Pompe disease

National Institute of Neurological Disorders and Stroke (NINDS)

Source

National Institute of Neurological Disorders and Stroke (NINDS). Pompe Disease Information Page.

Pompe disease is a rare (estimated at 1 in every 40,000 births), inherited and often fatal disorder that disables the heart and skeletal muscles. It is caused by mutations in a gene that makes an enzyme called acid alpha-glucosidase (GAA). Normally, the body uses GAA to break down glycogen, a stored form of sugar used for energy. The enzyme performs its function in intracellular compartments called lysosomes. Lysosomes are known to function as cellular clearinghouses; they ingest multiple substances including glycogen, which is converted by the GAA into glucose, a sugar that fuels muscles. In Pompe disease, mutations in the GAA gene reduce or completely eliminate this essential enzyme. Excessive amounts of lysosomal glycogen accumulate everywhere in the body, but the cells of the heart and skeletal muscles are the most seriously affected. Researchers have identified up to 300 different mutations in the GAA gene that cause the symptoms of Pompe disease, which can vary widely in terms of age of onset and severity. The severity of the disease and the age of onset are related to the degree of enzyme deficiency.

Early onset (or the infantile form) is the result of complete or near complete deficiency of GAA. Symptoms begin in the first months of life, with feeding problems, poor weight gain, muscle weakness, floppiness, and head lag. Respiratory difficulties are often complicated by lung infections. The heart is grossly enlarged. Many infants with Pompe disease also have enlarged tongues. Most babies die from cardiac or respiratory complications before their first birthday.

Late onset (or juvenile/adult) Pompe disease is the result of a partial deficiency of GAA. The onset can be as early as the first decade of childhood or as late as the sixth decade of adulthood. The primary symptom is muscle weakness progressing to respiratory weakness and death from respiratory failure after a course lasting several years. The heart is usually not involved. A diagnosis of Pompe disease can be confirmed

by screening for the common genetic mutations or measuring the level of GAA enzyme activity in a blood sample. Once Pompe disease is diagnosed, testing of all family members and a consultation with a professional geneticist are recommended. Carriers are most reliably identified via genetic mutation analysis.