

## Wetenschap voor Patiënten (Science to patients)

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### Seminar 39: ME, exercise and the mitochondria

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#### **What are the effects of exercise on someone with ME?**

The effect of exercise on people with this illness is very characteristic and it is really a diagnostic key, a diagnostic feature of the illness. So that when people exercise their muscles run out of energy, they run out of the capacity to perform exercise. So what we term exercise induced muscle fatigue is, I believe, what is probably the hallmark of this illness. Interestingly enough, when people exercise beyond their limitations they will also get what we call post exertion malaise, post exertion fatigue. This can sometimes be delayed for several hours or even 24 hours. So they go to the point to their exercise tolerance and stop, but the following day perhaps, they then feel that they've got an exacerbation of their symptoms because of this symptom of post exertion malaise.

#### **What is exercise tolerance time?**

Exercise tolerance is a term that we would normally apply to exactly how long someone can exercise for before fatigue sets in, quite often pain sets in and then if they continue after that actual weakness and unsteadiness of the muscles will occur. It's a very variable factor with people with ME. So someone at the mild end of the spectrum with this illness they may be able to go for a walk for half a mile, perhaps even longer before they're starting to feel fatigue and weakness. Whereas someone who is more moderately affected may only be able to walk perhaps a hundred or two hundred yards. An absolute maximum before they reach the point at which they cannot carry on any further. And of course people at the severe end of the spectrum, who are wheelchair bound, bed bound and house bound, they would have very very limited tolerance for any form of physical activity or exercise.

The other, I suppose, characteristic of this is it depends what sort of exercise activities are being undertaken. If it's a short burst of terribly strenuous or physical activities like saying trying to go for a ride on a bike or a run or something which someone with ME would not be able to do, but if you put someone with ME through that sort of exercise their ability to sustain that form of high-intensity exercise will be very very short. Whereas if it's low-intensity exercise, walking for instance as I say, there would be a wide variation in the tolerability as to how far someone would be able to do that.

#### **What is the effect of ME on the muscles?**

The effect of ME on the muscles is this symptom which I already described of exercise induced muscle fatigue. So we have this range of muscle symptoms which develop progressively after someone has been doing any form of activity. So fatigue will set in in the

muscle, pain will probably set in in the muscle - but not always – and then if the activity is pushed on beyond the persons limitations, actual weakness will occur in the muscles.

### **How can one avoid exerting oneself too much?**

To avoid getting these muscle symptoms and overexertion, to a certain extent it requires a process of trial and error. It's something that people with this illness learn to develop and the way which we try to make people understand the best way to cope with this key symptom of ME is through a process what we call pacing. This involves very careful management of activity and rest or relaxation.

So what we would advise patients with this illness to do is to pace their activities. So that they are not exceeding their limitations, they are dividing their physical and their mental activities into little small chunks, so they do a little bit of physical activity within their limitations. They then have a period of rest or relaxation. Perhaps after a bit of physical activity they might do a bit of mental activity, and then they have a period of rest or relaxation.

What is important not to do is, and this takes people into what we call a boom and bust cycle, is to push on to the point of physical exhaustion, fatigue and then stop because then you're just going to get a prolonged period when you'll not be able to do anything and return to activity. So it is very important to try and pace activities, with little bits of activity, gaps in between, followed by little bits of activity.

### **What's the difference between pacing and GET?**

The difference between pacing and graded exercise therapy very much depends on who is recommending the particular form of treatment. But in very simple terms pacing is living within your limitations. But at the same point within those limitations, given the fact that you are having little gaps, little periods of rest or relaxation between activities, gradually trying to increase the amount of time you are spending on a physical or mental activity. But certainly not pushing yourself beyond your fatigue barrier.

Graded exercise is a rather more structured and pro-active form of activity management in which people are, if you like, often encouraged to push beyond their boundaries and not necessarily take a rest when you would be taking a rest during pacing. Our experience, certainly in patients surveys, is that 90 % of people who respond to patient surveys on activity management find that pacing is a very effective form of activity management. Very few people report any sort of adverse effects to it. Whereas if you look at patient opinion on graded exercise you will find that up to about 50% of people in these surveys report graded exercise actually makes them worse. But there is a small number of people who find graded exercise to be helpful in their management.

I suspect this reflects the fact, going back to my previous points about this big umbrella of people that come under this term chronic fatigue syndrome, that there are people who have an illness of one end of the spectrum which may well be more of a psychiatric type of illness who respond to this type of approach. Opposed to the people at the other end of the spectrum with very much a physical ME type illness, who are much more likely respond to pacing.

## **How to deal with relapses while pacing?**

The way to deal with relapses in relation to pacing is first of all to try and make sure that you can recognize as soon as possible that you've got an exacerbation of symptoms going on or that your illness is going into a relapse phase. To a certain extent this is fairly recognizable because most of the things that we know cause ME are also the sort of things that tend to cause a relapse. So relapses are in particular caused by infections, sometimes they can be caused by vaccinations, stress seems to play a particularly important role in causing relapses and sometimes a physical trauma. We talk about road accidents, we talk about surgical operations could cause a relapse. So if you are aware that any factors are going on, like an infection, that is likely the cause of a relapse, you need to modify your pacing program to take that into account.

So you would drop the degree of activity you were doing, both physical and mental within those little chunks, to a lower level. You would decrease the time you were doing involved in those activities and you would at the same time extend the period of rest and relaxation between your activities. So it's a very careful balance that has to be struck, and again as we are learning how to do pacing, it's very often a question of trial and error before you actually pick up and learn how to do it properly.

## **What role do the mitochondria play in ME?**

The mitochondria play a very important role in ME. Mitochondria are tiny little, what we call organelles within the muscle and they're rather like Duracell batteries within the muscle. They're the places where chemical reactions take place which break down sugars, which were taken from our diet to actually form energy in the form of something called ATP. We know from our work. Actually the very initial stuff on mitochondrial dysfunction in this illness was done on some of my own skeletal muscle, this was done over thirty years ago, and the results were published in the Lancet. We demonstrated with someone called professor George Radda from Oxford the fact that when I exercised there was an abnormal increased amount lactic acid being produced in the muscle. Which is indicative of a problem within the mitochondria.

At the same time some research was being done by a colleague of mine, professor Peter Behan up in Glasgow which was actually again taking little bits of muscle and looking them up under the microscope. These experiments under the microscope show that there were actual structural changes in the mitochondria. So we have evidence of biochemical abnormalities in the mitochondria from the magnetic resonance spectroscopy studies at Oxford, and structural abnormalities from the electron microscopy studies that were being done in Glasgow. So we know that this seems to be a problem with mitochondrial function in ME. Which may play a very important part in explaining why people have this very characteristic symptom of exercise-induced muscle fatigue, and sometimes pain in this illness.