Sporadic Inclusion Body Myositis (sIBM)

A). Key Facts
B). Coping
C). Other
D). Information checklist
E). References
F). Disclaimer

A). Key Facts

sIBM overview:

This disease is usually called sporadic inclusion body myositis (sIBM). It is called sporadic because it develops unexpectedly. You will usually be the only one in your family who has this disease. It is called inclusion body because under the microscope the muscle cells display what they call inclusion bodies. It is called a myositis because it appears as an inflammation of the muscle. It is sometimes called an idiopathic disease – this means that they do not know what causes it.

sIBM is a type of muscular dystrophy (there are also many other types of muscular dystrophy that are quite different). sIBM attacks the long striated muscles in the body, usually affecting the arms and legs first. It can also affect the diaphragm (impacting breathing) but does not affect the heart. Nerves are not affected, and, although you may lose strength in your limbs, you will not lose sensation. sIBM leads to progressive disability over a period of years usually ending with severe (total) disability.

In the past, it has been reported that sIBM has no effect on one's lifespan. However, a recent study (see Barghout, et al, 2014 [below]) identified a shorter lifespan in patients with sIBM compared with the general population.

People often confuse muscle disorders with multiple sclerosis which is a neuron/nerve disease.

sIBM is often initially confused with another type of muscle disease called polymyositis. Polymyositis has similar symptoms and is much more common in the population, so doctors often assume that it is polymyositis. Patients are often treated with medications and do not respond as doctors would expect if they had polymyositis and further investigation reveals that they actually have sIBM.

About 30% of sIBM cases are initially incorrectly diagnosed with one or another disease. On average, it takes about five years to diagnose sIBM.

sIBM is very rare in the overall population; about 5 to 15 people per hundred thousand. But, it is a disease related to aging: As people get older, sIBM becomes much more common, and, in people over 50, the estimates of prevalence range from about 50

(the commonest figure) to as many as 139 per hundred thousand people (Tan et al, 2013, p. 334). With the approaching age bubble in our population, the burden of sIBM as a disease on society will likely increase. Although the disease is most common after 45-50, about 10-20% of cases present symptoms before 50. Average age of onset is about 60-65. Slightly more males are affected than females. The common form is the sporadic form and it is not considered inherited – that is, it is not passed on from parents to children. There are also several types of inherited IBM that are exceedingly rare (some have only a few hundred identified patients in the world).

sIBM symptoms come on extremely slowly, over months or years (whereas the symptoms of polymyositis come on over weeks or months). sIBM is a progressive disease, it does not appear to go into remission periods. It just slowly keeps getting worse and worse as muscles become weaker and weaker.

The rate and progression of the disease varies widely from person to person. As well, the initial symptom presentation (the exact pattern of muscles affected) can also vary widely from person to person. Most cases affect one side of the body more than the other (usually the non-dominant side).

Causes:

There is no recognized cause for sIBM.

What sIBM does:

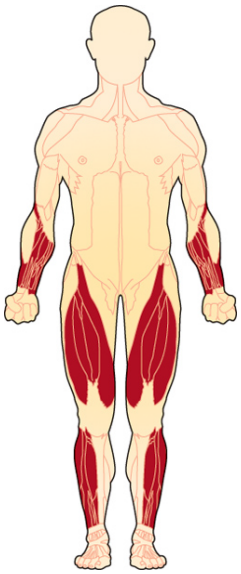
IBM causes problems within the cells that make up the muscles. (It does not affect nerves). Somehow, in each muscle cell, the internal chemistry is thrown off and the muscle cell dies. The problem continues and, over time, fewer and fewer cells are left functioning. Eventually the muscle becomes very weak and ultimately turns into a brittle fiber.

A recent (2014) review listed 10 distinct mechanisms leading to muscle damage in sIBM (Machado, Dimachkie, & Barohn, 2014). How these 10 different mechanisms are related to each other, what causes what, and ultimately, what triggers the problems to begin, remains a mystery.

The effect of sIBM on the body:

sIBM does not affect all muscles at the same time. You may initially find some muscles are affected and others will try to compensate. For example, as muscles in the front of the leg are weakened, enlargement of the calf muscles may be seen.

As you can see from the diagram below, the large quadriceps muscles in the front of the leg are often affected, causing weakness felt in climbing stairs, in getting up from chairs, etc. It often leads to frequent falls. “Toe drop” (the leg muscles don’t raise the toe high enough when taking a step) commonly causes tripping. Weakness of the muscles in the arm is a common, early symptom. This causes loss of wrist strength, finger dexterity and weak grip strength (weakness making a fist).



Diagnosis of sIBM:

The diagnosis of muscle diseases is complicated in general. The diagnosis of sIBM is more complicated because it is rare and because the symptoms presented very widely in each case. Generally speaking, as mentioned above, it is not unusual to take up to five years to achieve a diagnosis.

Usually diagnosis is made by a specialist in muscles – a neurologist – or sometimes by a rheumatologist. It is not uncommon to have to have a second opinion in the diagnosis. As well, it is not uncommon to have a biopsy that is ambiguous. Patients have to be diligent but patient during the process of diagnosis. There are various indicators used in making a diagnosis, the main ones appear below. As research goes on, new tests are becoming available that are more specific to sIBM.

1). Clinical signs: what the doctor can see when you are examined. The doctor looks for a characteristic pattern of muscle weakness.

2). A blood test is done for creatine kinase (CK) an enzyme in the blood showing muscle damage. CK is at most about 10X normal, although this may vary. A new blood test for antibodies against cN1A (or NT5C1A) is now becoming available.

3). Electromyography (EMG): Electrical studies of the muscle done with a computer (an electromyograph) will display abnormalities in these disorders.

4). Muscle Biopsy: Surgical removal of a piece of muscle and its study in the laboratory. Most cases will require at least one muscle biopsy for diagnosis.

Direct treatment of sIBM:

Today (2014) there is no direct treatment. The cause of sIBM is unknown and the exact way that sIBM affects the muscle cells is not well understood. Until this is better understood it will be very difficult to develop a treatment directly aimed at sIBM.

In the past, a number of different medications have been tried, primarily prednisone and IVIG. None of these medications have been shown to be effective. All of

the medications used have serious and significant side effects. About half of sIBM patients receive some sort of immunosuppressive treatment and it appears that the group receiving treatment end up displaying greater weakness than those who did not receive treatment (Benveniste et al, 2011).

Some clinics recommend creatine monohydrate (3 grams per day) to help maintain muscle bulk. This supplement has no known side effects, and has been shown to improve muscle strength in patients with different muscle diseases (Kley, Tarnopolsky, & Vorgerd, 2011).

The main focus of treatment is on the prevention of complications and on maximizing quality of life as long as possible. This is often done in consultation with a physical, and, or, occupational therapist. When necessary, speech therapy may be part of the treatment as well (they also monitor swallowing issues). The planning of appropriate palliative care during the end stages of sIBM is strongly recommended.

Indirect treatments:

Until a specific treatment can be developed for sIBM, one strategy is to try to develop treatments that will counterbalance the impact of the disease, for example, to try to increase the amount of muscle with the idea that if there is an increase in overall mass, there may be gains in function. Thus, by indirect, I mean that these treatments are not directly focused on sIBM and would not alter the sIBM disease process itself.

Several treatments along these lines are in experimental stages. Bimagrumab (BYM338), has achieved preliminary positive results (it is a myostatin inhibitor). Another approach uses gene therapy (using follistatin) to inhibit myostatin.

Other forms of "treatments:"

Many different types of treatments are often promoted for diseases like sIBM (and cancer). Unfortunately, companies often prey upon people with such illnesses and make very emotional and exaggerated claims of various cures. None of these different diets or potions or supplements (except the one mentioned above) have been shown to have any effect whatsoever on sIBM.

B). Coping

Adaptations:

Unfortunately, sIBM is a progressive disease and presents somewhat of a moving target. An adaptation that works today may not work in a year from now. This is important in planning ahead. For example, house renovations should not be based on your condition today but rather look at where you will likely end up in the future.

Falls:

Because the muscles in the legs are affected early in the disease, falls are one of the early symptoms. People often experience what is called "foot drop" this means that

when you take a step your toes do not fully rise up and you tend to drag your toes and trip, falling forward on your face.

I will describe two other characteristic types of falls. The first "the slow-motion tree falling in the forest." You end up losing your balance and slowly tip over and fall. You can feel yourself falling but you cannot do anything about it. This kind of fall is dangerous because you can hit your head.

The second kind of fall I will call "straight down in a crash." In this fall, usually you are taking a step forward and your knee gives out and you literally fall straight down. These falls tend to be instantaneous and you are on the ground before you even realize you are falling. These falls can be very dangerous because all of your weight is going straight down on your ankles and knees.

One thing for certain is that you cannot "catch yourself" by grabbing onto something when you fall. Prevention is everything.

Swelling of the feet:

This is a very common problem that can best be addressed by using compression socks on a daily basis. Prevention is the key. Usually this swelling of the feet is caused by inactivity, especially in people who are in wheelchairs. The only downside of using compression stockings is that they are difficult to put on. You will usually need help putting them on. You can get these in different compressions (strengths) and it's best to talk to your doctor about what is recommended for you.

Edema (that's what the swelling is called) can become a major problem if it becomes excessive. When the swelling becomes too excessive, it can cut off your circulation and this is why the skin in your feet may turn a purple color. If your toes are purple, you need to discuss this with your physician.

Exercise:

This is a very controversial topic in sIBM. Some doctors suggest mild exercise of the muscles that are still functional; others suggest no exercise. The research does not give us a clear answer. Some doctors believe that the more you exercise the faster the muscle will deteriorate and that after extreme exercise there is no recovery. Strenuous exertion should be avoided. In my opinion, from what I have seen, if you overdo it, it is very hard to recover. One doctor told me "run a marathon – get a wheelchair."

Diet:

Because sIBM is a movement disorder and impairs movement, and because you cannot exercise as a normal person would, the single most important thing is to eat well and to eat less. When you are inactive and you eat a normal diet you will gain weight. Naturally, the more you weigh, the more problems you will have in general because you don't have the muscle structure to support normal body weight. So the best advice is to try to curtail the amount you eat.

Attitude:

This is a serious and chronic disease. You will have it for the rest of your life. Attitude becomes a critical factor in being able to cope and not become bitter, cynical or depressed. Don't give up – find ways to adapt. Our lives will change – for example, I had to give up my job, but now I have different things in my life to keep me busy. Attitude is critically important when you have a long-term disease that has no treatment.

Using a walker or cane:

A cane can help you with balance in the initial stages of the illness. Likewise, the use of a walker can be beneficial in the early stages. As your disease progress you have to continue to adapt and change your strategy. For example, you may find yourself falling down on top of your walker (as I did) – this is time to move to a wheelchair.

Wheelchair:

Understandably, there are a number of drawbacks, problems and perhaps stigma associated with being in a wheelchair. However, a wheelchair is far safer than falling and risking broken bones. I have met many people who realize they should be in a wheelchair, however, they stubbornly refuse to consider the possibility. In my opinion, if you are using a cane or a walker and you are still falling, you should seriously consider that your safety becomes more important than pride. Recovery from a broken bone or concussion presents a very serious prospect for the patient with sIBM.

Note: Many sIBM patients will never require a wheelchair. Many factors enter into this, including: when symptom onset occurred; how rapid the progress is; and the patient's overall health. Many patients will pass away from other causes before reaching the stage where they need a wheelchair due to sIBM. Eventually, many people do end up with what they call total disability and, in general, the mean/median time to wheelchair use is about 14 to 16 years after symptom onset.

Swallowing:

Many sIBM patients (about 50-70%) develop weakened swallowing (dysphagia). This is a major complication leading to the potential of choking. As soon as a person is diagnosed with sIBM he or she should be assessed for swallowing weakness and this should be monitored as the disease progresses.

Sometimes you try to swallow and nothing will happen or, food will get stuck halfway down. This can lead to choking that can be life threatening. As well, if this happens, food can get into the lungs (aspiration), resulting in a type of pneumonia that is often fatal in older people.

Some people with sIBM eventually have to have tubes inserted into their stomachs because they can no longer swallow. Sadly, some people simply stop eating and die of malnutrition.

Pay attention when you are eating. Do not be in a hurry. Do not be trying to have conversations while eating. Eat smaller portions and chew the food well. If you notice problems swallowing, you should have this evaluated and keep an eye on any potential progress.

In general, you should always have a noncarbonated liquid available when eating. I find that drinking with a straw is the most practical. If you are with others and you began to have problems you should try to draw their attention to your situation. Try to take a very small sip of liquid to dislodge the blockage. I have discovered the most important thing in the situation is to try to remain calm. If you choke frequently you should not eat alone and those who are with you should be very attentive and know what to do, for example, how to apply the Heimlich manoeuvre.

Breathing:

Sometimes sIBM can weaken the diaphragm. This can lead to reduced air volumes, especially during sleep. This has a long-term effect that can kill you – over time, carbon dioxide can increase in the blood slowly poisoning you (it has nothing to do with oxygen). The treatment is to use a BiPAP machine at night to give the necessary amount of airflow in order to exhale enough carbon dioxide. Respiratory failure through weakness of the respiratory muscles is a recognized cause of death in sIBM. As soon as a person is diagnosed with sIBM he or she should be assessed for diaphragmatic weakness and this should be monitored as the disease progresses.

Pain:

Generally speaking, when you read about sIBM, it is not associated with pain however, people with sIBM often report pain. Pain can result from several things. If a muscle is pressed or stretched it can cause pain. Likewise, if you are in a position for a long time, the body can become stiff and this can lead to pain in the muscles.

Skin:

People sitting in one position for a long time, either in a wheelchair or just in an ordinary chair are often prone to developing soreness and breakdown of the skin on the buttocks. In sIBM the nerves are not affected and you will have normal pain receptors. If you are sitting and it begins to hurt, then you need to move, even if someone has to move you to a different position. Pain is a sign that pressure is becoming excessive. Pressure sores in the skin can be very painful and can become a major problem if they become infected. As well, pressure sores take a long time to heal.

Beds:

One of the major challenges of this disease is that you generally have trouble turning over in bed. If your bed is too soft you will end up “in a hole” and unable to move. If your bed is too hard you will have problems with pressure, usually felt on the hips. This can be very painful. Generally speaking a lot of experimentation is necessary to find the proper fit for you.

As the disease progresses, falling while getting in or out of bed is a major threat. Adaptive devices may be necessary, for example, the use of a ceiling lift for safe transfers.

Bathroom:

The bathroom presents many obstacles for the sIBM patient. Early on, it may become very difficult to get out of a bathtub. As well, rising from a toilet can be challenging as the symptoms progress. Adaptive devices may be necessary, for example the use of a shower chair (both for showering and usually, rolling over a toilet).

C). Other

Myositis associations:

Muscular Dystrophy Association USA (http://mda.org/)
Muscular Dystrophy Canada (http://muscle.ca)
The Myositis Association (myositis.org)

Research on sIBM:

sIBM is a very complex and challenging disease to research. In approximately the last 40 years of research, much has been learned about the disease, but frustratingly, more remains unknown. The understanding of sIBM and its description is a bit of an evolving phenomena as more is learned over time.

For technical reviews of research (aimed at doctors) see, for example, Dimachkie and Barohn (2013) or Machado, Dimachkie, and Barohn, (2014).

Theories of sIBM:

sIBM has two major features: one having to do with the immune system attacking and killing muscle cells (an autoimmune aspect); the other, a deterioration of the proteins in muscle cells (a degenerative aspect). The two aspects appear to occur in parallel in muscle cells. It is not clear which aspect comes first, if one causes the other, or if some other factor causes both aspects.

It is likely that a combination of multiple features will be discovered as causing sIBM, involving both immune and degenerative aspects, environmental and genetic factors and their interaction with each other.

An early theory was that a virus triggers sIBM, setting in motion an ongoing immune response which attacks and kills the muscle cells (no virus has been found).

sIBM was named for the observation that “inclusions” (inclusion bodies = clumps) and strands of abnormal proteins form in the affected muscle cells. Based upon this, a second major theory is that abnormal proteins somehow form in the muscle cells causing sIBM and then triggering an immune response.

Third, some researchers believe sIBM is primarily a type of autoimmune disease.

Research continues, although, at a very methodical (step-by-step) and incremental (slow) rate. Today, the available evidence does not form a coherent picture of how sIBM might develop. More discoveries and/or a new theory of sIBM will have to emerge before this impasse is resolved (and thus leading the way to new treatment strategies).

Polymyositis (PM) and sIBM:

Patients with sIBM are very often initially diagnosed as having polymyositis (PM). sIBM is quite rare and relatively unknown, whereas PM is quite well known. PM has a different onset – it comes on over weeks, whereas, sIBM has a very slow onset over months or years. PM responds quickly to medication whereas sIBM shows no response to medication. If you have been diagnosed with PM and given medication and you have not responded then clearly your diagnosis should be reviewed again.

Genetics and IBM:

The sporadic form of IBM (sIBM) is not considered an inherited disorder: It is not passed on to the children of people with sIBM. However, it appears that a predisposition to developing sIBM may be linked to a group of genes commonly seen in Caucasians from Northern European ancestry. People with these genes are predisposed to develop autoimmune disorders. sIBM is associated with a small group of such genes (HLA-DR3) in about 70% of patients (see Badrising et al, 2004). If you happen to have this particular set of genes, you may be somehow predisposed to develop sIBM.

Is also possible that some combination of genes may interact with each other and with environmental variables to increase the likelihood of sIBM developing in a given individual.

Familial Inclusion Body Myositis (fIBM):

fIBM occurs in two or more siblings in a family in the same generation (but it's not passed on to their kids). The symptoms and features of fIBM are very similar to those seen in the sporadic form of IBM. fIBM is also linked to the same genes as sIBM, raising the possibility that fIBM and sIBM share similar inherited predispositions. The familial occurrence of such a rare disorder likely highlights the importance of genetic predisposition in the causation of sIBM (Needham, Mastaglia, & Garlepp, 2007).

Other genetic forms of IBM:

Several different types of hereditary inclusion body myopathies (hIBMs) are now recognized. See Broccolini and Mirabella (2014) for information. Notice that these are called myopathies (literally, pathology of the muscle) as opposed to the sporadic and familial forms that are referred to as myositis conditions (literally, inflammation of the muscles). The different forms display different symptoms but all share similar underlying structural features. These are very, very rare disorders, altogether, likely affecting less than a few hundred people worldwide. The various hereditary types can be passed on to children and follow either autosomal recessive or autosomal dominant patterns of inheritance.

Summary of IBM types:

In summary, there are three basic forms:

Sporadic inclusion body myositis (sIBM) (the form most commonly seen).
Familial Inclusion Body Myositis (fIBM).
Several hereditary inclusion body myopathies (hIBMs) (exceedingly rare).

Familial and hereditary forms of IBM existing along with sporadic IBM is a challenge to understand: How are they related? What does this say about underlying causes?

D). Information checklist

✔ sIBM has been known since the late 1960s but it is quite rare and it is not unusual for physicians to be unfamiliar with the disease.

✔ Muscle diseases are complex and many have similar symptoms. Diagnosis is always a long and sometimes frustrating process. Misdiagnosis is common. The best advice on diagnosis is from your physician: not the Internet. My best advice is to be patient and become a strong advocate for yourself throughout the process. As I've said before, this is a serious disease that you will have for the rest of your life and my philosophy is that the more you know about it and the more professional you can be in your approach as an sIBM patient, the better.

✔sIBM has many variations in symptom presentation making it virtually impossible to compare two different patients. This also makes it hard to predict the rate of progression.

✔ sIBM has no recognized medical treatment today. All treatments that have been tried have failed and all have significant side effects that outweigh any short-term or marginal benefits. Likewise, generally, no supplements or other diets have been shown to make a difference.

✔ At least four complications need to be considered and managed: unexpected falls; weakness swallowing; weakness in the diaphragm; and lower leg edema.

✔ Very careful management of the disease and its complications will lead to the highest quality of life and maximize one's lifespan.

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F). Disclaimer

I am not a medical Doctor and this information is not intended to be read as medical advice nor is it a substitute for medical advice. Please consult your Physician if you have medical concerns. I have done my best to offer a layman's interpretation of this material based upon my experience with the illness and my reading of the literature. I have tried to avoid references here although I have included a few where critical. Any opinions offered are personal and do not reflect those of my employer. Thank you.

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August 27, 2014