsey, CPNP</td>
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<tr>
<td>• David Wilson, MD, PhD</td>
<td>• Regina Abel, PhD</td>
</tr>
<tr>
<td>• Debbie Woods, CPNP</td>
<td>• Suzanne Bell, MS</td>
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<tr>
<td>• Alison Towerman, CPNP</td>
<td>• Catherine Hoyt, OTD, OTR/L</td>
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<tr>
<td>• Kim Ferguson, LCSW</td>
<td>• Mackenzie Ray, MPH</td>
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<tr>
<td>• Ta’Lisa Davis, RN</td>
<td>• Ashley Houston, MPA</td>
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<td>• Tammy Taylor, RN</td>
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<td>• Tinishia Greene, NBS coordinator</td>
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<td>• Kelley Chadwick-Mansker, RRT</td>
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MO Newborn Screening
Nancy Althouse-Hill