CLSI NBS10™

Newborn Screening for Congenital Hypothyroidism

Sample

CLSI NBS10 describes a newborn screening system for detecting congenital hypothyroidism (CH). It discusses both first-tier and second-tier screening tests performed on newborn dried blood spot specimens, as well as screening strategies for identifying newborns at increased risk for CH.

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

Newborn Screening for Congenital Hypothyroidism

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Abstract

Clinical and Laboratory Standards Institute NBS10—*Newborn Screening for Congenital Hypothyroidism* describes newborn screening (NBS) processes used worldwide to identify newborns at increased risk for congenital hypothyroidism (CH). CH is one of the most common diseases detected by NBS, occurring in as many as 1 in 2000 live births and even more frequently in iodine-deficient areas. Presymptomatic detection through NBS can lead to early diagnosis and treatment, which reduces or eliminates the permanent intellectual disability and growth failure that occurs in individuals with untreated CH. CLSI NBS10 describes the laboratory screening tests for detecting primary CH, as well as the various laboratory screening algorithms in use, including the advantages and disadvantages of each. It also describes other types of CH that may be detected by NBS, such as central, transient, or subclinical CH. CLSI NBS10 is intended for use by health care providers, birthing facilities, NBS laboratories, regulatory agencies, public health policy makers, and manufacturers of instruments, reagents, and related NBS products.

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Foreword

The goal of newborn screening (NBS) is presymptomatic detection of at-risk newborns, generally through use of dried blood spot (DBS) specimens that are analyzed in specialized NBS laboratories. Ideally, NBS systems provide well-organized, highly effective, population-based services that apply preventive medicine principles to reduce death and disability from many congenital diseases or disorders. NBS systems should be comprehensive. They may include health care providers (HCPs), birthing facilities, public health programs, policy makers, insurers, and families, among others. NBS programs should be linked to follow-up HCPs for rapid diagnosis and initiation of treatment. NBS systems encompass preanalytical, analytical, and postanalytical activities, which include education; collection and laboratory analysis of DBS specimens; results reporting; referral to clinical care (short-term follow-up); diagnosis, intervention, programmatic evaluations, and evaluation of health outcomes (long-term follow-up); quality assurance; and quality improvement.

Congenital hypothyroidism (CH) is one of the most common diseases detected by NBS, occurring in as many as 1 in 2000 live births in most populations and even more frequently in iodine-deficient areas. Presymptomatic detection through NBS leads to early diagnosis and treatment, which drastically reduces or eliminates the permanent intellectual disability and growth failure that occurs in children with untreated CH. Since the 1970s, NBS for CH has been introduced in many countries. Presently, all high-resource and many low-resource jurisdictions screen newborns for CH. However, two-thirds of the world's newborns are not screened.[1] In those locations, including places where iodine deficiency makes CH more common, newborns with CH are usually not detected or treated early. The economic and social burden of intellectual disability due to CH remains a public health challenge.

CLSI NBS10 describes laboratory screening algorithms for CH detection that use thyrotropin (ie, thyroid-stimulating hormone), total thyroxine (T4), or both as first-tier screening tests. It also summarizes variations in screening protocols, including measurement of free T4 and thyroxine-binding globulin and point-of-care testing. The advantages and disadvantages of each strategy are explained. This globally applicable guideline is intended to help new and existing programs evaluate and refine procedures and practices for all aspects of CH NBS.

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

congenital hypothyroidism	**thyroid-stimulating hormone**	**thyroxine-binding globulin**
dried blood spot specimens	**thyrotropin**	
newborn screening	**thyroxine**	

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Chapter ❶

Introduction

Newborn Screening for Congenital Hypothyroidism

① Introduction

1.1 Scope

CLSI NBS10 provides recommendations for using dried blood spot (DBS) specimens to perform newborn screening (NBS) for congenital hypothyroidism (CH) and discusses the preanalytical, analytical, and postanalytical aspects of CH NBS. It describes:

- Etiology and clinical manifestations of CH
- Analytical methodologies for thyroid-stimulating hormone (TSH) and total thyroxine (T4)
- Screening strategies and laboratory screening algorithms currently used, including single- or multi-tier testing, that begin with measurements of TSH, total T4, or both
- Variations in TSH and/or total T4 screening strategies, including explanations of the advantages and disadvantages of each strategy
- Successful laboratory practices, including method validation and/or verification, QA, and results interpretation
- Recommendations on implementing CH NBS for emerging programs

The intended users of CLSI NBS10 are NBS laboratories, follow-up and program personnel, birthing facilities, public health program administrators, medical laboratories, pediatric endocrinologists, neonatologists, other health care providers (HCPs), regulatory agencies, public health policy makers, and manufacturers of instruments, reagents, and related NBS products.

CLSI NBS10 does not cover:

- Methodologies for free thyroxine (FT4), thyroglobulin, or point-of-care (POC) testing
- Laboratory testing performed to confirm or exclude a diagnosis (ie, diagnostic testing)
- Recommendations for diagnosis or treatment of CH
- Comparative cost information

1.2 Background

NBS with DBS specimens began in the 1960s, when a bacterial inhibition assay for detecting phenylalanine as a marker for phenylketonuria was introduced.[2] In the 1970s, radioimmunoassays for detecting total T4 and TSH in DBS specimens were developed, providing a tool for inclusion of CH in NBS programs (see Additional Resources).[3-5] Since then, NBS for CH has been introduced in most NBS programs. Testing and treatment for CH are simple, inexpensive, and effective. Also, CH has a relatively high prevalence, particularly in areas where iodine deficiency is common. Globally, the birth prevalence of CH is approximately 1 in 2000 and even higher in iodine-deficient areas. Unfortunately, about 70% of newborns worldwide are born in areas without an established NBS program. Thus, CH is usually not detected or treated early. The prevention of the cognitive impairment and developmental delay associated with CH is possible only with early treatment. The initiation of treatment as soon as possible is crucial for normal intellectual outcome.[6-8]

Appendix B. (Continued)
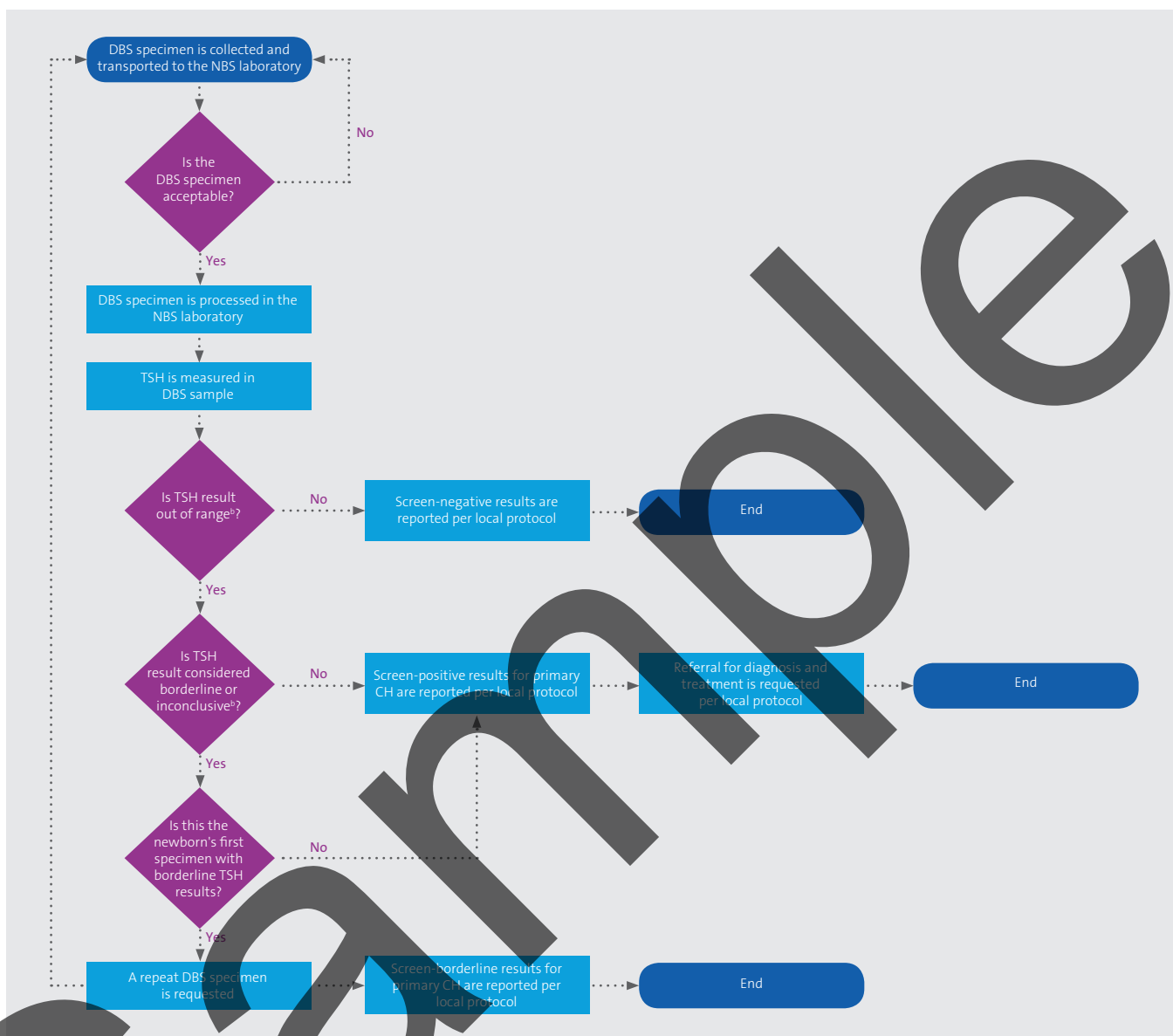
Abbreviations: CH, congenital hypothyroidism; DBS, dried blood spot(s); NBS, newborn screening; TSH, thyroid-stimulating hormone.
[a] Four basic symbols are used in this process flow chart: oval (signifies the beginning or end of a process), arrow (connects process activities), box (designates process activities), diamond (includes a question with alternative "Yes" and "No" responses).
[b] Standard laboratory practice is to retest in duplicate for any abnormal result.

Figure B1. First-Tier TSH Screening.[a] This model is a simplification of laboratory screening algorithms used by many NBS programs. Programs that perform second-tier T4 testing have more complex algorithms. Cutoff values vary among programs, and age-adjusted TSH cutoffs should be considered (eg, higher cutoffs for newborns < 24 hours, lower cutoffs for newborns > 72 hours). Borderline results are considered screen positive. In the case of a borderline TSH result from a second DBS specimen, most programs request referral for diagnosis and treatment. If retest results are inconclusive, a repeat specimen is requested. This protocol does not enable detection of central CH.

Sample