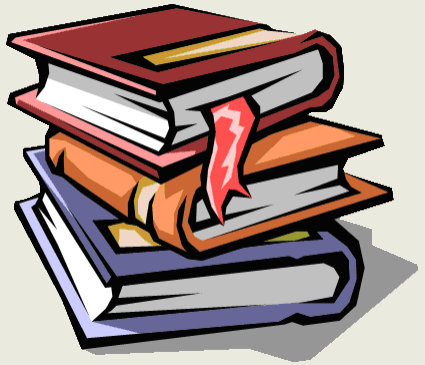
Building and Enhancing Laboratory Capacity for Screening and Diagnosis of Hemoglobinopathies

Presented by M.Christine Dorley -TNDOH

Reasons

- Millions are affected globally
- i.e. Sickle Cell Disease
  - 1/500 African Americans
  - 1/36000 Hispanic Americans
  - 1/12 African American born with SCT
  - SCD incidence higher in certain areas
    - Liberia – 10.31% SCT & 1.19% SCD
    - Uganda – prevalence study
      - 13.3% SCT & 0.7% Disease
      - prevalence of SCT > 20%
      - Other Hb variants at 26%

- Many published articles on Hemoglobinopathies Screening and Diagnosis
- Lack of a comprehensive reference



White Paper

56 page document

- Executive Summary
- Acknowledgements
- Introduction
- History of Screening
- Methods
- Advantages, Limitations & Testing Strategy
- Algorithms
- QA
- Follow-up
- References
- Appendices

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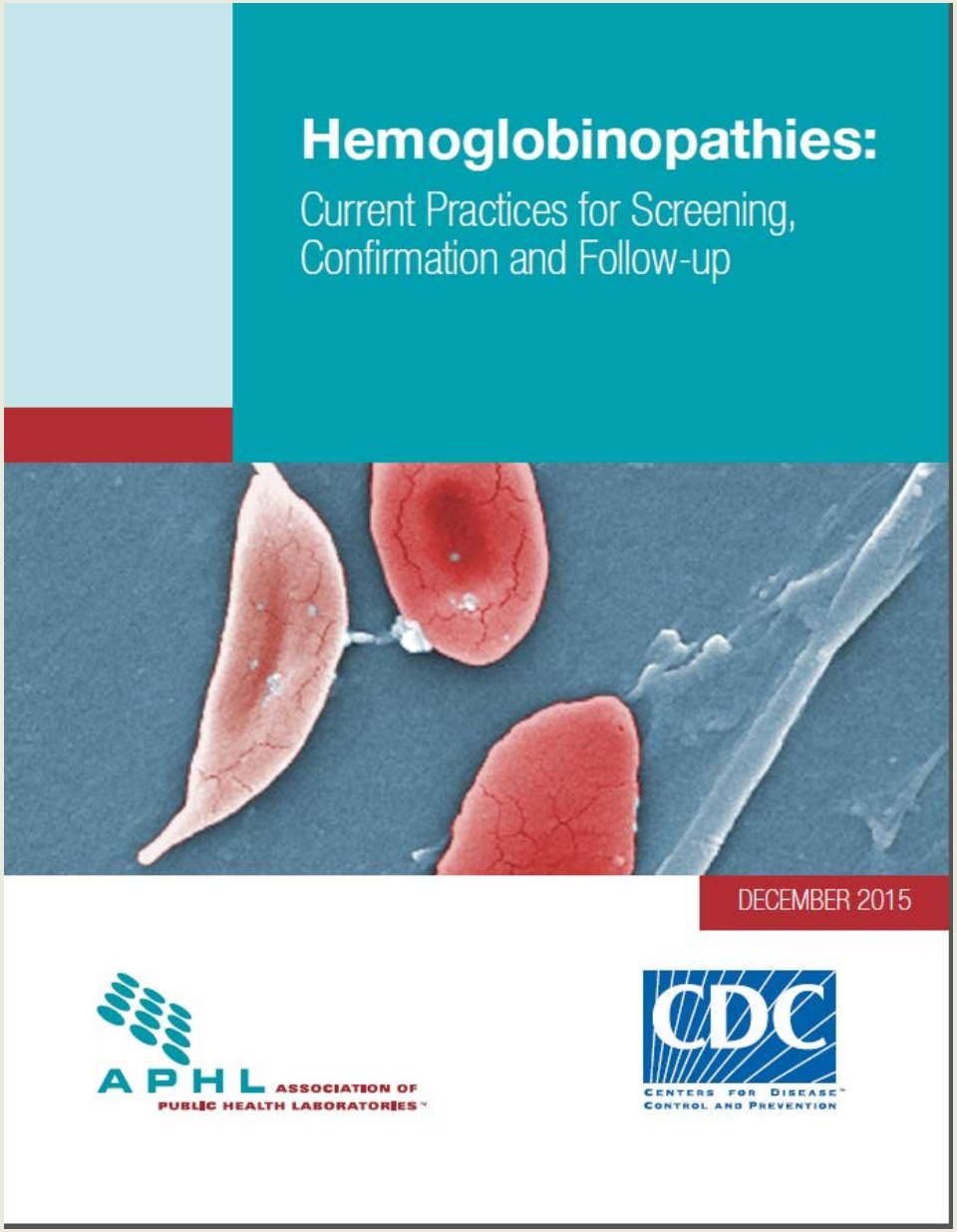


How It Began

Workgroup

Joint Effort

- 6 States Public Health Labs
  - WA, TX, TN, NV, NJ, & FL
- 1 Diagnostic lab – Meharry
- APHL
- CDC
  - National Center on Birth Defects and Developmental Disabilities
  - National Center for Environmental Health

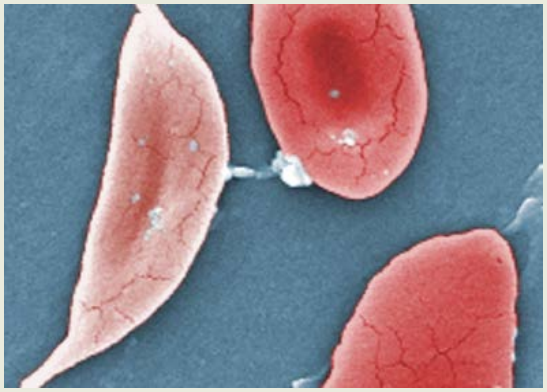
I. Executive Summary

- States Workgroup Objectives:
  - Discuss issues related to lab capacity
  - Conduct inventory of labs with capacity for SCD testing
  - Develop a training program for implementing lab technology
  - Evaluate current lab methods and make recommendations for improvement
  - Identify and document best practices

II. Acknowledgements

- Maria del Pilar Aguinaga – MMC, Tennessee
- Ming Chan, Florida DOH
- Tim Davis, Washington DOH
- Christine Dorley – Tennessee DOH
- Jojo Dy – Nevada DOH
- Marie Earley – CDC
- Althea Grant – CDC
- Mary Hulihan – CDC
- Suzanne Karabin – New Jersey DOH
- Joanne Mei – CDC
- Christine Moore – Texas DOH
- Laxmi Nayak – New Jersey DOH
- Kwaku Ohene-Frempong – CHOP, Pennsylvania

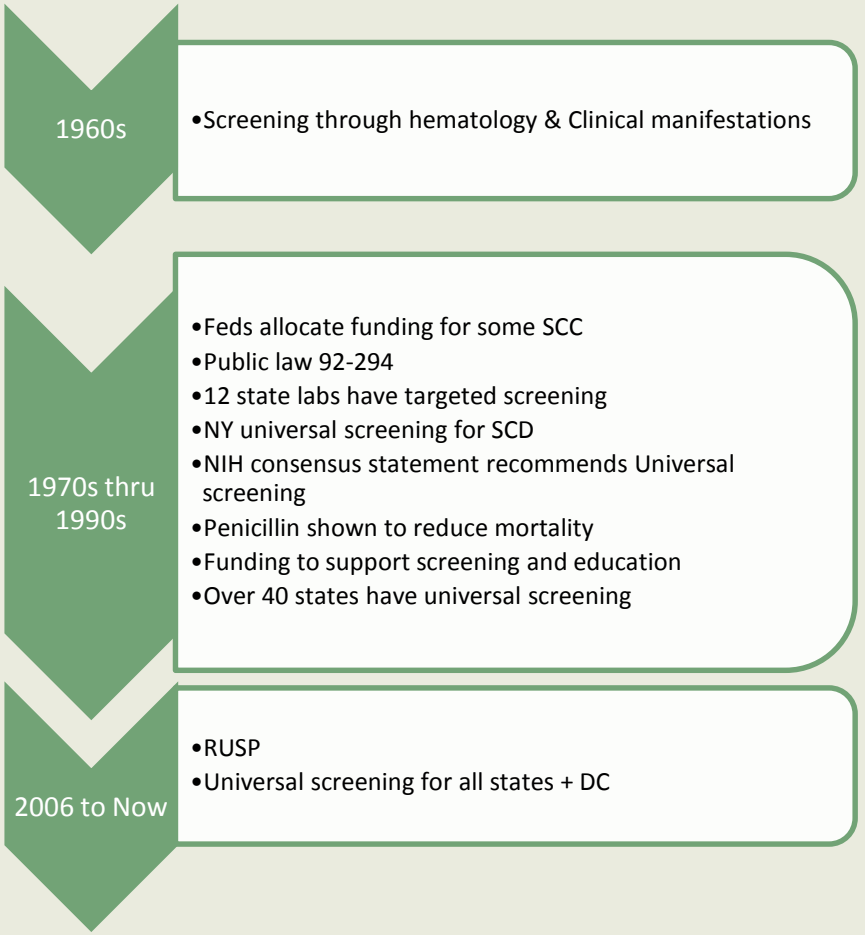
III. Introduction



- Discusses Hemoglobin structure
  - Normal Hb
  - Quantitative changes to Hemoglobin
    - Thalassemias – i.e. αthal
    - One gene deletion vs. four gene deletions
  - Qualitative changes to Hemoglobin
    - Beta globin variants i.e. Hb S, C, D, E, and G
  - Severity of disease can vary from insignificant to life threatening
  - Highlights differences in methods and screening programs

IV. History

- Historical perspective beginning in the 1970s up to present day with addition to the RUSP



V. Specimen Types

- Satisfactory specimens

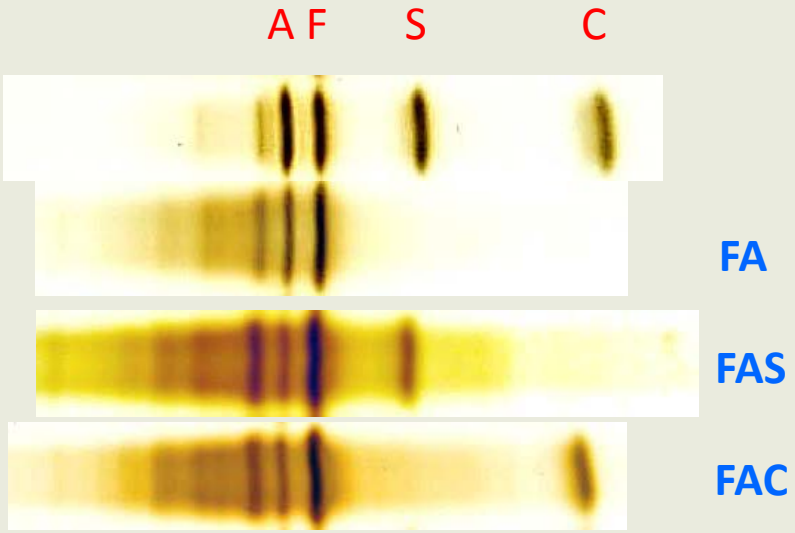
- Unacceptable samples and transfusion

VI. Methods

- Isoelectric focusing
- High Performance Liquid Chromatography
- Cellulose Acetate Electrophoresis
- Citrate Agar Electrophoresis
- Alkaline Globin Chain Electrophoresis
- Capillary Electrophoresis
- Molecular Methods

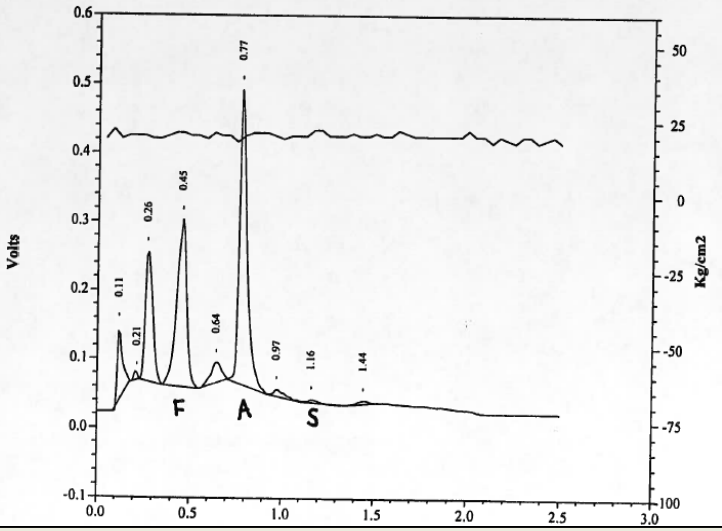
VII. Advantages, Limitations, and Testing Strategy

- Advantages
- Limitations



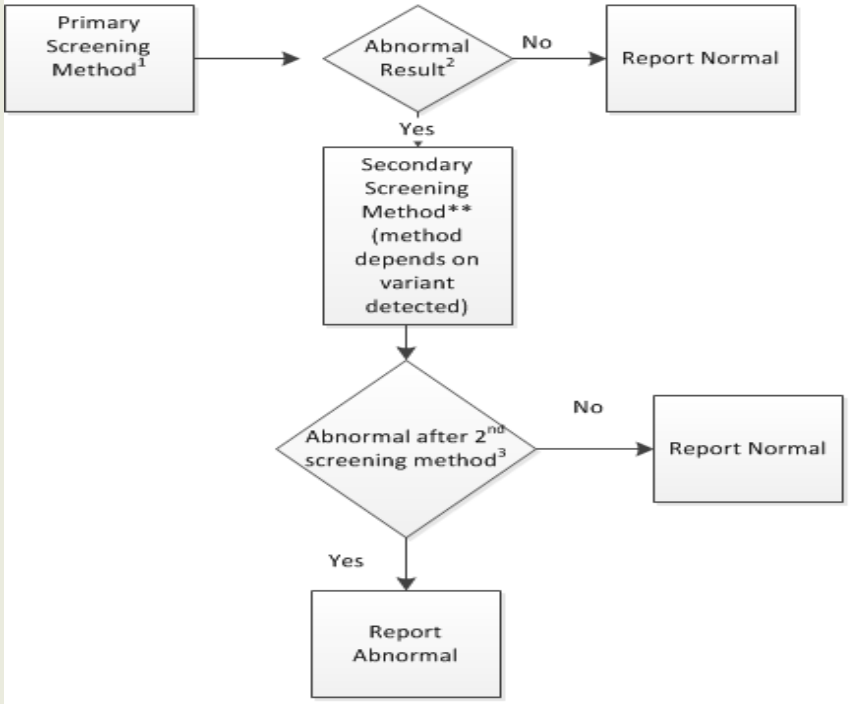
Peak	Peak Name	Retention Time (min)	Height	Area	Area %
1	FAST	0.112	110971	216914	7.0
2	Unknown	0.210	6625	17271	0.6
3	F1	0.264	188622	512679	16.5
4	F	0.450	242757	898514	29.0
5	OTHER(1)	0.636	29845	122276	3.9
6	A	0.768	427563	1263027	40.7
7	E/A2	0.967	10033	39342	1.3
8	S	1.156	4181	12865	0.4
9	OTHER(5)	1.437	4797	19952	0.6

Pattern: *FA
Total Area: 3102840



VIII. Algorithms

Typical Screening Algorithm

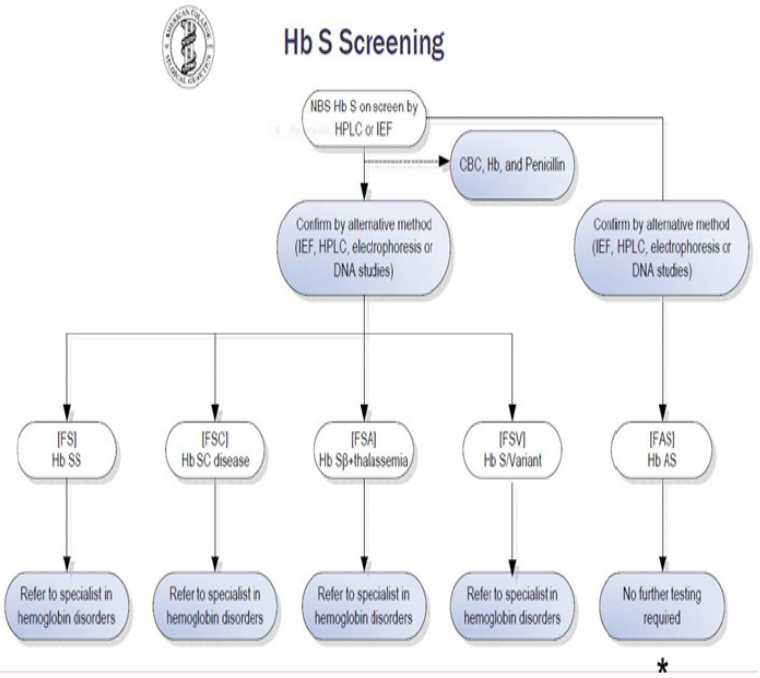


1. Primary screening methods are commonly IEF or HPLC depending laboratory

2. Note if unsuitable (because of specimen or test quality) result is obtained from primary screen, primary screen method is usually repeated before moving to next step

3. Secondary screeni methods are commonly IEF, HPL or Molecular metho depending type of variant detected b primary screening method and laboratory

Confirmatory Algorithm HbS



Abbreviations/ Key: F, S, A, C, and V = The hemoglobins seen in neonatal screening; HPLC: High performance liquid chromatography; IEF: Isoelectric focusing; ‡ = Repeat testing at 6 months age is required if genotyping to confirm the newborn screening result is not done.

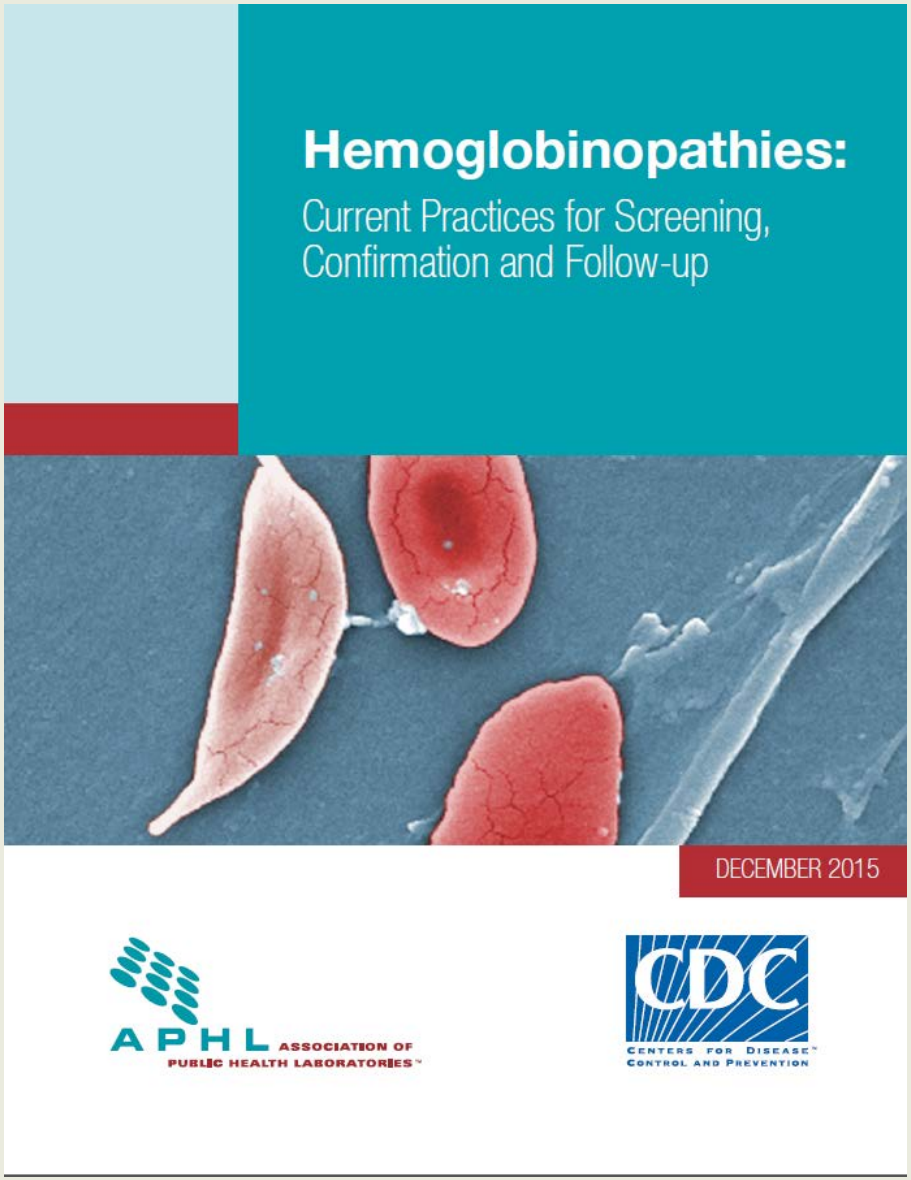
Source: Adapted from American College of Medical Genetics, 2009 and Dr. Aguinaga-NBS for Hemoglobinopathies in TN, from the 11th Annual Research Symposium in Obstetrics and Gynecology at Meharry Medical College-Nashville, TN. 2014.

IX. Quality Assurance

- Pre-analytical
- Analytical
- Post-analytical

X. Follow-up

- Short-term follow-up
- Relationship of lab and follow-up staff
- Training of follow-up staff
- Process algorithms for disease versus trait
- Follow-up activities for adult screening



Hemoglobinopathies: Current Practices for Screening, Confirmation and Follow-up

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Acknowledgements Again

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- Kwaku Ohene-Frempong – CHOP, Pennsylvania
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References

Centers for Disease Control and Prevention. (2015). Sickle Cell Disease: Data and statistics. Retrieved from http://www.cdc.gov/ncbddd/sicklecell/data.html

Centers for Disease Control and Prevention (n.d.). Sickle Cell Foundation of Georgia: Jackie George, Beverly Sinclar (photographer: Janice Haney Carr).

Ndeeezi G, Kiyaga C, Hernandez AG, Munube D, Howard TA, Ssewanyana I, Nsungwa J, Kiguli S, Ndugwa CM, Ware RE, Aceng JR. (2016). Burden of sickle cell trait and disease in the Uganda Sickle Surveillance Study (US3): a cross-sectional study. The Lancet. Retrieved from http://www.thelancet.com/pdfs/journals/langlo/PIIS2214-109X(15)00288-0.pdf

Tubman VN, Marshall R, Jallah W, Guo D, Ma C, Ohene-Frempong K, London WB, Heeney MM. (2016). Newborn screening for Sickle Cell Disease in Liberia: A pilot study. Pediatric Blood Cancer. doi: 10.1002/pbc.25875.

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