NORTH CAROLINA NEWBORN SCREENING PROGRAM

Pompe Disease Fact Sheet for Providers

What is Pompe disease?

Pompe disease, also known as Glycogen Storage Disease Type II, is a genetic disorder caused by deficiency of the enzyme acid alpha-glucosidase (GAA). As a result of this deficiency, the substance glycogen accumulates in cardiac and skeletal muscle cells and causes damage. There are two distinct types of Pompe disease: infantile-onset Pompe disease (IOPD) and late-onset Pompe disease (LOPD).

What are the signs and symptoms of Pompe disease?

- IOPD: This is the most severe form of the disease. Infants develop profound, rapidly progressing muscle weakness and cardiomyopathy within the first few days, weeks, or months of life. They may present with failure to thrive, feeding problems/tongue weakness, or signs of cardiac failure. Left untreated, IOPD is fatal by 2 years of age. **A positive newborn screen for IOPD is an ABNORMAL (URGENT) result that requires immediate action.**
- LOPD: This represents a wide spectrum of disease. Patients do not present with cardiomyopathy. Instead, symptoms include more slowly progressive muscle weakness and are generally milder than IOPD. Symptoms can become apparent at any age, from within the first few months of life to adulthood. Treatment is dependent on age of symptom onset and/or disease progression. Symptoms are typically not apparent in newborns. **A positive newborn screen for LOPD is considered ABNORMAL (NOT URGENT), but does require timely follow-up.**

How is Pompe disease diagnosed?

A positive newborn screen does not confirm a diagnosis of Pompe disease. Additional testing is required to confirm the diagnosis and, if confirmed, to determine the type of Pompe disease. Additional testing includes the following:

- **Enzyme Testing:** A biochemical test that measures the level of GAA enzyme in blood and/or tissue
- **Molecular Testing:** Sequencing and deletion/duplication analysis of the *GAA* gene to identify gene mutations
- **Clinical Evaluation:** Echocardiogram, electrocardiogram, labs, and physical exam

How is Pompe disease treated?

There are treatment options available to prevent progression of symptoms and improve quality of life. Treatment of Pompe disease includes enzyme replacement therapy (ERT), a recombinant form of the deficient GAA enzyme given via weekly or biweekly IV infusion. A genetics team experienced in the treatment of Pompe disease should manage treatment with ERT.

- IOPD: Babies with IOPD should begin receiving weekly ERT as soon as possible to maximize outcomes. *Even days can make a difference.* There are two sub-types of IOPD:
  - Cross-reactive immunologic material (CRIM) negative (most severe) and CRIM positive
  - All CRIM negative patients will receive immune tolerance induction (ITI) with ERT initiation. Some CRIM positive patients will also receive ITI.
  - **Note:** ITI impacts vaccine schedules. You should work closely with the Duke Genetics team to plan a vaccine schedule for your patient.
- LOPD: Treatment with ERT is not usually required for infants with LOPD. These patients should be monitored closely for symptom progression. Initiation of treatment is often based on the discretion of the genetics team.

Regardless of the type of Pompe disease, most children with Pompe disease receive interventional therapies, such as physical therapy, speech/feeding therapy, and occupational therapy.

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How do I handle an abnormal screen for Pompe disease?

Your patient has had a positive newborn screen for Pompe disease. The newborn screen result will state ABNORMAL (URGENT) or ABNORMAL (NOT URGENT). Based on the results, the following actions should occur:

- **Abnormal (Urgent):** This result is concerning for IOPD. Your patient needs an urgent clinical evaluation with confirmatory testing by Duke University Pediatric Medical Genetics (PMG). If your patient is confirmed to have IOPD, treatment with ERT will be started immediately at Duke, and you will be notified of the results.
- **Abnormal (Not Urgent):** Your patient's initial newborn screen was a borderline result. Your patient's sample was then sent for second tier testing, which was positive. This result could represent LOPD, carrier status, or a pseudodeficiency. Your patient will need a non-urgent clinical evaluation within 3 business days.
- ACTION ITEMS:
  - Inform your patient's parent of the positive newborn screen.
  - Connect with Duke University (PMG)
  - Inform your patient's parent that they will be receiving a call from Duke PMG
  - Place a referral for your patient in your EMR and/or fax to Duke PMG. Referrals can be faxed to: 919-668-0414 attn: Duke Pompe NBS Team.
- If you see the patient in clinic in the interim or if any of the following signs were present on your first visits, please contact Duke PMG (919-970-2200).
  - Hypotonia or muscle weakness
  - Cardiac concerns
  - Tongue weakness/feeding difficulties
  - Breathing difficulties

  If your patient has any signs/symptoms of Pompe disease, or if you have any other questions about your patient's clinical care, please page Duke PMG (919-970-2200) immediately for clinical evaluation.
- If you have questions about the newborn screening result, a Duke PMG genetic counselor is available during business hours at 919-613-0948.

Where do I go for more information?

Use your phone's camera to scan the QR codes below.

ACMG Pompe ACT Sheet

Gene Reviews

Where do I send parents for more information?

Use your phone's camera to scan the QR codes below.

Baby's First Test

Duke Pediatric Genetics

MedlinePlus

NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

State of North Carolina Department of Health and Human Services Division of Public Health
www.ncdhhs.gov
http://slph.ncpublichealth.com
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