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1st Edition

NBS08

Newborn Screening for Hemoglobinopathies

This guideline describes the recommended protocols for detecting hemoglobinopathies and thalassemias by population-based newborn screening using dried blood spot specimens. Early, presymptomatic detection to identify newborns with abnormal hemoglobins is critical because it improves treatment effectiveness.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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NBS08, 1st ed.
October 2019

Newborn Screening for Hemoglobinopathies

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Abstract

Clinical and Laboratory Standards Institute guideline NBS08—*Newborn Screening for Hemoglobinopathies* describes the newborn screening (NBS) processes for testing dried blood spot specimens to detect hemoglobinopathies and thalassemias not usually evident at birth. Hemoglobinopathies and thalassemias are clinically significant congenital red blood cell disorders caused by structural or other hemoglobin abnormalities, resulting in various clinical manifestations. Early detection is critical, because without treatment, these conditions lead to increased morbidity and mortality. This guideline discusses various NBS approaches, including equipment considerations, laboratory screening methodologies, short-term and long-term follow-up processes, and future screening possibilities.

Clinical and Laboratory Standards Institute (CLSI). *Newborn Screening for Hemoglobinopathies.* 1st ed. CLSI guideline NBS08 (ISBN 978-1-68440-059-1 [Print]; ISBN 978-1-68440-060-7 [Electronic]). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2019.

Suggested Citation

CLSI. *Newborn Screening for Hemoglobinopathies.* 1st ed. CLSI guideline NBS08. Wayne, PA: Clinical and Laboratory Standards Institute; 2019.

ISBN 978-1-68440-059-1 (Print)
ISBN 978-1-68440-060-7 (Electronic)
ISSN 1558-6502 (Print)
ISSN 2162-2914 (Electronic) Volume 39, Number 12

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NBS08

Acknowledgment for the Expert Panel on Newborn Screening

CLSI, the Consensus Council, and the Document Development Committee on Preterm Newborn Screening gratefully acknowledge the Expert Panel on Newborn Screening for serving as technical advisors and subject matter experts during the development of this guideline.

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Contents

Contents (Continued)

Foreword

Since the implementation of universal newborn dried blood spot (DBS) screening, mortality in children with sickle cell disease (SCD) aged 1 to 4 years has decreased by 50%.[1-5] This dramatic decline in mortality is believed to result from multiple interventions, including early initiation of penicillin prophylaxis.[6] Timely interventions are made possible by early diagnosis, which results from newborn DBS screening coupled with comprehensive follow-up diagnostic testing.

Sickling disorders and thalassemias are among the most prevalent monogenetic diseases worldwide. The screening techniques currently used are primarily based on US experiences and have the longest history and most comprehensive use. The significant effects of hemoglobinopathies on US health care over time, particularly sickle cell anemia and other forms of SCD, can be measured by the availability of various SCD-related federal and state public health programs and funding streams.[7] Partially because of these programs, universal newborn DBS screening for hemoglobinopathies is now required in all 50 states, the District of Columbia, and many US territories. As of 2016, full-population hemoglobinopathy DBS screening also exists in eight Canadian provinces, seven European countries, and three Latin American countries. Additionally, pilot or targeted hemoglobinopathy screening exists in several other European, Latin American, Asian, Middle Eastern, and African countries.[8] Although newborn DBS screening has primarily focused on sickle hemoglobinopathies, there is increasing interest in newborn DBS screening for thalassemias, particularly in the Middle East and parts of Europe and Asia.

Various approaches to newborn DBS screening for hemoglobinopathies are used internationally. Variability exists not only in newborn screening (NBS) laboratory procedures but also in screening algorithms, results reporting, and patient follow-up. This guideline has been developed recognizing that although hemoglobinopathy NBS is expanding worldwide, no other informational, harmonizing resource is currently available. The comprehensive training and methodological guidance originally developed in the 1970s and 1980s are no longer readily available. Additionally, available hemoglobinopathy screening manuals are outdated.[9-11] Although some regulatory and quality improvement assistance is available to laboratories in the United States[12] and Europe,[13] it was not designed to harmonize the NBS program differences that currently exist. Guidance is needed to provide an accessible reference for basic newborn DBS screening and to assist NBS programs and medical professionals worldwide who may be initiating, expanding, or harmonizing newborn DBS screening for hemoglobinopathies.

NOTE: The content of this guideline is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

Key Words

Hemoglobinopathy, newborn screening, sickle cell anemia, sickle cell disease, thalassemia

Newborn Screening for Hemoglobinopathies

Chapter 1: Introduction

This chapter includes:

- Guideline's scope and applicable exclusions
- Background information pertinent to the guideline's content
- Standard precautions information
- "Note on Terminology" that highlights particular use and/or variation in use of terms and/or definitions
- Terms and definitions used in the guideline
- Abbreviations and acronyms used in the guideline

Hemoglobinopathies are a group of inherited blood disorders characterized by the presence of structural hemoglobin variants or quantitative differences in globin chain production. Results reporting, particularly for carriers, may sometimes be complicated by regulatory and ethical issues. Although many newborn screening (NBS) programs primarily focus on detecting and reporting sickle cell disease (SCD), they may also detect and/or report the presumptive presence of other clinically significant hemoglobin disorders, including both α and β thalassemias, as well as heterozygotes (carriers).

1.1 Scope

This guideline focuses on the NBS laboratory analytical processes for detecting SCD and other clinically significant hemoglobin disorders, including basic information about the biological and clinical features of clinically significant hemoglobinopathies detectable through NBS. It also provides information on preanalytical considerations affecting laboratory detection of hemoglobinopathies in NBS, including dried blood spot (DBS) specimen stability considerations. Various NBS procedures for hemoglobinopathy detection are discussed, with details of the methods included in the appendixes following a general template to allow easier comparisons between the different screening technologies. Terminology and reporting recommendations are included, along with other postanalytical NBS activities, including both short-term follow-up (STFU) activities (tracking and confirmatory testing) and long-term follow-up (LTFU) activities (outcome indicators, registries, care coordination, and access to services).

The guideline's overall purpose is to provide sufficient information for worldwide quality NBS process implementation, evaluation, and harmonization. This guideline may also inform policymaking for ensuring quality NBS results. Intended users of this guideline include:

- NBS laboratory and associated follow-up personnel
- Hospital personnel managing newborn DBS specimen collection activities, including:
  - Newborn DBS specimen collection supplies management
  - Newborn DBS specimen collection and transmittal process
  - NBS patient follow-up
  - NBS recordkeeping
- Medical personnel advising NBS programs and caring for affected newborns