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

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Both authors are members of the Pompe Disease Newborn Screening Working Group and have experience in newborn screening and in treating and caring for patients with Pompe disease, and both authors provided input and reviewed and approved the content for all articles of the supplement.

DOI: https://doi.org/10.1542/peds.2016-0280B

Accepted for publication Mar 8, 2017

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Sanofi Genzyme (Cambridge, MA) facilitated and provided financial support for the meeting of the Pompe Disease Newborn Screening Working Group to discuss and develop the recommendations provided in all articles comprising the Newborn Screening, Diagnosis, and Treatment for Pompe Disease guidance supplement and also paid for editorial and writing support for this supplement. The recommendations and opinions expressed in this article and in all others in the Supplement are those of the authors based on their clinical expertise and experience and do not necessarily reflect those of Sanofi Genzyme.

POTENTIAL CONFLICT OF INTEREST: Dr Kishnani received consulting fees, honoraria, and/or research funding from Sanofi Genzyme, Amicus Therapeutics, Baebies, Shire Pharmaceuticals, Alexion, and the Lysosomal Disease Network and is a member of the Pompe and Gaucher Disease Registry Advisory Boards for Sanofi Genzyme; and Dr Hwu received research grants and consultation fees from Sanofi Genzyme.

The guidelines/recommendations in this article are not American Academy of Pediatrics policy, and publication herein does not imply endorsement. 2017; 140(s1):e20160280B

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.9 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...
Pompe disease is a good candidate for
NBS. 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. 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.

ACKNOWLEDGMENTS

The members of the Pompe Disease
Newborn Screening Working
Group (in alphabetical order) are
as follows: Andrea M. Atherton,
MS, CGC, Children’s Mercy Hospital
for critical review of the manuscripts and Marianne B. Zajdel of Sanofi Genzyme for medical writing support.

**ABBREVIATIONS**

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

**REFERENCES**

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*Pediatrics* 2017;140;S1

DOI: 10.1542/peds.2016-0280B

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