Newborn Screening Act Sheet
[Decreased acid alpha-glucosidase]

Pompe disease

Condition Description: Pompe disease is a lysosomal storage disorder (LSD) caused by a defect in acid alpha-glucosidase (GAA), resulting in glycogen accumulation primarily in cardiac and skeletal muscle. There is wide variability in severity and age of onset. Pompe disease is an autosomal recessive disorder.

MEDICAL EMERGENCY - TAKE THE FOLLOWING IMMEDIATE ACTIONS:

- Contact family to inform them of the newborn screening result and ascertain clinical status (Poor feeding, muscle weakness, respiratory concerns).
- Consult with Clinical Genomics (4-8198, off-hours via the clinic operator at 4-2511).
- Evaluate the newborn for signs of muscle and/or heart disease (hypotonia, generalized muscle weakness, feeding difficulties, respiratory distress). If any sign is present or infant is ill, transport to hospital for further evaluation and treatment in consultation with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing and management, as recommended by Clinical Genomics.
- Provide family with basic information about Pompe disease.

Diagnostic Evaluation: Confirmatory alpha-glucosidase enzyme assay, muscle enzymes (CK, LDH, AST, ALT), urine oligosaccharides, and - if clinically indicated - assessment for cardiomyopathy (ECG, ECHO). When patients have low enzyme activity, GAA gene analysis and other laboratory studies may be required in consultation with the pediatric metabolic specialist.

Clinical Expectations: The clinical presentation of Pompe disease ranges from a rapidly progressive infantile variant, which is uniformly lethal if untreated, to a more slowly progressive late-onset variant. All disease variants are eventually associated with progressive muscle weakness and respiratory insufficiency. Cardiomyopathy is associated almost exclusively with the infantile form. Pompe disease is caused by mutations in the GAA gene and has an estimated incidence of approximately 1 in 15,000 live births. Enzyme replacement therapy (ERT) is available for all variants and should be started as soon as possible for patients with the infantile variant and at the first signs of muscle weakness in the later onset variants. ERT administration is highly complicated and should only be given under the guidance of a specialist with expertise in lysosomal storage disorders.

Additional Information:

Genetics Home Reference
Genetic Testing Registry
Baby's First Test

Referral:

Testing
Mayo test 89210, GAABS, Acid Alpha-Glucosidase, Blood Spot
Mayo test 64889, OLIGU, Oligosaccharide Screen, Urine
Mayo test 35430, GAAZ, Pompe Disease Full Gene Analysis

Clinical
Clinical Genomics at 4-8198, off-hours via the clinic operator at 4-2511

Local Resources:
Mayo Clinic Biochemical Genetics Laboratory (BGL)
Mayo Clinic Department of Clinical Genomics
Minnesota Department of Health (MDH)
NBS for Pompe Disease
Follow-up

Decreased acid alpha-glucosidase (GAA) & 2nd tier test abnormal
Assess clinically
Routine labs: CK, LDH, AST, ALT
Cardiac evaluation

Acid Alpha-Glucosidase, Blood Spot #89210 – GAABS
Oligosaccharide Screen, Urine #64889 - OLIGU

GAA activity – deficient
Oligosaccharides/Glc4 – elevated
Evidence of cardio-myopathy

GAA activity – deficient
Oligosaccharides/Glc4 – normal
Evidence of cardio-myopathy

GAA activity – normal
Oligosaccharides/Glc4 – normal
No evidence of cardio-myopathy

GAA activity – normal
Oligosaccharides/Glc4 – elevated
No evidence of cardio-myopathy

Pompe Disease, Full Gene Analysis
#35430 - GAAZ

Genotype consistent with Pompe disease
Referral to Genetics Specialist
CRIM western blot
If genotype is not informative of CRIM status

One mutation identified
GAA deletion/duplication analysis
Genotype suggestive of Pompe disease
Testing consistent with carrier status
Negative

No mutations identified

CRIM western blot
If genotype is not informative of CRIM status

Abbreviations:
GAA – acid alpha-glucosidase
LDH – lactate dehydrogenase
CK – creatine kinase
AST – aspartate aminotransferase
ALT – alanine aminotransferase
Glc4 – glucose tetrasaccharide

* Refer to Genetics Specialist if clinical suspicion is high.
† Review perinatal history and check for other causes of hyperCKema and/or cardio-myopathy.
‡ Evaluate for other causes of elevated Glc4 (glycogen storage disease).

Actions are shown in shaded boxes; results are in the unshaded boxes.