Update
Hemoglobinopathy Issues and Answers Conference
CHORI – May 25, 2010
SACHDNC – September 16, 2010

Brad Therrell, PhD
NNSGRC - Austin, Texas

Jelili Ojodu, MPH
APHL – Silver Spring, Maryland
Current Status of Newborn Hemoglobinopathy Screening in the United States

May 25, 2010

Brad Therrell, Ph.D., Director
National Newborn Screening and Genetics Resource Center
Austin, Texas
Laboratory Service Delivery Models 2010
States Using Contract Screening Laboratories and Public and/or Commercial/Non-profit
Laboratory Service Delivery Models 2010
Hemoglobinopathy Screening
Laboratory Service Delivery Models 2010
Hemoglobinopathy Screening

IEF as Primary Screen
IEF and HPLC as Primary Screen
HPLC as Primary Screen

Laboratory Service Delivery Models 2010
Hemoglobinopathy Screening
Laboratory Service Delivery Models 2010
Hemoglobinopathy Screening

- HPLC Not Available
- IEF and HPLC on All Newborns
- HPLC Available – First or Second Tier Screen
DNA Available as Second Tier
DNA Available to Some Infants as Second Tier
DNA Not Commonly Used as Second Tier Screen

Laboratory Service Delivery Models 2010
Hemoglobinopathy Screening
D.C.

U.S. History of Hemoglobinopathy Screening
April 1, 1975

Universal Newborn Hemoglobinopathy Screening Mandated
Newborn Hemoglobinopathy Not Universally Mandated

U.S. History of Hemoglobinopathy Screening
April 1, 1975

U.S. History of Hemoglobinopathy Screening
By January 1, 1995

Universal Newborn Hemoglobinopathy Screening Mandated

Newborn Hemoglobinopathy Not Universally Mandated

U.S. History of Hemoglobinopathy Screening
By January 1, 2005

Universal Newborn Hemoglobinopathy Screening Mandated
Newborn Hemoglobinopathy Not Universally Mandated

U.S. History of Hemoglobinopathy Screening
By May 1, 2006
All 51 Programs

Issues and Answers Series
Hemoglobinopathy Newborn Screening

Nomenclature
and
Hemoglobinopathy 101

Kwaku Ohene-Frempong, M.D.
The Children’s Hospital of Philadelphia
University of Pennsylvania
Genetics of Hemoglobinopathies

Human Hemoglobin Genes and Products

Chromosome 16  Globin proteins  Chromosome 11

Globin genes

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# Nomenclature in SCD

## Common Types of Sickle Cell Disease

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Common Term</th>
<th>Preferred Term</th>
<th>Preferred Acronym</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta^s / \beta^s$</td>
<td>Sickle cell anemia</td>
<td>Sickle cell disease SS</td>
<td>SCD-SS</td>
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<tr>
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<td>Hemoglobin SS disease</td>
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<td></td>
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<td>Sickle cell hemoglobin C disease</td>
<td>Sickle cell disease SC</td>
<td>SCD-SC</td>
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<td>Hemoglobin SC disease</td>
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<td>$\beta^s / \beta^o$</td>
<td>Hemoglobin S beta-zero thalassemia</td>
<td>Sickle cell disease S$\beta^o$ thalassemia</td>
<td>SCD-S$\beta^o$ th</td>
</tr>
<tr>
<td>$\beta^s / \beta^+$</td>
<td>Hemoglobin S beta-plus thalassemia</td>
<td>Sickle cell disease S$\beta^o$ thalassemia</td>
<td>SCD-S$\beta^+$ th</td>
</tr>
</tbody>
</table>
Hemoglobinopathies Newborn Screening

Newborn with Hemoglobin Bart’s

Hemoglobin St. Bartholomew’s (Hb Bart’s):
• Abnormal tetramer of gamma globin ($\gamma_4$) suggests excess gamma globin and by inference, deficiency of alpha globin ($\alpha$ thalassemia) to make Hb F ($\alpha_2\gamma_2$)
• Relative quantity of Hb Bart’s reflects degree of alpha thalassemia

Reporting Hemoglobin Bart’s
- FA + Bart’s
- FX + Bart’s
- FYZ + Bart’s
Sickle Cell Disease and Other Hemoglobinopathies

Proficiency Testing Program

Carla Cuthbert, PhD FACMG
Newborn Screening and Molecular Biology Branch
Centers for Disease Control and Prevention
Hemoglobinopathy PT program

• Hemoglobinopathy PT program has been in operation since 1991

• Current participants include 51 domestic and 26 international laboratories

• Extent of participant enrollment by NSQAP is limited by availability of materials
# Results by Year (2000-2009)

<table>
<thead>
<tr>
<th>Year</th>
<th>Total # Specimens</th>
<th>Percentage of Errors</th>
<th>Phenotype</th>
<th>Clinical Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td>Phenotype</td>
<td>Clinical Assessment</td>
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<td>0.5</td>
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<td>0.3</td>
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<td>920</td>
<td>0.4</td>
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<td>1020</td>
<td>0.1</td>
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<td>0.1</td>
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<td>2003</td>
<td>884</td>
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<td>0.3</td>
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<td>2004</td>
<td>1080</td>
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<td>0.9</td>
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<td>1100</td>
<td>0.5</td>
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<td>2009*</td>
<td>1056</td>
<td>1.2</td>
<td></td>
<td>1.2</td>
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</tbody>
</table>

* 1st year single donor specimens used
Future Directions for Hb Program

• NSQAP is expanding our current program to increase the number and variety of specimens

• New partnerships are being developed to achieve expansion

• Expansion will allow us to serve those laboratories currently on the waiting list
Testing for Hemoglobinopathies in the Texas Newborn Screening Program

Rachel C. Lee and Chris Moore

Texas Department of State Health Services
Austin, Texas
Hemoglobinopathy Screening Procedures in Texas

- Isoelectric Focusing (IEF) to screen all specimens
  - ~800,000 specimen per year
  - ~2,700 specimens per day (6 days a week)
- Retest IEF for all abnormal specimens
  - ~100 specimens per day
- HPLC for certain abnormal specimens
  - ~10 specimens per day
- 2nd tier molecular testing
  - ~500 per year
- Identify an average of 35 clinically significant results per month
Newborn Screening Laboratory Methodology

- High pressure liquid chromatography (HPLC)

- Identifies hemoglobins F, A, S, D, C, E, Bart’s, and 5 unknown Variants
Non-Targeted Hemoglobinopathies: Challenges and Considerations

Kathryn Hassell, M.D.
Professor of Medicine, Division of Hematology
Director, Colorado Sickle Cell Treatment and Research Center
NBS Hemoglobinopathy Follow-Up Program, Colorado and Wyoming
Harmonizing laboratory reporting
Is It Possible?

Issues and Answers Series –
Hemoglobinopathy NBS
Children’s Hospital Oakland
Research Institute
May 25, 2010

Roger B. Eaton, PhD, Director
New England Newborn Screening Program
The BIG ISSUE
Standardization vs. Idiosyncracy

- 54089-8 Newborn Screening Panel, American Health Information Community (AHIC)
  - HPLC: 79 codes
  - IEF: 79 codes

- 15 State NBS labs (after grouping): about 272 patterns
Remaining Issues

- LA12057-8 = “Hb F, A, and other than C,D,E,S,O-Arab”
  Similar for FSV, FV, FACV, FADV, FAEV, FASV
  FSV, FVB, FAVB, SV, V, AV

- LA11982-8 = “Hb F, D”
  Many labs acknowledge they cannot reliably distinguish D/G

- Have not discussed “Disorder List” today
- Have not addressed “method specificity” issue
- >20 labs not represented
- Hundreds of patterns still not covered …
Introduction to Hb H-Disease
Epidemiology and Natural History

Elliott Vichinsky, MD
Hematology/Oncology

May 25, 2010
Hemoglobin H Disease
Longitudinal Observations During Childhood

Ash Lal, M.D.
Hematology/Oncology
Nutrition & Metabolism Center
California Newborn Screening Program for Thalassemias

APHL Hemoglobinopathy Lab Workshop
Children’s Hospital Oakland
May 26, 2015

Fred Lorey, Ph.D
Genetic Disease Screening Program
CA Department of Public Health
California Newborn Screening Program for Thalassemias: Confirmatory Testing and Follow-up

Issues and Answers Series
Hemoglobinopathy Newborn Screening
May 25, 2010

Carolyn Hoppe, MD
Hemoglobinopathy Reference Laboratory
Children’s Hospital & Research Center Oakland
Report from Evidence Review

Advisory Committee on Heritable Disorders in Newborns and Children

May 14, 2010

Alex R. Kemper, MD, MPH, MS
Department of Pediatrics, Duke University
http://genes-r-us.uthscsa.edu