Introduction to the Newborn Screening, Diagnosis, and Treatment for Pompe Disease Guidance Supplement

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Started in 1963 by Robert Guthrie, newborn screening (NBS) is considered to be one of the great public health achievements.[1] The original goal of NBS was to screen newborns for conditions that could benefit from presymptomatic treatment and therefore reduce associated morbidity and mortality. As new methods became available that allowed for better screening of newborns (eg, tandem mass spectrometry), the scope of NBS broadened and the number of disorders included in NBS programs increased significantly.[1,2]

Lysosomal storage disorders (LSDs), which include >50 genetic disorders caused by dysfunctional or deficient activity of specific lysosomal enzymes, are good candidates for NBS.[3–7] Pompe disease, a rare, autosomal recessive inherited LSD, is caused by mutations in the acid α-glucosidase (*GAA*) gene that lead to a deficiency of the lysosomal GAA enzyme. As a result, excess glycogen accumulates in many tissues throughout the body and causes cellular dysfunction and progressive damage to respiratory, cardiac, skeletal, and smooth muscle; considerable clinical debilitation; organ and system failure; and often death.[8] There is a low index of clinical suspicion due to the rarity and heterogeneous nature of Pompe disease's clinical presentation, often resulting in delays in diagnosis.[9–11] The availability of a specific treatment for Pompe disease, namely enzyme replacement therapy (ERT) with alglucosidase alfa,[12,13] that can treat this progressive disorder makes early diagnosis crucial, especially in infants with classic infantile-onset Pompe disease, the most severe form of the disease. Without treatment, these patients die before 2 years of age. Early initiation of ERT for these patients can impact and often determine survival. Thus, Pompe

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disease is a good candidate for NBS.[5,14] In March 2015, Pompe disease was approved by the US Secretary of Health and Human Services for inclusion on the Recommended Uniform Screening Panel (RUSP), the list of diseases recommended for NBS.

THE POMPE DISEASE NEWBORN SCREENING WORKING GROUP

Although NBS programs have been implemented in several countries around the world, including the United States, programs and efforts for the LSDs, including Pompe disease, have been inconsistent, mainly due to the fact that decisions are made at regional and local levels.[2,15] With this in mind, the Pompe Disease Newborn Screening Working Group, a group comprising international experts in Pompe disease and NBS, met to share their clinical experience and expertise, with the hopes of stimulating the best practice in NBS for Pompe disease globally. The Working Group's primary goal was to develop a general guidance document for NBS for Pompe disease for practitioners around the world. The group also recognized that the recommendations they provide are general and will have to be adjusted as needed due to differences in the characteristics of patient subgroups and regional delivery of care that must be considered and integrated into the management and care of individual patients.

The result of the Working Group's efforts is the "Newborn Screening, Diagnosis, and Treatment for Pompe Disease" guidance supplement, a compilation of 4 separate articles each covering an important topic in NBS, published in this issue of *Pediatrics*. Each article was authored by a subgroup of Working Group members who summarized and reported the entire Working Group's recommendations for each respective topic. All articles were reviewed and approved by the entire Working Group before publication. The articles included in the supplement with the Working Group members who were authors for each section are:

- "Newborn Screening for Pompe Disease" (Olaf A. Bodamer, C. Ronald Scott, and Roberto Giugliani);
- "The Initial Evaluation of Patients After Positive Newborn Screening: Recommended Algorithms Leading to a Confirmed Diagnosis of Pompe Disease" (Barbara K. Burton, David F. Kronn, Wuh-Liang Hwu, and Priya S. Kishnani);
- "Management of Confirmed Newborn-Screened Patients With Pompe Disease Across the Disease Spectrum" (David F. Kronn, Debra Day-Salvatore, Wuh-Liang Hwu, Simon A. Jones, Kimitoshi Nakamura, Torayuki Okuyama, Kathryn J. Swoboda, and Priya S. Kishnani); and
- "The Role of Genetic Counseling in Pompe Disease After Patients Are Identified Through Newborn Screening" (Andrea M. Atherton and Debra Day-Salvatore).

The guidance in this supplement from these experts is meant to provide an overview of NBS and screening programs for Pompe disease; share insight into what steps lead to a confirmed diagnosis of Pompe disease and raise awareness of current challenges facing clinicians and NBS laboratories that may impact an accurate diagnosis of Pompe disease; highlight factors that influence and determine the appropriate timing of initiation of treatment that warrant careful consideration, detail the monitoring and appropriate follow-up of patients who are being treated with ERT, and increase understanding of the nuances involved in the management of the different subgroups of patients; and explain the need for and importance of genetic counseling for all patients and their families and caregivers.

The Pompe Disease Newborn Screening Working Group emphasizes that the recommendations made in this supplement are based on their current knowledge and experience and will be revised periodically as the medical community's knowledge of Pompe disease expands and changes as they learn more from patients who are living longer. The Working Group also wishes to emphasize that this guidance summary is intended to provide a review of NBS and Pompe disease and overall recommendations and not to provide an overview of Pompe disease.

These guidelines and recommendations do not necessarily reflect the policy of the American Academy of Pediatrics, and publication herein does not imply endorsement.

The Working Group recognizes that there are a number of challenges that present with NBS for Pompe disease. Despite the challenges, however, they emphasize the importance of NBS for Pompe disease and the need for early identification of patients with this progressive, debilitating disease. It is with this goal in mind that the members of the Pompe Disease Newborn Screening Working Group, who are experts in both NBS and Pompe disease, wish to share their recommendations based on their current knowledge and experience, thus providing a general standard framework for early identification of patients and accurate diagnosis of Pompe disease through NBS.

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ABBREVIATIONS

ERT: enzyme replacement therapy
LSD: lysosomal storage disorder
NBS: newborn screening

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