

## McArdle's disease

### What is McArdle's disease?

McArdle's disease is a metabolic muscle disorder first described in 1951 by Dr Brian McArdle. The disorder is also called Glycogen Storage Disease Type V (GSD V). People born with McArdle's disease are unable to produce an enzyme called muscle phosphorylase. This enzyme is important in producing the fuel source required by the skeletal muscles for exercise.

### What are the symptoms?

People with McArdle's disease develop severe muscle pain and fatigue in the first few minutes of exercise. If exercise is continued despite the pain, a severe muscle spasm or contracture will develop. This results in muscle damage leading to myoglobinuria, a dark discolouration of the urine.

Many people with the condition remember painful symptoms from early childhood but the disorder is rarely diagnosed before adulthood. Some people notice a worsening of their symptoms in middle-age and this may be accompanied by some muscle wasting, especially over the shoulders and back. Most people live normal lives and learn to improve their exercise tolerance using a "second wind".

### What is a second wind?

There are two types of exercise: aerobic exercise includes walking, gentle swimming, jogging and cycling. Anaerobic exercise is more intense or sustained exercise and includes running, walking uphill and carrying loads. The first few minutes of any exercise are usually anaerobic. Normally, during anaerobic exercise, muscle phosphorylase converts glycogen (stored starch) to glucose (sugar). The glucose enters a metabolic pathway known as the glycolytic pathway, which ultimately produces ATP (energy). During aerobic exercise, the main energy source comes from free fatty acids carried in the blood stream. These fatty acids enter a different metabolic pathway, called oxidative phosphorylation, which takes place in the mitochondria (these are the power houses of the cell) the end result is the production of ATP (energy

A second wind is like a key opening the door, enabling exercise without pain for people with McArdle's disease. After a few minutes of exercise when pain occurs, if the individual rests for a moment or two, exercise can be continued without severe pain. The second wind probably results from a switch in metabolic pathway from the glycolytic pathway to oxidative phosphorylation.

### Which muscles are affected?

Any skeletal muscle is affected. Usually walking brings on symptoms in the legs and carrying heavy shopping affects the arms. Sawing, digging or squatting may affect the back muscles and some people develop pain eating chewy foods.

### **How is McArdle's disease diagnosed?**

A blood test will usually reveal a raised muscle enzyme known as creatine kinase (CK). Sometimes a forearm lactate test is performed, although this is not essential. The diagnosis is confirmed by a muscle biopsy, which shows an excess of glycogen and absence of the muscle enzyme phosphorylase. In up to 85% of patients from Northern Europe, an abnormality in the gene encoding for muscle phosphorylase, called R50X (previously known as R49X), can be detected on a DNA test (blood test). In practice such testing is rarely helpful and not always available and is not essential to make the diagnosis.

### **Is there any treatment?**

The ability to develop a second wind is greatly increased by keeping physically fit. Taking regular gentle aerobic exercise, such as walking is important. At the start of exercise, when pain occurs, slow right down or stop until the pain has subsided, then try again. Sustained or severe exercise, such as weight lifting, or sprinting, must be avoided because of the high risk of muscle damage. Continuing to exercise in the presence of severe pain will also result in muscle damage and myoglobinuria, which will in turn increase the risk of acute renal failure.

Many different diets and supplements have been tested in McArdle's disease such as high protein diet, vitamin B6 and creatine supplements, as yet there is insufficient evidence to suggest that any of these benefit people with McArdle's disease. There is some evidence to suggest that a sugary drink prior to planned exercise might help. This however, needs to be balanced against excessive weight gain, which should be avoided at all cost. Carrying increased weight will lower your body's aerobic threshold and make exercise more difficult. Keeping aerobically fit is the best way to condition McArdle's muscles to improve performance and improve quality of life.

### **What happens if myoglobinuria occurs?**

Most people with McArdle's disease will develop myoglobinuria at some time in their lives. Myoglobinuria is a dark discolouration of the urine from a red- brown colour (mild) to a brown-black colour (severe). This is a warning sign for acute renal failure, which can occur if severe muscle damage has occurred. If this happens the kidneys stop producing urine because the draining tubules become blocked with the products of muscle breakdown.

If the episode of pain and contracture was not too severe myoglobinuria will be transient and lighter in colour. After more severe episodes the muscles may be swollen and tender and there may be flu like symptoms. Minor symptoms are managed by increasing fluid intake to maintain a good urine output. More severe episodes will require an admission to hospital for intravenous fluids and if kidney failure occurs, a period of dialysis may be required. Kidney failure is almost always reversible, but expert treatment is required immediately to prevent complications during the acute stage. It is, therefore, very important to seek medical help early should any of these symptoms occur.

### **Are there any other precautions?**

There is a reported risk of acute muscle damage, with certain general anaesthetics (usually muscle relaxants and inhaled anaesthetics), although in practice problems appear to be very rare. The anaesthetist should be made aware of the diagnosis of McArdle's disease, and may choose to avoid certain anaesthetic agents. Tourniquets should not be used during operative procedures in patients with McArdle's disease.

Affected women do not seem to be disadvantaged by pregnancy or childbirth. A natural childbirth is a realistic possibility for women with McArdle's disease.

### **Will I become disabled?**

McArdle's disease does not affect life expectancy. Some people do notice a slow deterioration in their symptoms over many years but by far the majority of people remain independent and able to walk.

### **Can it be passed on to my children?**

The condition is caused by a recessive gene. This means that one abnormal copy of the gene is passed from each parent to the affected child, who in turn will have inherited two abnormal copies of the gene. The risk for both carrier parents to have an affected child is 1:4 for each pregnancy.

People who have McArdle's disease do not usually pass the condition onto their own children because one normal copy of the gene will have been provided by their partner. However, all of their children will be carriers. Generally speaking carriers do not have symptoms.

### **Is there a support group?**

The Association for Glycogen Storage Disease UK provides information, support, and a regular newsletter.

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