Screening for and Treatments of Congenital Immunodeficiency Diseases

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KEYWORDS

- Severe combined immunodeficiency (SCID) • T-cell lymphopenia
- T-cell receptor excision circles (TRECs) • Newborn screening (NBS)
- Hematopoietic stem cell transplantation (HSCT)

KEY POINTS

- Newborn screening (NBS) for severe combined immunodeficiency (SCID) is possible with the T-cell receptor excision circle assay.
- This program has proved effective at diagnosing SCID as well as other disorders associated with T-cell lymphopenia.
- With early diagnosis and infection prophylaxis, infants born with SCID have the best opportunity for successful treatment with stem cell transplant.
- The successful development and implementation of the T-cell receptor excision circles assay for SCID raises the possibility of other immune deficiency screening programs.
- Challenges remain for the NBS program for SCID, such as vulnerable populations that are reluctant to screen, as well as the need for qualified immunologists to care for the children detected.

INTRODUCTION

Newborn screening (NBS) programs are highly successful public health programs designed to detect rare, but treatable, inborn errors of metabolism. A NBS program for severe combined immunodeficiency (SCID) was developed recently and was implemented in several states. This article provides a description of this screening program, summarizes its initial findings, and reviews the pitfalls of this program.

HISTORICAL PERSPECTIVES OF NEWBORN SCREENING

Population-based screening programs began in 1963 with the demonstration that phenylketonuria can be detected in the neonatal period for all newborns, before the

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onset of cognitive symptoms, allowing dietary modification and prevention of long-term disability.[1] The ability to screen for other disorders has increased dramatically, leading to controversies about expanding screening programs. To address these concerns, Wilson and Jungner[2] published a pivotal report that attempted to strike a balance between the desire for early detection and treatment of disease, and the potential harms to patients and society.[2] This report defined the characteristics of disorders that were amenable to NBS, such as disease incidence and severity, the presence of a sensitive test to detect the disorder, as well as a curative treatment (**Box 1**). Although the characteristics outlined by Wilson and Jungner[2] guided the development and implementation of NBS programs and created a platform for understanding of the ethics of screening tests, there is an ongoing need for expansion and reassessment of these criteria as novel medical technologies are developed.[3–5] The Health Resources and Services Administration (HRSA) commissioned the American College of Medical Genetics (ACMG) to develop national NBS standards. This task force ultimately recommended that NBS for 31 conditions be mandated in all states.[5] Despite these national efforts at uniformity for NBS programs, each state administers its own panel of tests.

The primary imperative of NBS remains the identification and early intervention of treatable disorders. These screening programs have been highly successful in preventing the long-term disability associated with inborn errors of metabolism, and congenital hypothyroidism is one of the best examples of this.[6] Congenital hypothyroidism is one of the most common inborn errors of metabolism, occurring in 1 in 2500 infants. Congenital hypothyroidism is characterized by progressive neurologic dysfunction that can lead to mental retardation, which can be prevented by early treatment with hormone replacement. With the implementation of NBS for hypothyroidism, the incidence of mental retardation caused by this disorder has been reduced by more than 90%.[6] NBS for congenital hypothyroidism has proved to be a highly cost-effective when the long-term costs of caring for individuals who develop mental impairment caused by congenital hypothyroidism are considered.

As understanding of the molecular basis of diseases improves, novel methods to detect disorders that are amenable for high-throughput population-based screening are increasingly available and are constantly being evaluated for possible additions

Box 1
Wilson and Jungner NBS criteria

1. The condition sought should be an important health problem.
2. There should be an accepted treatment of patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care.
10. Case finding should be a continuing process and not a once-and-for-all project.