

Issues relating to
Severe ME/CFS and Graded Exercise
Greg Crowhurst Sept 3 2005

Any one considering Graded Exercise for someone with severe ME/CFS needs to reflect very carefully upon the devastating neurological nature of this illness :

SYSTEM	EXPERIENCE (Carruthers et al 2003) ^v	POSSIBLE CAUSES
Immune System Manifestations	<ul style="list-style-type: none"> ▪ Tender lymph nodes ▪ Sore throat ▪ Flu-like symptoms ▪ General malaise ▪ Development of new allergies ▪ Hypersensitivity to medications and/or chemicals 	Impaired function of natural killer cells and increased numbers of activated CD8+ T cells (McLaughlin 2003); Abnormalities found in the 2-5 synthetase/RNase L anti viral pathway; Suhadolnick (2004) ⁱⁱ Low molecular weight RNaseL in ME/CFS patients (Montague and Hooper 2001) A "profound loss of growth hormone " in patients with ME/CFS (Severling 2005) ⁱⁱⁱ This helps explain why ME/CFS sufferers are very sick; the question for Dr Cheney is "How are these people surviving?"(Severling 2005) ^{iv}
Neuroendocrine System Manifestations	<ul style="list-style-type: none"> ▪ Loss of Thermostatic stability ▪ Heat/Cold intolerance ▪ Anorexia or abnormal appetite ▪ Marked weight gain ▪ Hypoglycemia ▪ Loss of adaptability and tolerance for stress. ▪ Worsening of symptoms with stress and slow recovery and emotional lability 	Abnormalities in the output of hormones ; a chronic depression of cortisol and DHEA (which is not seen in depressive illnesses.) (Wright 2003) ^v ; depletion of central opioid tone (Wright 2003) ^{vi} ; a reduction in adrenal gland size (Wright 2003) ^{vii} ; functional hypothyroidism at a cellular level (Wright 2003) ^{viii} ; low levels of pituitary hormone output , which may be the cause of the fatigue. (Wright 2003) ^{ix} Creatine, a sensitive marker of muscle inflammation, is secreted in significant amounts in the urine of ME/CFS patients, as well as choline and glycine. (Richards and Clare et al 2001) ^x
Autonomic System Manifestations	<ul style="list-style-type: none"> ▪ Postural orthostatic tachycardia syndrome ▪ Delayed postural hypotension ▪ Vertigo ▪ Light-headedness ▪ Extreme pallor ▪ Intestinal or bladder dysfunction ▪ Palpitations with or without cardiac arrhythmia ▪ Vasomotor instability ▪ Respiratory irregularities 	An excess of sympathetic over parasympathetic tone ^{xi} ; autonomic nervous system (ANS) dysfunction in up to 90% of CFS patients (Hooper & Montague 2000) ^{xii} ; including orthostatic intolerance and neurally mediated hypotension. (Komaroff 2000)
Neurological/Cognitive System Manifestations	<ul style="list-style-type: none"> ▪ Confusion ▪ Difficulty with information processing ▪ Perceptual/sensory disturbances ▪ Overload phenomena ▪ Photophobia and/or Hyperacusis 	Low blood flow in multiple brain areas of brain (Schwartz et al 1994) ^{xiii} (Costa et al 1995) ^{xiv} Significant 8% reduction in gray matter volume compared with health controls (de Lange et al 2005) (Okada et al 2004) Cellular metabolic abnormality (Chadhuri & Behan 2004) ^{xv}

As Wright (2003)^{xvi} puts it : "given the bi-directional flow of information between the nervous, endocrine and nervous systems we are presented with a perfect example of

Chaos Biology."

Holgate and Kerr et al (2005) have recently found that patients with ME/CFS have reproducible alterations in gene regulation and that sixteen genes have an expression profile associated with the disorder that can be grouped according to immune, neuronal, mitochondrial and other functions." ^{xvii} This effect is known to be linked to organophosphate exposure. ^{xviii} In other words, as Williams (2005) states ^{xix}: " there are more gene abnormalities present (in CFS/ME) than are found in cancer sufferers."

Cheney (1999) warns : *“The most important thing about exercise is not to have (patients with ME / CFS) do aerobic exercise. I believe that even progressive aerobic exercise is counter-productive. If you have a defect in mitochondrial function and you push the mitochondria by exercise, you kill the DNA”* ^{xx}

The severe ME sufferer, at any one time , will be experiencing a host of violent symptoms , both inside and outside their body :

INSIDE	OUTSIDE
<p>Sleep problems: insomnia; non-refreshing sleep; difficulty in waking up. Brain fog Difficulty processing information Struggling to stay awake/go to sleep Word forgetfulness Lack of ability to make sense of external information Dizziness Tinnitus Acute noise hypersensitivity Inner ear pain Poor reaction to anaesthetics & dental treatment Hypothalamus/ Pituitary imbalance Whole body muscle spasms Nerves firing continually Adrenal glands affected Adrenalin over-stimulation Hypoglycaemia Muscles not functioning properly Gastritis Irritable Bowel Syndrome Candida / Fungal infection Joint pain Noise sensitivity Light sensitivity Hypotension Sound sensitivity Transient paralysis Severe headache/pain Nausea</p>	<p>Problems walking Numb face, eyebrows, nose, cheeks, ears, neck/hands/body Whole body paralysis/increased pain Acute sensitivity to touch Falling over / Spacial problems Skin itching, burning, throbbing. Need silence Numb tongue Problems swallowing Difficulty in coping with dental surgery Difficulty talking Thyroid imbalance Menstrual problems (increased pain/spasms) Body shaking/ tension Irritability Emotional lability Increased stress reaction Black outs Fainting Desperate need to eat/drink Inability to <ul style="list-style-type: none"> • stand • walk • hold things • write, • eat • cook • get dressed • sit up. Danger of falling (increased pain, numbness, fatigue, weakness) Stomach pain / bloating/food sensitivity Genital pain Reduced sexual activity Increased difficulty with using joints and muscles.</p>

Drawing upon her personal experience of 12 years of suffering from severe ME, Linda Crowhurst has many concerns about Graded Exercise Therapy:

- The person has to be able to get out of bed, which a high proportion of people with severe ME might not be able to do.
- The person has to be able to stand upright which is a huge issue for people with severe ME suffering from hypotension, dizziness, muscle weakness, nausea and multiple other symptoms.
- Any activity can be too much at any moment with a worsening after-impact and decline.
- Being expected to do anything on a regular basis at a set time or on a set date is unlikely and impractical given the severe nature of the symptoms.
- If the person somehow manages to perform some level of exercise once, the likelihood of doing it again and increasing it more and more, is likely to lead to an adverse, out-of-proportion reaction and decline.
- It is irresponsible to subject somebody to exercise that will almost certainly result in a worsening of symptoms.
- Exercise just does not tire the muscles, the person with severe ME is likely to suffer a multitude of worsening symptoms including severe pain/headaches/muscle spasms/breathing difficulties/ increased numbness/ increased paralysis, which could lead the person who may be just about coping to become more disabled, more dependent and have a total knock-on effect on their whole ability to cope or could put people at risk or mean they need a higher level of care.
- The person with severe ME is unlikely to be able to attend a centre where there are other people because of: noise sensitivity; fatigue issues; difficulty in travelling, sitting upright, coping with motion, noise, vibration, balance, perception and fatigue.
- The person with severe ME is unlikely to be able to cope with conversation, given the problems of: physically speaking; processing information; understanding what is being asked; coping with the loudness and tone of speech; fatigue and the physical and mental effort of trying to engage in dialogue. For people with severe ME most of this is not possible, most of the time.
- The hardest thing for people with severe ME is to be with other people. The impact of others can make the sufferer very ill within moments.
- You also need to consider the effect of expecting someone with severe ME, which is a neurological illness to participate in an intervention that is based on the underlying beliefs that the person is not physically ill. This is an attack on the person's integrity, self esteem and whole being. To not be believed, even in the "nicest" possible way, is going to undermine any intervention and have a negative impact in the relationship and relationship is the key to working with people with severe ME.
- The assumption that people do not really want to try or they are not trying hard enough or they just think they cannot do it is wrong. People desperately do want to be well and some people will try GET and CBT trusting in the professional, especially people new to the illness who just want to be better. What about the impact emotionally as well as physically on them? It would be devastating to be willing to do that and try it and end-up in a downward spiral, a worsening of illness and symptoms.

Clinically, the research shows that :

- It takes the ME sufferer an inordinate amount of time to recover from exercise.^{xxi}
- Patients with CFS describe characteristic worsening of their symptoms following exercise as well as exercise limitations, defects in functional capacity, neuroendocrine defects in response to exercise, as well as defects in respiratory control mechanisms.^{xxii}
- As much care should be taken in prescribing exercise as in prescribing pharmaceuticals.^{xxiii}
- ME/CFS patients do not respond to exercise in a manner that is expected of healthy people.^{xxiv}
- ME/CFS patients receive less blood and oxygen to the brain after exercise making them feel worse.^{xxv}
- The maximum oxygen uptake of ME patients is approximately only half that of sedentary controls. This could indicate the heart is functioning at a sub-optimal level and that exercise could be dangerous.^{xxvi}
- In one study ME/CFS patients demonstrated significantly lower cardiovascular as well as ventilatory values at peak exercise, compared with the control group, this could indicate either cardiac or peripheral insufficiency embedded in the pathology of ME/CFS patients.^{xxvii} as Williams (2004) states : "many people with ME / CFS may have a serious heart problem."^{xxviii}
- Because of cerebral hypoperfusion , exercise in ME/CFS patients can cause a further marked decrease in cerebral blood flow and a marked worsening of symptoms.^{xxix}
- In ME/CFS patients body temperature normally decreases in response to exercise - the opposite of normal.^{xxx}
- In ME/CFS patients cognitive processing becomes impaired in response to physical exertion.^{xxxi}
- Recovery period is greatly prolonged and can take days or weeks.^{xxxii}
- The severity of post-exertional symptoms ranges from mild to severe, or may be life-threatening (seizures and cardiac events). The onset of post-exertional symptoms may be very sudden, but more often are delayed by 12 - 24 or 48 hours (or longer) and may then persist for hours, weeks or months afterward.^{xxxiii}
- Orthostatic intolerance, low circulating blood volume and blood pooling in the legs often play a role in post-exertional malaise and fatigue.^{xxxiv}
- Gait abnormalities have been found in ME/CFS patients which may be due to balance problems, muscle weakness or central nervous system dysfunction.^{xxxv}
- The response of CFS patients to incremental exercise associates a lengthened and accentuated oxidative stress together with marked alterations of the muscle membrane excitability. These two objective signs of muscle dysfunction are sufficient to explain muscle pain and postexertional malaise reported in patients.^{xxxvi}
- Research from The University of Adelaide suggests that exercise worsens ME/CFS symptoms because it triggers a flood of excess lactic acid. In some trials, ME/CFS patients were found to produce double the amount of lactic acid than people without CFS, even when taking lack of fitness into account.^{xxxvii}
- The Canadian Clinical Case Definition^{xxxviii} , currently being lobbied for by the 25% Group in the UK, requires that a person's condition worsens following exercise and that other symptoms must be present for a diagnosis of CFS/ME to be made. These include :

- Sleep dysfunction
- Pain
- Neurological manifestations
- Autonomic manifestations
- Neuroendocrinal manifestations
- Immune manifestations

Overall there appears to be very little clinical or research evidence upon which to recommend Graded Exercise Therapy for the severe ME sufferer. The Chief Medical Officer (2002) warns that exercise-based regimes advocated for less severely affected patients tend not to have been studied among those most severely affected.^{xxxix}

The issue is not so much setting "baselines" - highly unlikely in severe ME anyway- but of learning :

- how to be aware of the subtly of the illness : *when you can, when you can't and when you might.*
- how you are in any one moment so you can cope with it
- how to be accepting of yourself in whatever state of illness you are in without giving up hope that it might/will/can change, at least on a micro-level, if not in an external obvious way. (Crowhurst & Crowhurst 2005)^{xl}

Overall there appears to be very little clinical or research evidence upon which to recommend Graded Exercise in severe ME . It is important for people to be aware that participation in GET for those with severe ME is a potentially dangerous and abusive step to take.

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Evidence for their organic basis: A summary of the suggested underlying pathophysiologies and treatment approaches CFSResearch 2005

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vii *ibid*

viii *ibid*

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x SCM Richards, A Cleare et al. Conference Proceedings of the British Society of Rheumatologists, Edinburgh, April 2001

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