Inclusion Body Myositis

Inclusion body myositis (IBM) is a muscle condition that causes muscles to become thin and weak. Symptoms usually start in middle to late life and it is the most common muscle disease diagnosed after the age of 50. Nevertheless it is still considered rare with between 3 and 4 people out of every 100,000 people over 50 having the condition.

The cause of IBM is not well understood but it is not thought to be a genetic condition and it generally does not run in families. For this reason it is often called sporadic IBM or sIBM. It is grouped with the conditions called the “inflammatory myopathies” which includes the related conditions polymyositis and dermatomyositis. There is another more rare condition called hereditary inclusion body myopathy which does have a genetic cause, but this will not be covered in this factsheet.

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What are the symptoms and what is the prognosis?
People with IBM experience slowly progressing muscle weakness and wasting in the arms and legs. The quadriceps (the main muscles of the thighs) are usually affected first leading to frequent falls, trouble climbing stairs and difficulty with standing from a seated position. Forearm muscles that flex the fingers and wrists are commonly weak and people with IBM may notice a weakened hand grip. Tripping can be a problem due to weakness of muscles below the knees which causes the foot to drop and toes to catch when walking. Often one side of the body is more affected than the other. Swallowing muscles may be affected in some people.

The muscles of the heart, lungs, eyes, gut and bladder are not affected by IBM and neither is the brain or sense of touch. Speech is rarely affected. Pain or discomfort and fatigue may be experienced as muscles weaken, though often patients report no pain. In general patients do not die of IBM, but most meet with some degree of disability as the disease progresses. Most people with IBM remain able to walk, although they may require a cane or wheelchair for long distances. Walking progressively becomes more difficult and some people will require a wheelchair fulltime 10 to 15 years after the onset of symptoms.
It has been noted that people with IBM are more likely to also have other medical conditions such as lupus (SLE), Sjögren’s syndrome, mitochondrial disease, scleroderma, sarcoidosis, thyroid dysfunction, high blood pressure and diabetes.

**What causes inclusion body myositis?**

The cause of inclusion body myositis is not fully understood. Researchers think that there are two processes happening in the muscle at the same time causing the symptoms. One process is inflammation which damages the muscles. Viruses and autoimmunity have both been implicated in causing the inflammation. However, since treatment with anti-inflammatory medication generally does not improve the symptoms of IBM, something else must be going on.

More recently researchers have been studying degenerative processes occurring in the muscles of people with IBM. When viewed under a microscope the muscle cells of people with IBM contain what are called inclusion bodies, which give the condition its name. These are abnormal clumps of proteins which are thought to be toxic to the cell and cause them to deteriorate.

How these two processes of inflammation and degeneration interact, and if one causes the other is not yet fully understood.

**How is inclusion body myositis diagnosed?**

IBM is thought to be underdiagnosed and frequently misdiagnosed as polymyositis. So getting the correct diagnosis can be a long and frustrating process.

Getting a diagnosis involves gathering various pieces of evidence that when put together point to IBM:

- Blood test: When muscles are damaged they release a protein into the blood stream called creatine kinase. In some people with IBM the level of this protein in the blood is slightly raised. This blood test may therefore alert the physician to the possibility of muscle disease.
- Electromyography (EMG): A test that assesses the electrical activity of the muscles and the nerves controlling the muscles. In IBM abnormal electrical impulses may be detected. However, although EMG may be helpful it cannot make a definite diagnosis.
- Muscle biopsy: The definitive test for IBM is a muscle biopsy. The biopsy involves taking a small sample of muscle under general or local anaesthetic. This is examined under a microscope and different stains used to highlight different parts of the muscle. In IBM, muscle cells will contain inclusion bodies, which are abnormal clumps of proteins seen in damaged cells.

There is also a new blood test that detects a certain antibody called ‘anti-cN1A’ or ‘anti-NT5C1A’ in the blood. The blood test comes back positive in about 70 percent of patients with IBM. However, this blood test may not be widely available yet.

Because of the slowly progressing nature of muscle weakness in IBM, a diagnosis is sometimes delayed for years after the onset of weakness. In some patients, the initial biopsy may give inconclusive results, and a second biopsy may be necessary.
In other forms of myositis steroid treatment may be helpful. If steroids fail to help then this may give rise to consideration of IBM as a possible diagnosis.

**How can the symptoms be managed?**

There is currently no treatment for IBM but much can be done to manage the symptoms.

Immunosuppressive drugs such as corticosteroids can be helpful in other types of myositis but usually people with IBM do not see any improvement with these medications or if they do, the improvement is only short lived. One study has even suggested that people with IBM who take immunosuppressive medication are actually worse off in the long term. In addition, unwanted side effects are possible, so these medications are not recommended.

A physiotherapist can help maximise the efficiency of the relatively unaffected muscles. They can also advise on the use of walking aids and teach people how to transfer between chairs, beds and wheelchairs (if they become necessary). Advice on exercise to do at home may also be given.

Occupational therapists (OTs) can provide advice and equipment to assist in overcoming the everyday practical problems that people with IBM may face. Examples include cutlery with chunky handles to make gripping easier, aids to help stair climbing and advice on bathing or showering difficulties.

Trouble swallowing may cause fragments of food or drink to enter the windpipe resulting in coughing after meals, chest infections and significant weight loss. Speech therapists can help with the management of swallowing difficulties if this develops. Occasionally minor surgery is performed to improve swallowing.

Recent research has shown that regular exercise is generally helpful for people with IBM and may even modestly improve strength. Care must be taken to avoid falls and injuries though. When undertaking a new exercise program it should be tailored for your ability and closely monitored by a health professional to avoid over exerting the muscles. If there is significant and long lasting muscle pain or weakness – you are probably overdoing it!

There is no specific exercise prescription for IBM but combining both aerobic and resistance exercise is generally recommended. For example, a short walking or swimming session one day and then the next day a short session of exercise using light weights. The exercise program could also include some hydrotherapy. Further research is ongoing to help to define the optimal exercise regime for people with IBM.

Keeping to an ideal weight is also advised because weakened muscles may struggle to carry excess weight. There is no scientifically recognised diet specific for people with IBM. Healthy diets which are high in protein, low in fat and carbohydrates are recommended, with at least five serves of vegetables and two of fruit per day.
What research is being done?

Research is ongoing to learn more about IBM and test potential treatments.

One research strategy is to test drugs already in use for other conditions to see if they may also be useful for IBM. One such drug is oxandrolone which is an anabolic steroid which has the effect of building more muscle and increasing body weight. A small trial of oxandrolone in 19 people with IBM showed some improvement in muscle strength, particularly upper body strength. However further trials are needed to assess in detail the benefits and risks of this drug for people with IBM.

A pilot trial of etanercept, a drug used to treat autoimmune diseases like rheumatoid arthritis, did not show significant benefit in muscle strength scores at 6 months. However, with 12 months of treatment, slight improvement in grip strength was noted. A larger clinical trial is currently underway to assess the effectiveness of etanercept treatment for IBM in more detail. More information about the etanercept trial.

There has been a small clinical trial involving 13 people with IBM who were treated with alemtuzumab (Campath), a drug used to treat a type of leukaemia and multiple sclerosis (MS). This drug depletes the immune system of white blood cells. It was reported that disease progression was slowed and strength improved in some patients. A larger placebo-controlled trial is now required to confirm this result and ensure that the risk of side effects does not outweigh the benefit.

Several promising new drugs are also being developed. One of these is arimoclomol - a drug that is primarily being developed to potentially treat another neuromuscular condition called amyotrophic lateral sclerosis (ALS) in which toxic clumps of proteins form in the motor neurons. It is hoped that for both ALS and IBM arimoclomol will help proteins fold correctly and therefore prevent the formation of toxic clumps. A clinical trial of arimoclomol for IBM was completed at the end of 2012 in the UK and USA but no results have been published as yet. More information about the arimoclomol trial.

Another strategy for the development of a treatment for IBM is to boost muscle growth. One way to do this is to interfere with the mechanisms naturally present in the muscle that put the brakes on muscle growth so that muscles remain within the normal size range. This involves a protein called myostatin which inhibits muscle growth when it binds to certain receptors on the muscle. Interfering with this process could result in increased muscle growth and strength.

Drug company Novartis is testing an investigational drug called BYM338 (also known as bimagrumab) for IBM. BYM338 is an antibody that binds to receptors on muscle thereby blocking myostatin from binding to them. A phase 2 clinical trial apparently showed that BYM338 benefited patients with IBM compared to placebo but the full results have not yet been released; they are expected to be out in late 2014. A phase 3 trial to be carried out at approximately 35 study locations worldwide has now begun. In Australia clinicians are recruiting patients to participate in the trial in Melbourne, Sydney and Perth. More information about the BYM338 trial.
Other researchers in the USA are aiming to inhibit the myostatin mechanism using a form of gene therapy. It involves increasing levels of a protein called follistatin which is a natural inhibitor of myostatin. A harmless virus is used to deliver the follistatin gene inside muscle cells and these instructions are used to make the follistatin protein. A phase 1 clinical trial is underway to test this in people with IBM and those with Becker muscular dystrophy. More information about the follistatin trial.

NOTE: Research is moving forward at a fast pace, so this research summary may not be up-to-date at the time of reading. Feel free to contact MDA’s Scientific Communications Officer for an update on the latest developments - kristina.elvidge@mda.org.au.

Further information

- Clinical trials – your questions answered
- The Myositis Association of Australia and The Myositis Association of America
- A glossary is available on the MDA website which explains terms in this factsheet that you may not be familiar with
- You can get regular updates by becoming a friend of the MDA Facebook page or follow our Scientific Communications Officer on Twitter (@kelvidge).

For further information on any of the areas discussed above, please contact MDA on (03) 9320 9555, email info@mda.org.au

References


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