**Pompe Disease (Glycogen Storage Disease Type II)**

Pompe Disease is one of the lysosomal storage disorders. It is caused by the defect in the acid alpha-glucosidase (GAA) gene. The enzyme GAA breaks down glycogen to glucose. If not broken down, glycogen builds up in the lysosomes causing them to swell, eventually burst and damage the cells. There are several forms of Pompe ranging from a rapidly progressive infantile form, which is uniformly fatal if untreated, to more slowly progressive later onset forms. However, all forms of the disorder are associated with progressive muscle weakness and respiratory insufficiency. Cardiomyopathy is associated almost exclusively with infantile form.

Forms:

* Classic infantile
  + 28% of cases have the infantile-onset form – no GAA activity
  + Signs of classic infantile onset usually appear before the baby is born or within the first two months of life. Death can occur within 1st year of life.
    - Decreased tone
    - Hepatomegaly
    - Cardiomyopathy (almost exclusively with infantile form)
    - Macroglossia
* Non-classic infantile-onset Pompe disease
  + Symptoms usually appear within the first year of life
    - Muscle weakness, which leads to breathing problems
    - Delayed motor skills
  + Without treatment, fatal respiratory failure in early childhood
* Late-Onset Pompe Disease
  + Can be divided into childhood, juvenile and adult-onset forms
  + Symptoms include:
    - Progressive muscle weakness
    - Breathing problems
    - Difficulty exercising
    - Hepatomegaly
    - Difficulty chewing or swallowing
  + Generally, later symptoms present, slower they will progress

Incidence: It is estimated that one in every 40,000 births worldwide is born with Pompe; however, an exact rate of occurrence cannot be determined until more states are screening newborns for the disease

Diagnosis: Diagnosis is made by confirmatory testing conducted by or through consultation with an experienced metabolic geneticist.

Confirmatory Tests include:

* GAA Enzyme Activity – blood or tissue - if low – DNA
* Urine Hex 4 (Urinary Glucose Tetrasaccharides – more of a particular carbohydrate in their urine, but this is not exclusive to Pompe)
* CK, CKMB, LFTs, LDH (Serum Creatinine Kinase (CK) – people with pompe disease will often have more CK in their blood, but this is not a definite diagnosis.)
* Cardiac evaluation ECHO and EKG

Treatment:

* Enzyme replacement therapy – goal is <3 weeks of age to start, as soon as possible after evaluating cross-reacting material (CRIM) status.
* Individuals with + CRIM status usually benefit more from ERT. Usually 75% of patients are CRIM +.
* ERT may improve survival in infantile-onset Pompe.
* It can reduce heart size, help the muscles work, decrease the need for a ventilator and help some gain motor skills.

False Positives: Low GAA can sometimes be found in people who never develop Pompe disease – pseudodeficiency (high in East Asian populations)