MUSCULAR DYSTROPHY CANADA
DYSTROPHIE MUSCULAIRE CANADA

NMD4C

Webinar Report

RESEARCH Spotlight
#LetsTalkNMD

Pompe Disease: Clinical Research Updates
06-07/2021

NMD4C (Neuromuscular Disease Network For Canada)

NMD4C launched in January 2020, is a Canadian network that is funded by Muscular Dystrophy Canada and the Canadian Institutes for Health Research.

NMD4C **brings together the country's leading clinical, scientific, technical, and patient expertise on neuromuscular disease.** The rarity and diversity of neuromuscular diseases make interdisciplinary collaboration and networking essential to future progress.

NMD4C strives to train and educate neuromuscular disease stakeholders

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NMD4C

Muscular Dystrophy Canada (MDC) and the Neuromuscular Disease Network For Canada (NMD4C) have been working on a monthly webinar series to provide clinical and research updates by highlighting cutting-edge research, current state of clinical care and providing up-to-date information on interdisciplinary guidelines for a variety of neuromuscular disorders to clinicians, researchers, academics and medical/graduate trainees.

The Royal College of Physicians and Surgeons of Canada have accredited our webinars for Continuing Medical Education (CME) credits as part of the Maintenance of Certification Program (MOC).

In line with this new accreditation (CMA Policy; Guidelines for Physicians in Interactions with Industry; standard 22), the primary purpose of the “Neuromuscular Disease Rounds & Educational Webinars” is to address the educational needs of the clinical and research community in order to improve the health care of patients affected by neuromuscular disorders and improve health and quality of life. MDC shares a common interest with NMD4C in improving patient care, improving health outcomes and building clinical and research neuromuscular expertise.

WEBINAR DISCUSSION TOPIC

Pompe Disease: Clinical and Research Updates

Dr. Mark Tarnopolsky

Disclaimer: Please note the speakers in this webinar might have involvement in the subject matter with real or perceived relationships

POMPE DISEASE
CLINICAL AND RESEARCH UPATES

Dr. Mark Tarnopolsky, MD, PhD
Professor of Pediatrics and Medicine

MCMASTER UNIVERSITY
(HAMILTON, ONTARIO)

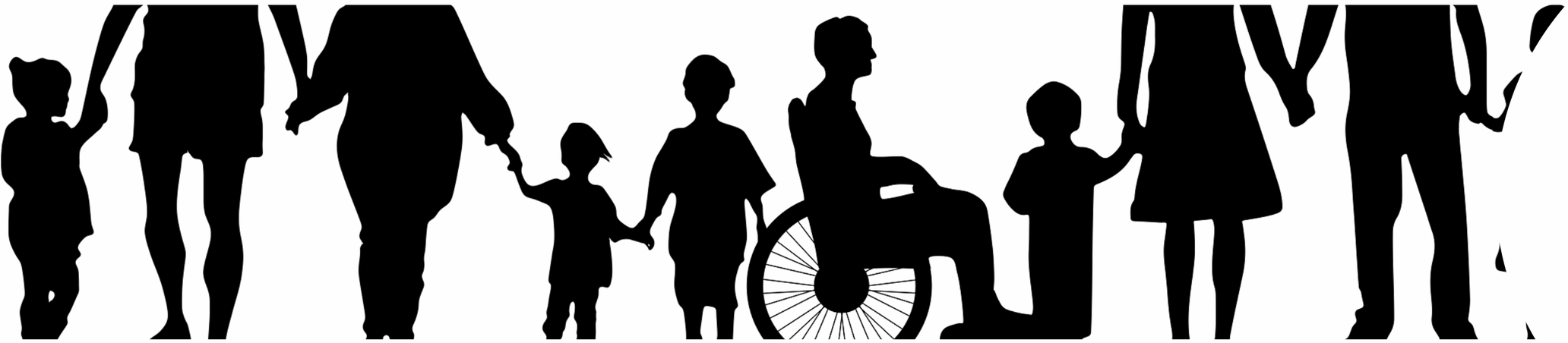
Pompe Disease was first described by Dutch Pathologist J.C Pompe

Pompe disease, also known as Acid Maltase Deficiency or Glycogen Storage Disease II, is described as a disease that causes significant cardiomyopathy (heart disease) and respiratory (breathing) issues in addition to muscle weakness.

There are two types of Pompe Disease: Infantile Pompe disease, progresses rapidly and can be fatal before age one; Late-onset Pompe Disease is identified by progressive weakness of the muscles, heart, and lungs and can possibly be life-limiting later in life.

The diagnostic process can take up to 7-10 years on average.

The age that symptoms begin to show and severity of disease can vary among those living with Pompe disease. Generally, it depends on what level of working enzyme activity a person has (high activity =typical; low activity =Pompe disease). In the late-onset type, which is more common, individuals typically start to notice symptoms in their mid 20's; leg weakness is usually the primary concern. On average, individuals are diagnosed in their mid 30's.



Pompe disease typically progresses more rapidly in males than females.

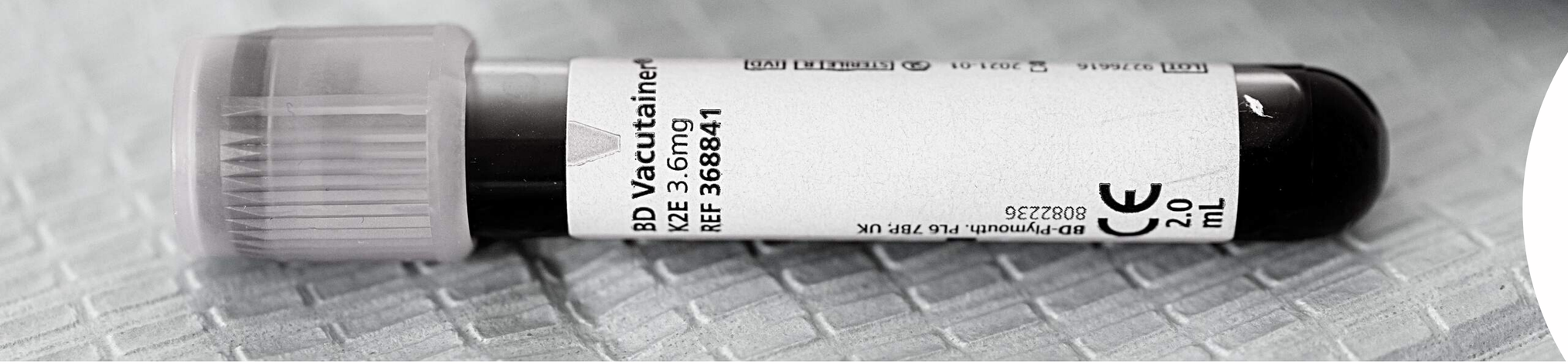
It is common for individuals to require walking aids, wheelchairs, and support with activities of daily living, such as dressing and bathing, later in life. Breathing can also become worse with age and individuals may require a BiPap machine (a machine that pushes air into your lungs) while sleeping to exhale enough carbon dioxide. These aids are typically used around age 40, but it varies depending on the individual.

POMPE GENETICS

Muscle strength decreases approximately 1.3% per year as the glycogen (a form of sugar stored in the body) accumulates in the muscles.

Pompe disease is a genetic recessive disorder (a disorder passed down from parents that may be hidden by a dominant gene). Pompe disease occurs when a non-working acid-alpha-glucosidase(GAA) gene (a gene that gives instructions to an enzyme to make GAA that breaks down glycogen) is passed down to the child from each parent. The gene has the instruction to make a lysosomal enzyme called GAA. This disease is caused by spelling changes in the GAA gene that carries the instructions to make the lysosomal enzyme. GAA prevents the build-up of glycogen. When there is not enough of this working enzyme, build up occurs.

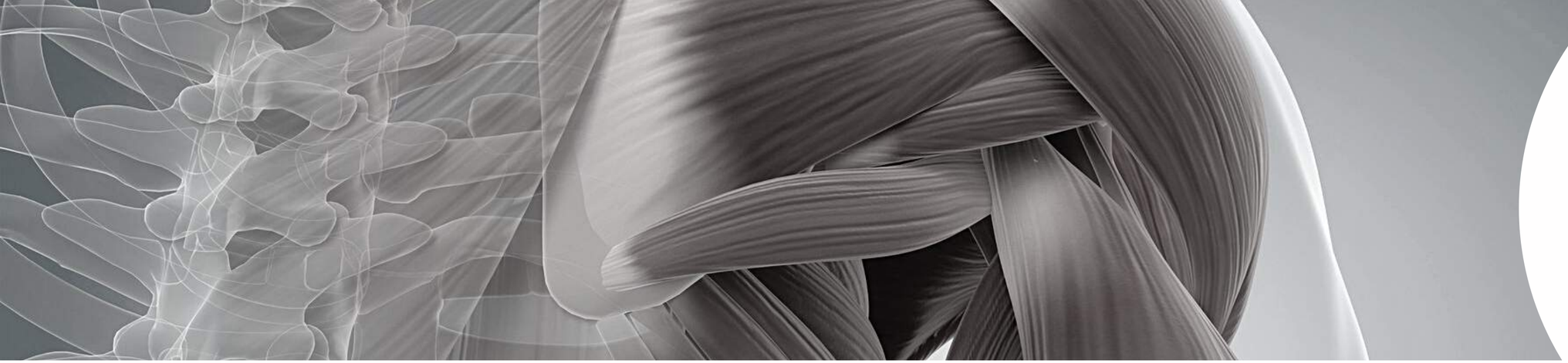
DIAGNOSTIC TESTING AND EXAMINATION



Blood spot tests speed up the diagnostic process by measuring enzyme activity. If enzyme activity is low, it is likely to be Pompe disease. Typically enzyme activity of 30% means there is a deficiency and the body can not keep up with the glycogen.

Clinicians perform numerous tests to determine a Pompe disease diagnosis such as:

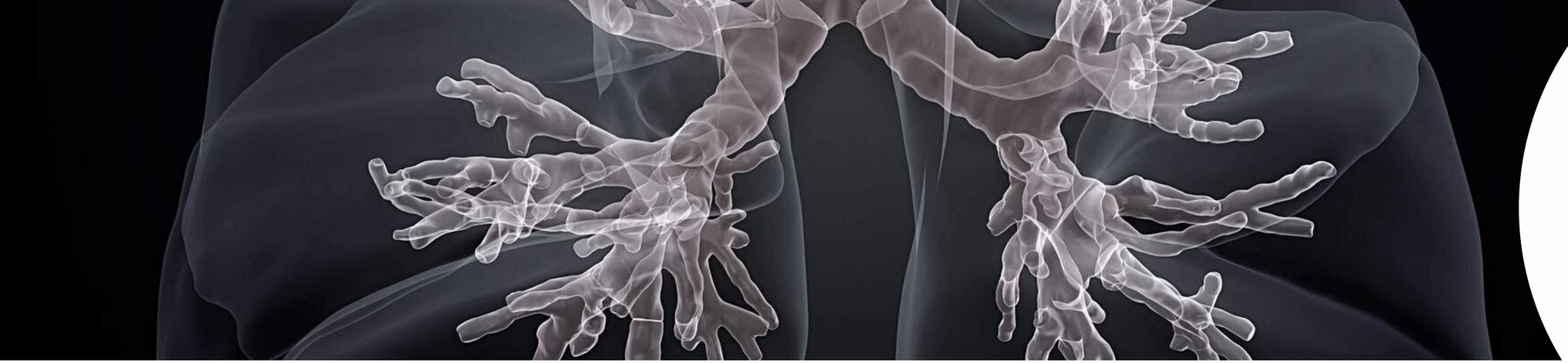
- Neurological examination to detect a muscle disorder
- Measuring Creatine Kinase (responsible for energy metabolism in cells) levels, which reflect damage to muscles.
- Electromyography (measures muscle response with nerve stimulation)
- Muscle biopsy (test done to diagnose diseases involving muscle tissue)
- Measuring enzyme activity of GAA



Late Onset Pompe Disease

Signs that skeletal muscle is affected by Pompe disease may include:

- Type II fibers of muscle build up more glycogen and are more affected
- A decrease in muscle strength (approximately 1.3% per year as glycogen accumulates)
- Highly affected muscle areas include deltoids (shoulders), hip adductors, hip flexors, and knee extension
- Lordosis (curve of the spine) can be seen in up to 60% of patients
- Up to 30% will have scapular winging (shoulder blade sticking out)
- Bulbar findings (swelling at the top of the spinal cord) very common in infantile pompe patients



Late Onset Pompe Disease

Signs that the respiratory system is affected by Pompe disease may include:

- Forced Vital Capacity (FVC: the maximum amount of air you can exhale) can decline up to 1.5% per year
- If there is a 20% drop in FVC from sitting to supine (back) this is a strong indicator of diaphragm weakness
- If FVC is lower than 60% than expected, there is a high risk of nocturnal hypoventilation (breathing that is too shallow and slow to meet the needs of the body)

It is important to complete a full history, clinical exams, neurological examinations, test Creatine Kinase levels, perform an Electromyography (to assess the health of the muscle and nerve cells), nerve conduction studies and in some cases a muscle biopsy to get to the diagnosis.

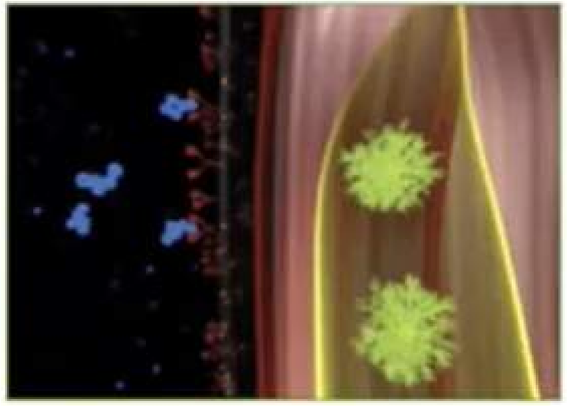
- **Similar disorders that present as Pompe disease include:**
  - **Sarcoglycanopathies**
  - **Limb Girdle Type 2A**
  - **Myoshi Myopathy**
  - **LGMD**
  - **FSHD**

SUPPORTIVE TREATMENTS

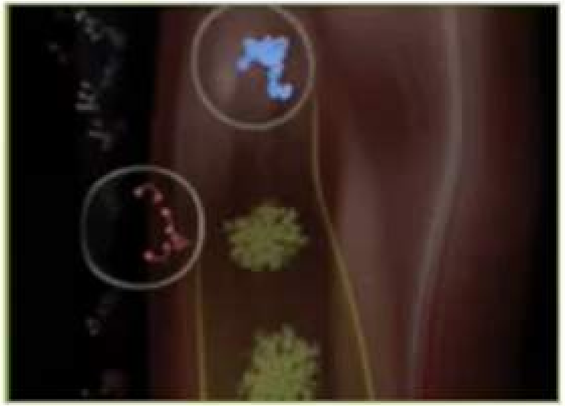
Myozymes are an enzyme replacement therapy that help the body to be able to start breaking down sugars.

Myozyme (algucosidase alfa) is the brand name of a drug used to treat Pompe Disease. It is an enzyme replacement therapy which means that an exttra working version of GAA enzyme is delivered into the body to compensate for the non-working enzyme that the body produces. It makes its way into the lysosomes (part of the cell that contains digestive enzymes) where it helps by breaking down some of the built up glycogen to glucose.

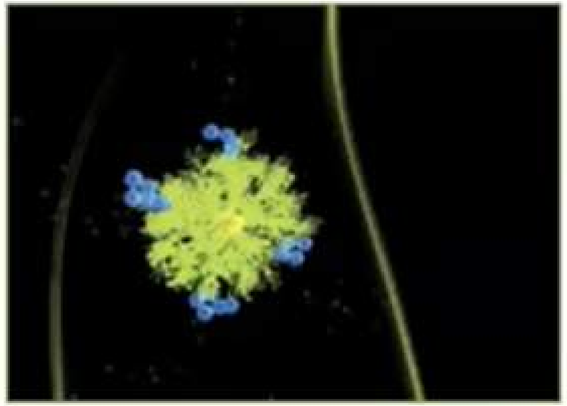
Myozyme Mechanism of Action



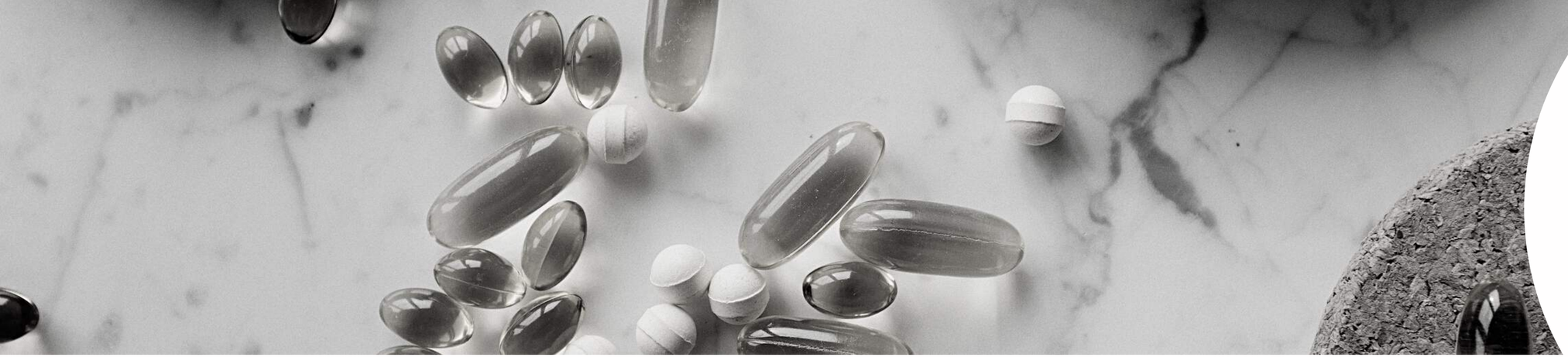
Myozyme (alglucosidase alfa) "docks" on M6P receptors on cell surface



Inside cell, Myozyme molecules disassociate from M6P receptors, which cycle back to cell surface



Inside lysosome, Myozyme breaks down glycogen to glucose



STUDIES. A few studies have assessed the effects of dietary supplements on Pompe disease. As evidence continues to emerge, it is important to consult your physician before starting any of the following supplements.

Supportive dietary recommendations include:

- Adequate protein intake of 1.2g/kg/d
- Vitamin D supplements
- Creatine monohydrate (helps your muscles produce energy) (100mg/kg/d)
- Ferritin (a blood protein that contains iron)
- B12 supplements

EXERCISE

Emerging evience shows that endurance and resistance exercise can be beneficial for individuals living with Pompe Disease. Please consult with your physician before beginning any physical activity

Endurance exercise can help:

- Improve cardiovascular health (heart health)
- Activate autophagy (cleaning up damage in muscles)

Resistance Exercise

- Increase muscle strength
- Increase bone mineral density
- Lower Type 2 Diabetes risk

***Patients who combined endurance and resistance exercise showed strong improvements**

CLINICAL TRIALS

There are a number of clinical trials in Canada. If you need support finding a clinical trial, please contact the Research Hotline.

research@muscle.ca

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QUESTIONS?

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