McArdle disease is a rare, metabolic condition that is genetic. It results from changes in your DNA, called mutations, that affect your body's ability to provide muscles with the energy they need to function. People living with McArdle disease generally experience muscle cramps/pain during regular activities and exercise. McArdle's is also known as Glycogen Storage Disease Type 5 (GSD V).

Everyone experiences the disease differently. Symptoms can range from mild and manageable to severe and life-threatening.

Our bodies make, store and access energy. We convert the foods we eat into a simple sugar called glucose. If we have more glucose than we need, these molecules join together to form glycogen which can be stored in our muscles.

When we need energy, an enzyme called phosphorylase (or myophosphorylase) breaks down the stored glycogen. People with McArdle disease have inactive phosphorylase, so their muscles cannot access the stored glycogen. Without the energy they need, muscles cramp and fatigue during exercise.

McArdle disease is a recessive genetic disorder meaning the mutated gene is inherited from both mother and father. It is important for people to know if they carry the gene when it comes to family planning. Carriers will pass the abnormal gene on to their child(ren). If both parents are carriers and pass the abnormal gene on to the child, that child will have McArdle disease.

Symptoms of McArdle Disease

The most common symptoms of McArdle disease are listed below. They begin within the first 20 seconds after starting activities that require high energy and then ease up once the activities stop.

- **Exercise Intolerance** means you become extremely tired, stiff and/or weak soon after you begin activities that require quick bursts of energy.
- **Muscle Pain and Cramping** occur because your muscles cannot access stored energy.
- **Contractures** describe muscles that tighten and don’t release. This prevents movement, usually involves swelling, and can be quite painful.
- **Second Wind Phenomenon** describes how symptoms improve after approximately 8 - 10 minutes of rest or continuous exercise at a lower intensity. This happens as your body changes from unsuccessfully trying to access glycogen to using oxygen to make energy. This is called aerobic exercise. An increase in heart rate and breathing occurs for everyone during this type of activity but is accentuated for those with McArdle disease.
- **Rhabdomyolysis** describes the breakdown or death of muscle cells.
- **Myoglobinuria** is a type of kidney injury. Damaged muscles release a form of waste called myoglobin which is usually removed by the kidneys. However, if myoglobin levels rise too high and too quickly as muscles break down, the kidneys can’t keep up and myoglobin appears in urine that is a dark, tea-colour. Quickly getting to a hospital is important if this happens.
- **Permanent Muscle Weakness** of the thigh or other muscles may occur in rare cases or those impacted by age.

Marsha has McArdle disease but she does not allow it to limit her. She lives life to the fullest by paying attention to her body, resting when she needs to, and finding creative ways to share her energy.
Who Develops McArdle Disease?

Children with McArdle disease usually experience symptoms before the age of 10 years. Unfortunately, symptoms are often ignored or dismissed. Too often, kids are thought to be lazy or uncoordinated. Most patients are not diagnosed until their mid to late adulthood. For them, life can be frustrating, difficult and dangerous, especially for those with severe symptoms.

Getting a Diagnosis

Getting an accurate diagnosis early is very important. Knowing you have McArdle disease empowers you to make choices that can protect your health and maximize your quality of life.

However, getting a diagnosis can be challenging. The disease is rare and many healthcare professionals are not familiar with it. The more information you can share with your doctor about your symptoms and family history, the more likely you are to get the proper diagnosis and care.

Your doctor may recommend one or more of the tests listed below.

- **Physical exam** that may involve testing your muscle strength.
- **Blood tests** to check for gene mutations and increased levels of creatine kinase (CK). This is an enzyme that flags muscle breakdown and is seen in nearly all cases.
- **Electromyography** to measure muscle or electrical activity response to nerve stimulation. This is usually normal when people with McArdle disease are at rest.
- **Forearm exercise test** to look for markers such as the absence of a lactate rise and an exaggerated rise in ammonia. Both are characteristic of McArdle disease.
- **Muscle biopsy** removes a small piece of muscle then examines it under a microscope for glycogen buildup and/or phosphorylase enzyme activity.
- **Urine tests** are used during acute bouts of rhabdomyolysis to check for myoglobin.

Getting an accurate diagnosis is very important. You may be tested for other glycogen storage or mitochondrial-related illnesses that can have similar symptoms. Once you have a diagnosis, you may then be referred to a neurologist, geneticist or metabolic specialist.

**Neurologist** – a medical doctor who specializes in disorders of the brain and nervous system  
**Geneticist** – a medical doctor who focuses on how genetic information is passed from parents to their children  
**Metabolic Specialist** – a medical doctor who specializes in the processes that change food into energy to keep our cells healthy and working properly

Living with McArdle Disease

There are currently no approved drugs available to treat McArdle disease. However, new medicines are being developed. Until a cure or treatments are found, you may take comfort in knowing that McArdle disease should not change your life expectancy and that lifestyle choices may prevent or lessen your symptoms.

It is important to work with your health team to create an exercise and nutrition plan that is specific to your needs. Strategies for managing McArdle disease may include:

- avoiding activities that you learn will cause symptoms
- developing a fitness plan with a professional to maintain muscle health through moderate aerobic exercise.
- avoiding activities that are intense or strenuous, involve muscle contractions for extended periods of time, heavy lifting, and sports that require sudden bursts of energy like basketball, jumping, hockey.

**NOTE:** there are some people with McArdle disease who can do sports with careful planning.

- warming up gradually and listening to your body as you slowly adapt to activity.
- Eating a diet that provides protein at ~ 50% of the current recommendation (strive for > 1.2 g/kg/day).
- adding creatine supplements (no more than 100 mg/kg/day).
- eating or drinking sugar (in a drink or piece of fruit) about 10 - 15 minutes before exercise.

The good news is that McArdle disease does not get worse over time and, if managed properly, it is not fatal. Most people learn to adapt with lifestyle modifications that help reduce symptoms.

MitoCanada is the Canadian charity dedicated to creating a world where all lives are powered by healthy mitochondria. Visit us at: www.MitoCanada.org.