Newborn Screening for Pompe Disease

A Summary of the Evidence and Advisory Committee Decision

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EXECUTIVE SUMMARY

This summary reviews the information the federal advisory committee used when deciding whether to recommend adding Pompe Disease to the Recommended Uniform Screening Panel (RUSP) in 2013.

About the condition

Pompe Disease is a rare disease caused by a change in a single gene. Studies of patients with symptoms suggest that between 1 and 2.5 out of every 100,000 people have Pompe Disease. People with Pompe Disease do not have enough of the GAA enzyme that helps the body break down stored sugar. Babies with the disease appear normal. There are 2 types of Pompe Disease: infantile- and late-onset. The first type can cause muscle problems that begin in early infancy. Most children with Pompe Disease have the late-onset type. Problems from the disease can worsen quickly and cause death within the first year.

Treatment for Pompe Disease

There is no cure for Pompe Disease. Early diagnosis allows early treatment and improves outcomes for babies with Pompe Disease. Enzyme replacement therapy can stop Pompe Disease problems from getting worse.

Detecting Pompe Disease in newborns

Newborn screening for Pompe Disease can happen along with routine newborn screening for other conditions in the first few days of life. Newborn Pompe Disease screening measures GAA enzyme activity. This process uses the same dried blood spots already collected to screen for other disorders. Newborns with low GAA activity have higher risk for the disease. They need more testing to diagnose the condition.

Public health impact

Based on what is known about screening and the risk of being born with Pompe Disease, experts think that screening all newborns in the United States for Pompe Disease would find about 144 babies with the disease each year (about 3.6 out of every 100,000 children born). It would prevent up to 28 people with the disease from needing a breathing machine and up to 19 deaths due to the disease each year.

Committee decision

The Committee voted in 2013 to recommend adding Pompe Disease to the RUSP. As of 2015, the RUSP recommends that state newborn screening programs include Pompe Disease.

ABOUT THIS SUMMARY

What is newborn screening?

Newborn screening is a public health service that can change a baby's life. Newborn screening involves checking all babies to identify those few who look healthy but who are at risk for one of several serious health conditions that benefit from early treatment.

Certain serious illnesses can be present even when a baby looks healthy. If the baby does not receive screening for these illnesses early in life, a diagnosis may be delayed. Later treatment might not work as well as earlier treatment. Newborn screening programs have saved the lives and improved the health of thousands of babies in the United States (US).

Who decides what screening newborns receive?

In the US, each state decides which conditions to include in its newborn screening program. To help states determine which conditions to include, the US Secretary of Health and Human Services provides a list of conditions recommended for screening. This list is called the Recommended Uniform Screening Panel (RUSP).

Progress in screening and medical treatments can lead to new opportunities for newborn screening. To learn how a condition is added to the RUSP, see **Box A**.

What will this summary tell me?

In 2012, the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) requested an evidence review of newborn screening for Pompe Disease. This summary presents key review information that the Committee used to make its decision about whether to recommend adding Pompe Disease to the RUSP. It will answer these questions:

- What is Pompe Disease?
- How is Pompe Disease treated?
- How are newborns screened for Pompe disease?
- Does early diagnosis or treatment help patients with Pompe Disease?
- What is the public health impact of newborn Pompe Disease screening in the US?
- What did the Committee decide about adding Pompe Disease to the RUSP?

Box A: Adding a Condition to the RUSP

A committee, called the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC), makes a recommendation to the US Secretary of Health and Human Services about adding specific conditions to the RUSP. The Committee bases its decision on a review of the condition, the screen, the treatment, and the ability of newborn screening programs to check for the condition. To learn more about the ACHDNC, visit this website.

UNDERSTANDING THE CONDITION

What is Pompe Disease?

Pompe Disease is a rare genetic disorder. People with Pompe Disease have a change in a single gene called GAA. Normally, this gene makes the GAA enzyme, which helps the body break down stored sugar. In people with Pompe Disease, the enzyme does not work properly. As a result, stored sugar builds up in the muscles and causes serious health problems.

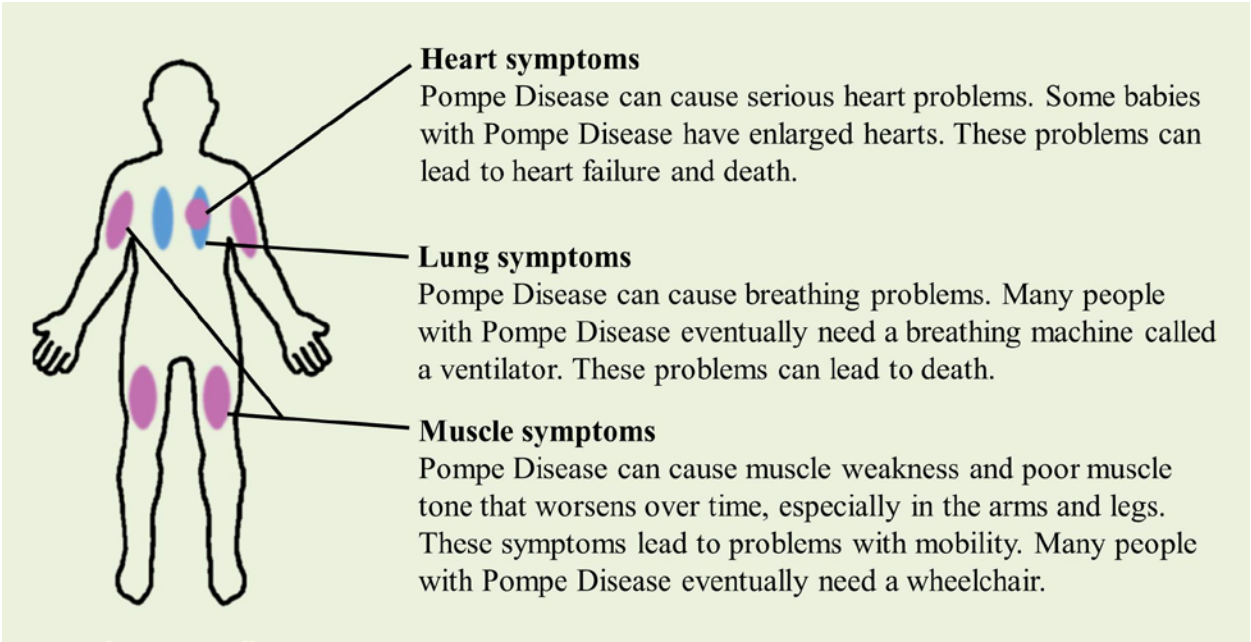
How common is Pompe Disease?

- Pompe Disease is rare. Between 1 and 2.5 out of every 100,000 children receive a diagnosis of Pompe Disease.
- This estimate is based on the number of people who develop symptoms and receive a diagnosis without newborn screening. Not everyone with Pompe Disease is diagnosed, so the estimate might be low.

What kinds of health problems does Pompe Disease cause?

Pompe Disease mainly affects the muscles, including the heart, arms and legs, and breathing muscles (Figure 1).

Figure 1: Pompe Disease Symptoms.



Are there different types of Pompe Disease?

Yes. Doctors classify Pompe Disease into 2 types based on when symptoms start:

- Infantile-Onset: This type of Pompe Disease is the most severe. Babies with this type usually have a GAA enzyme that does not work at all. They have symptoms early and can die within the first year of life. One out of every 3 or 4 people with Pompe Disease have this type.
- Late-Onset: This type of Pompe Disease varies in severity. People with this type usually have a partly working GAA enzyme. They may or may not get sick. If they do, symptoms arise from later childhood through adulthood. Most people with Pompe Disease have this type.

When do Pompe Disease symptoms develop?

The timing and type of problems caused by Pompe Disease differ for different people. Table 1 explains when Pompe Disease symptoms may arise.

Table 1: Symptom Timing and Type.

Age	Sign/Symptom	Details
Birth	No signs	• Pompe Disease is present at birth. However, newborns usually have no visible signs.
Early infancy	Infantile-Onset Pompe Disease symptoms	• Most babies with this type have symptoms in the first few months of life. • Symptoms include weakness and serious heart or muscle problems. • Without treatment, this type causes death during the first year of life or early childhood.
Childhood through adulthood	Late-Onset Pompe Disease symptoms	• Symptoms start later than in Infantile-Onset Pompe Disease. When they start can vary. • Symptoms include muscle weakness and breathing problems. • Without treatment, this type can cause death at middle or older ages.

TREATMENT FOR POMPE DISEASE

How is Pompe Disease treated?

There is no cure for Pompe Disease. Once a patient has symptoms, the patient needs treatment for each affected system of the body.

One treatment that may stop Pompe Disease problems from getting worse is enzyme replacement therapy (ERT). ERT works by replacing some or all of the missing GAA enzyme.

People who need ERT receive a 4-hour treatment every 1 or 2 weeks to put the GAA enzyme into their blood. Patients with Pompe Disease need ERT throughout their lives. ERT can slow or even prevent problems from the disease. ERT can lower the risk of death or needing a ventilator.

What are the risks of treatment for Pompe Disease?

Some people have serious allergies to ERT. These can be dangerous for people with Pompe Disease, particularly because of their breathing problems.

Some patients have an immune system response to ERT. This response can make ERT less effective. It can also make symptoms worse. Other treatments can help ERT work in these patients. Doctors monitor patients receiving ERT closely.

FINDING NEWBORNS WHO HAVE POMPE DISEASE

How are newborns screened for Pompe Disease?

Newborn screening for Pompe Disease can happen along with other routine newborn screening in the first few days of life. Most newborn screening begins when a doctor or nurse collects a few drops of blood from a baby's heel and dries them onto a special piece of paper. The hospital sends these "dried blood spots" to the state's newborn screening program. The program uses a laboratory to check the dried blood spot for many disorders.

To screen for Pompe Disease, laboratories use special equipment to measure GAA enzyme activity in the dried blood spots. Low GAA activity means a higher risk for Pompe Disease.

When a newborn has low GAA activity, the baby needs more tests. The newborn screening program works with the baby's doctor when screening results mean that the baby should receive other tests or see a specialist to tell for sure if the baby has Pompe Disease.

How well does screening for Pompe Disease work?

Screening identifies babies with low or no GAA activity. After further testing, some of these babies receive a diagnosis of Pompe Disease. Others do not have Pompe Disease. Screening cannot diagnose Pompe Disease, but it can determine which babies should receive more tests or see a specialist.

Experts think that screening detects all babies with infantile-onset and most babies with late-onset disease. Screening cannot distinguish between the disease types. Experts in the field and newborn screening programs continuously work to make screening better.

What happens if newborn screening indicates a high risk for Pompe Disease?

Doctors refer newborns at high risk for Pompe Disease for more testing. Doctors can diagnose Pompe Disease by checking for a problem with the GAA gene. They also examine babies to look for certain symptoms. These tests may tell doctors about how severe the disease is or how best to treat the baby. They cannot always distinguish between Pompe Disease types. Babies with Pompe Disease need close monitoring.

What are some of the benefits and risks of newborn Pompe Disease screening?

Table 2 describes benefits/risks of newborn Pompe Disease screening as of 2013.

Table 2: Benefits and Risks of Screening.

Benefits	Risks
• Earlier identification and evaluation of babies at high risk for Pompe Disease.	• Some babies identified from newborn screening do not have Pompe Disease. All babies with low GAA activity need more testing.
• Earlier diagnosis.	• The timing and type of problems caused by Pompe Disease are hard to predict. • Screening and follow-up testing cannot always distinguish the disease types.
• Earlier monitoring and treatment.	• Earlier exposure to treatment risks. • Most people with Pompe Disease detected through newborn screening have late-onset disease. They may not need treatment right away.
• More time to plan for the future.	• More anxiety about the future.
• Health counseling and family planning for family members.	• Sometimes, people do not want to know genetic risks. Some families do not like to share health information.
• Reassurance for the families of babies who do not have low GAA activity.	• Unnecessary anxiety for families of babies with low GAA activity who do not have Pompe Disease.

Does early diagnosis or treatment help patients with Pompe Disease?

Experts think that **early diagnosis** from newborn screening improves the lives of babies with Pompe Disease. Babies identified after newborn screening are less likely to die or need a ventilator than babies identified after symptoms develop.

Early diagnosis allows **early treatment**, which can lead to better outcomes for people with Pompe Disease.

- **Infantile-Onset Pompe Disease**

  For this type, early ERT lowers the risk of death or needing a ventilator. It may also help with movement and brain development. Babies who receive ERT before symptoms arise may benefit most.

- **Late-Onset Pompe Disease**

  For this type, experts need more data to know how much early ERT helps. ERT cannot fix muscle or heart damage that has already happened. However, it may prevent new damage from occurring.

Box B: Where Can I Learn More?

Follow the links below to learn more about topics from this summary.

- To learn more about Pompe Disease, visit the National Institutes of Health Pompe Disease website.
- Visit the Committee's website to learn more about:
  - Nominating conditions to the RUSP.
  - Full Pompe Disease evidence report.
  - The ACHDNC recommendation to the Secretary to add Pompe Disease to the RUSP.

PUBLIC HEALTH IMPACT

How would newborn Pompe Disease screening affect the health of the country?

Based on what is known about screening and the risk of being born with Pompe Disease, experts think that screening all newborns in the US for Pompe Disease would do the following:

- Find about 144 babies with Pompe Disease each year (about 3.6 out of every 100,000 children born).
- Prevent between 20 and 28 people with Pompe Disease from needing a ventilator each year.
- Prevent between 8 and 19 deaths due to Pompe Disease each year.

Without screening, diagnosing infantile-onset disease can take several months after a baby develops symptoms. For late-onset disease, diagnosis can take 8 years or longer after symptoms develop. Sometimes, the diagnosis is never made. Newborn screening for Pompe Disease allows diagnosis early in life before symptoms arise.

What is the status of US newborn Pompe Disease screening?

- At the time of the report, one state (Missouri) screened newborns for Pompe Disease. Three more (Illinois, New Jersey, and New Mexico) had mandates to start.
- Most states estimated that newborn Pompe Disease screening could begin several months to several years after funding became available.

ADVISORY COMMITTEE DECISION

What did the Committee recommend?

The ACHDNC voted in 2013 to recommend adding Pompe Disease to the RUSP. The Committee based its decision on the ability of screening to find babies with Pompe Disease and early treatment being better than later treatment. In 2015, the US Secretary of Health and Human Services recommended that all newborns receive Pompe Disease screening.

To screen for any condition, states must be prepared. They must have the right equipment and procedures. There must also be specialists who can work with families to determine whether a baby has the condition and, if so, the best treatment.

HELPFUL INFORMATION

Glossary

Term	Definition
ACHDNC	Advisory Committee on Heritable Disorders in Newborns and Children. The committee that oversees the RUSP.
Dried blood spot	A drop of blood that is collected from a baby's heel, dried onto a special piece of paper, and used to screen for many disorders.
ERT	Enzyme replacement therapy. A Pompe Disease treatment that works by replacing some or all of the missing GAA enzyme.
GAA gene	Problems with this gene cause Pompe Disease.
GAA enzyme	An enzyme that helps the body break down stored sugar.
Infantile-Onset Pompe Disease	The more severe type of Pompe Disease. It arises early and can cause death within the first year of life.
Late-Onset Pompe Disease	The less severe type of Pompe Disease. It arises in later childhood through adulthood.
Pompe Disease	A rare genetic disorder causing problems with the muscles, including the heart, arms and legs, and breathing muscles.
RUSP	Recommended Uniform Screening Panel. The list of conditions recommended for newborn screening.
Secretary of Health and Human Services	The head of the US Department of Health and Human Services. This person decides whether to add conditions to the RUSP.
Specialist	A doctor with expertise in a specific area of medicine.
Ventilator	A machine that helps with breathing.

Source

The information in this summary comes from the report *Evidence Report: Newborn Screening for Pompe Disease* (03 June 2013), which was commissioned by the ACHDNC. The report reviewed data on Pompe Disease screening and treatments in children through April 2013. It included both published and unpublished research. To see a copy of the report, visit this page.