

Post-Exertional Malaise in Chronic Fatigue Syndrome

By Jennifer Spotila, J.D. for The CFIDS Association of America, 2010

Part One - Unraveling Post-exertional Malaise

Muscle wilting meltdown, air gulping short of oxygen feeling, brain blood vessels flayed on a laundry line in the wind, metal rods in the back of head . . . someone crushing your ribcage, limbs giving out, mesh bag constricting head, 'pingers': those first small headaches that warn of bigger headaches, 'back of head clamp' . . . headache, increased gravity feeling, being pushed backward into bed, temple-to-temple headache, weak arms as if bound down by stretchy ropes, eyes and brain blanking with a kind of pulse through the head . . . Harm and damage often come from these collapses, though on the outside they may look like 'malaise'.

- Patient, speaking anonymously

A survey of more than 1,000 patients conducted by The CFIDS Association in 2009 found that post-exertional malaise (PEM)¹ is one of the most common and most severe symptoms reported by patients.² This article, the first in a series, examines the definition of PEM and how patients experience it.

How Is Post-exertional Malaise Defined?

Standard medical dictionaries define malaise as “a feeling of general discomfort or uneasiness, an out-of-sorts feeling.”³ This bland description bears little resemblance to the severity of PEM in CFS. It is not clear who first coined the term or applied it to CFS. Early definitions of the illness do not use the phrase, but they do describe something like it.

The 1988 Holmes criteria for CFS⁴ included the symptom of “prolonged (24 hours or greater) generalized fatigue after levels of exercise that would have been easily tolerated in the patient's premorbid state.” The Oxford criteria⁵ from 1991 said only that fatigue and myalgia (muscle pain) “should be disproportionate to exertion.” Neither Holmes nor Oxford required PEM for diagnosis of CFS. The 1994 Fukuda criteria⁶ was the first to explicitly include the symptom of “postexertional malaise lasting more than 24 hours,” but still did not require it in order to make a diagnosis of CFS.

The 2003 Canadian Consensus Definition⁷ was the first to define PEM in detail, and the first to require PEM for the diagnosis of ME/CFS:

Post-Exertional Malaise and/or Fatigue: There is an inappropriate loss of physical and mental stamina, rapid muscular and cognitive fatigability, post-exertional malaise and/or fatigue and/or pain and a tendency for other associated symptoms within the patient's cluster of symptoms to worsen. There is a pathologically slow recovery period—usually 24 hours or longer.⁸

How Does Post-exertional Malaise Feel?

PEM is not just a feeling of severe fatigue; it is a full-body assault. A physician with CFS says, “My PEM feels like a worsening of my baseline CFS symptoms - more fatigue, headaches, neck/ back muscle achiness (but not outright pain), problems concentrating/ reading. My insomnia also sometimes increases temporarily and at its worse, my throat hurts and my lymph nodes feel more tender.” PWC Andrew says, “I can’t focus enough to watch TV. Conversation becomes difficult. Any kind of stimulation feels like an assault on my senses.”

The use of the word “exertion” may create the impression that PEM is triggered by strenuous or intense activity, but this is not the case. Patient Sue Jackson says that “Any kind of exertion . . . can leave me, a few hours later, suddenly feeling as if I have a terrible flu.” Some patients need only attempt to make a simple meal or get dressed before PEM descends. Cognitive or emotional effort can also cause PEM. For Andrew, it takes very little to bring on PEM, such as “[s]itting at the computer too long a few days in a row. It seems like not enough bed time and too much activity time can cause it.”

The amount of activity that triggers PEM varies from patient to patient, or even for one patient on different days. “The safety zone moves around,” says another physician with CFS. It is very common for the onset of PEM to occur a day or more after the triggering activity, but sometimes it can happen immediately. A patient may be able to drive to a doctor appointment, but sudden PEM might make it impossible to drive home. Without clear and predictable boundaries to define tolerated activity levels, patients are forced to navigate with trial and error.

The cost of error is very high. One patient says, “It feels like somebody flips a switch and any sense of well-being disappears. I have to go lie down, and then I still feel like I have to go lie down! There is no relief.” PEM may last as short as 24 hours, but recovery can take days, weeks or even months. Andrew has found “the more I stress my body this way, the longer the exacerbation lasts.” He notes that recovery from PEM only means returning to baseline, and “I don’t even feel that well before exertion.”

There is no formula for PEM. Patients cannot reliably predict what activities will bring it on, and the duration of recovery does not always correlate to the level of effort that caused it. Ms. Jackson speaks for many patients when she says, “PEM is the worst part of CFS for me.”

Part Two - Post-Exertional Malaise: Perception and Reality

Dr. Anthony Komaroff of Harvard University recently described post-exertional malaise (PEM) as “an illness within an illness.”⁹ This article, the second in a series, examines objective evidence of PEM and how it differs from fatigue in other illnesses.

Is it Real?

PEM associated with CFS dominates the patient's experience of the illness, but PEM is generally considered a self-reported symptom because there is no clinical test to easily measure its occurrence and severity. However, researchers have been able to objectively demonstrate that PEM is a real phenomenon by inducing it with exercise testing and identifying differences in the physiological responses of people with CFS (PWCs) and healthy controls:

1. Exercise lowers the pain threshold in patients with CFS, while it raises the pain threshold in healthy sedentary controls. The amount of force applied to skin that caused pain was objectively measured with an instrument, and compared across subjects.^{10,11}
2. CFS patients and sedentary controls do not recover from muscle exertion at the same rate. The maximum amount of force exerted by leg muscles was objectively measured, and both groups showed the same pattern of decrease in force during repetitions. The controls recovered to full force within 200 minutes, and did not differ from their pre-exercise levels at 24 hours. In contrast, CFS patients not only failed to recover to full force, but an even further decline in force was observed at 24 hours.¹²
3. Cognitive tests performed before and after exercise demonstrated that CFS patients have both increased perception of effort and deficits in cognitive processing after exercise. Furthermore, these cognitive deficits distinguished CFS patients from both healthy and depressed controls.¹³

The full effects of PEM often do not emerge immediately after activity, and some researchers have examined the effects of exercise over a period of days. For five days following a maximum exercise test, CFS patients exhibited significantly greater fatigue of longer duration than controls, although they did not exhibit any change in activity levels.¹⁴ In another study, patients and controls recorded their symptoms for 7 days after a maximum exercise test.¹⁵ At 24 hours after the test, 20% of controls were completely recovered, and 100% were recovered after two days. None of the CFS patients were recovered after 24 hours, and only 4% recovered in two days. The majority (60%) took 5 or more days to recover from the single exercise challenge. A comparison of CFS patients and controls during four weeks of daily exercise indicated that the patients could not sustain increased activity beyond 7 days, and were more likely than controls to develop exercise intolerance.¹⁶

Single exercise tests do not always show significant differences between PWCs and controls, but conducting tests on two consecutive days can produce dramatic results. VanNess and colleagues at the Fatigue Lab at Pacific University measured cardiopulmonary function in patients and controls with a test/re-test protocol.¹⁷ During the first exercise test, CFS patients and healthy controls exhibited no significant differences in cardiopulmonary function. But when the subjects repeated the exercise test the following day, very significant differences emerged. Oxygen consumption varied by only 3% in the controls between the first and second tests. The CFS patients experienced decreases in oxygen consumption of more than 20% during the second test.

Is It Unique?

Fatigue is a significant and disabling symptom in many illnesses, including multiple sclerosis, lupus, and rheumatoid arthritis. Fatigue in lupus has been described as “an extreme fatigue that interferes with many aspects of your daily life.”¹⁸ MS fatigue or “lassitude” is severe fatigue that is unrelated to physical activity, occurs on a daily basis, and interferes with functioning.¹⁹ Both of these descriptions are similar to how CFS patients describe their fatigue, but it is the effect of exercise on these illnesses that may truly distinguish them.

There is a growing body of research showing that MS patients can tolerate aerobic exercise, and also benefit from it.²⁰ For example, in a four-week trial of aerobic exercise, MS patients improved their aerobic threshold, decreased fatigue, and only 6% of subjects experienced symptom exacerbation.²¹ The Medical Advisory Board to the National Multiple Sclerosis Society recommends regular aerobic exercise geared to the person’s ability as one of the clinical management strategies for MS fatigue, even for the 50-60% of MS patients who say fatigue is one of their most troubling symptoms.²² The same holds true for patients with lupus and rheumatoid arthritis. Aerobic exercise training in lupus patients has been shown to improve aerobic capacity and exercise tolerance, while also not exacerbating the disease.²³ In rheumatoid arthritis, studies show that regular exercise helps reduce joint pain, increase joint mobility and strength, and improve mood.²⁴ While all these illnesses require rest and pacing, exercise does not appear to have the same aggravating effect on symptoms that it does in CFS.

In fact, PEM can be used to differentiate CFS from other illnesses. The presence and severity of PEM was among several symptoms that distinguished PWCs from people with major depressive disorder with complete accuracy.²⁵ In the test/re-test protocol used by VanNess and colleagues, the 20% decrease in cardiopulmonary function in CFS patients during the second test is unique. Variation in cardiopulmonary function has been measured in people with pulmonary hypotension, end-stage renal disease, cardiac problems and cystic fibrosis; none of these patient groups exhibit more than a 7% variation in function. The authors conclude, “We believe that this difference may be a distinctive feature of the syndrome and allow differentiation between the fatigue produced by CFS and fatigue associated with other illnesses.”²⁶

Whether objective measures of PEM can be used to confirm a CFS diagnosis remains to be seen, but the evidence indicates that PEM is the result of disturbances in many body systems. The next article in this series will review that evidence and consider what might cause this “illness within an illness.”

Part Three - Post-Exertional Malaise: Cause and Effect

Post-exertional malaise (PEM) is one symptom of Chronic Fatigue Syndrome (CFS), but is itself more complex than a single symptom. Patients experience fatigue, pain, cognitive difficulties, sore throat, and/or swollen lymph nodes after previously tolerated

physical or mental activity. These symptoms may appear immediately after the activity or after a period of delay, and may last days or weeks. This article, the third in a series, examines what mechanisms may cause PEM.

What is not the cause?

As discussed in Part 2 of this series, PEM is a self-reported symptom without a clinical test to easily measure its occurrence and severity. Understandably, patients do not want to exacerbate PEM, and many reduce their activity levels or avoid certain activities altogether. This is a predictable response to PEM, but the pattern lends itself to theories that phobias or deconditioning actually cause PEM, or even CFS itself. Such theories, however, are not supported by research data.

Kinesiophobia, is defined as “an excessive, irrational, and debilitating fear of physical movement and activity resulting from a feeling of vulnerability to painful injury or reinjury.”²⁷ One theory claims that CFS patients avoid activity or exercise as a result of irrational fears. These fears can be objectively measured using the Tampa Scale for Kinesiophobia, originally developed and validated for use in patients with lower back pain. Researchers have adapted the Tampa Scale for use in people with CFS (PWCs), and some PWCs do appear to have a high level of kinesiophobia.²⁸

If kinesiophobia causes PEM or CFS, then one would expect patients with higher Tampa scores to be more disabled, have lower exercise capacity, and have more anxiety associated with exercise. While patients with kinesiophobia do report more activity limitations,²⁹ the other hypotheses are not supported by the data. High Tampa scores do not correlate with higher measures of disability, higher levels of exercise-related anxiety, or lower measures of exercise capacity. Even a study that proposed a cognitive-behavioral model for CFS admitted, “no evidence of exercise phobia was found” in subjects with CFS.³⁰

Physical deconditioning is the loss of fitness caused by a reduction in activity. By definition, CFS is an illness that substantially reduces the physical activity of the patient for a minimum of six months, and so every PWC experiences at least some deconditioning. One proposed explanation for CFS is that it is a self-perpetuating cycle of activity avoidance leading to further deconditioning, which in turn reduces the amount of activity that can be comfortably tolerated. The only way to test this theory is to compare CFS patients with sedentary, deconditioned controls. If poor fitness perpetuates CFS, then patients should exhibit more severe deconditioning than the controls. However, a study designed to test this hypotheses showed the opposite: there was no statistically significant difference in physical fitness between CFS patients and sedentary controls, based on several measures of exercise capacity.³¹

Another study used exercise tests on two consecutive days to examine the performance of patients and controls, and found a sharp decrease in performance by the CFS patients in the second test while controls showed no such decrease.³² The authors stated, “The profound reduction in physical activity that accompanies CFS symptoms certainly results in deconditioning. In isolation, the similarity of results between patients and controls for

the first test in this study do not contradict a deconditioning hypothesis for CFS performance. However, the fall in oxygen consumption among CFS patients on the second test appears to suggest metabolic dysfunction rather than a sedentary lifestyle as the cause of diminished exercise capacity in CFS.” This conclusion underscores the need for the use of the test-retest study design in order to reveal an accurate picture of CFS-related impairments.

So what might cause PEM in reaction to activity?

It is now generally accepted that CFS involves disruptions and disturbances of multiple body systems. Research on the physiological responses to exercise in CFS patients supports this principle, with demonstrated abnormalities in the central nervous system, cardiovascular and energy metabolism system, and immune system.³³

1. Central nervous system – When CFS patients and sedentary controls are asked to rate their perceived level of effort during an exercise test, PWCs perceive a higher level of exertion than controls.³⁴ This is true even when heart rate and other measures between the groups are similar, and suggests impairment of the mechanism that contributes to effort sense. Studies that demonstrate exercise lowers the pain threshold in CFS patients also suggest abnormalities in central pain processing.³⁵
2. Cardiovascular/Energy system – Studies have found that peak oxygen consumption and maximum capacity for oxygen consumption are lower in CFS patients than controls.^{36,37,38} Patients have difficulty achieving their predicted target heart rate, and their maximum workload at exhaustion is substantially lower than controls. The average level of maximum oxygen consumption in patients was similar to patients with chronic heart failure and other conditions.³⁹ Research has also suggested that muscle energy metabolism is impaired, as evidenced by higher levels of lactate and other measures of oxidative stress.⁴⁰
3. Immune system – Research provides evidence for associations between measures of intracellular immune deregulations and exercise performance in CFS patients.⁴¹ A twenty-minute bicycle ride caused increases in the levels of the immune protein C4a in CFS patients (but not controls), and the increase was significantly correlated with the severity of post-exercise symptom flare. C4a increases in healthy athletes as well, but after intense exercise such as a 2.5 hour run.⁴² A high symptom flare after exercise in CFS patients correlated with elevated levels of six immune cytokines; neither controls nor patients with lower levels of symptom flares showed the same cytokine activity.⁴³

Summary

Some CFS patients do have kinesiophobia, and many are likely deconditioned. But neither factor explains PWCs’ physiological response to exercise. In contrast, multiple abnormalities have been detected in the systems involved in the body’s response to physical activity. What do these many observed abnormalities really mean? Are they (in sum or in part) the cause of PEM, or merely the observable effects of some other process?

Davenport and colleagues suggest an integrative conceptual model in which “a spectrum of aerobic energy system impairments may be responsible for the reduced tolerance of physical activity.”⁴⁴ Any theory of the cause of PEM must take into account the multiple genetic, cellular, and systemic abnormalities that are associated with the PWC physiological response to exercise. It is probable that maladaptive responses in one or more body processes leads to the reduced tolerance of physical activity and cascade of symptoms associated with PEM.

No definite answer has been found, and more research is needed to understand the root causes of PEM. In the meantime, CFS patients are left to focus on how to manage, treat or avoid PEM themselves. These issues will be examined in the fourth article in this series.

Part Four - Post-Exertional Malaise: Power to the People

“It is not necessary to understand [PEM] before we respect it.”⁴⁵

This series of articles about post-exertional malaise (PEM) in Chronic Fatigue Syndrome (CFS) has reviewed the definition, experiences, measurement, and possible causes of PEM. This final part of the series examines what patients can do to cope with and avoid this incapacitating symptom.

When It Happens

People with CFS know that once PEM strikes, they are at the mercy of their symptoms. Rest, good nutrition and patience are the only “remedies.” Dr. Cindy Bateman advises patients experiencing PEM, “to ‘pull back’ on all fronts (i.e. rest), focus on getting good sleep, reducing unnecessary stress, hydrating, replacing electrolytes, and generally tending all aspects of CFS until they pull out of the relapse.”

Esther says, “The unpredictable nature of it is a real hardship.” But it is possible to plan ahead for periods of PEM to a certain extent, says George. “I keep a little cache of quick lunches like tuna and crackers in the cupboard for just such times when I know that the PEM will strike. Since cooking or any other activity is completely out, having food and water become the major concerns.”

Coping with PEM is not just about managing physical symptoms and environment. It is common, especially when PEM lasts for days or longer, to struggle with the emotional consequences of the physical crash. Dr. Bateman tells her patients, “to remember that it will go away, eventually, and not to fall into despair about the relapse. While we all know that sometimes a severe relapse represents a setback that some may never fully recover from, I try to keep it positive. Sometimes the despair is more problematic than the relapse itself. So keeping a positive attitude and staying proactively focused on gradual recovery is imperative.”

George agrees, saying, “Meditation helps me see that the PEM period is a period of healing, a form of payment for engaging in activity that was more than my body could endure. . . There is no cheating on the recovery times. Not giving adequate time for PEM recovery just costs me more time and more frustration.”

People with CFS do not have many alternatives once PEM has struck. But Dr. Bateman notes, “Treating PEM once it happens is much more difficult than preventing it.” If PEM can be prevented, CFS patients may not have to endure the misery of this disabling symptom.

Pace to Prevent

Preventing PEM largely depends upon an individual’s ability to limit activity to a safe level that will not exacerbate symptoms. People with CFS quickly learn that some activities, easily tolerated before becoming ill, are completely out of bounds for them. But patients also know that activity limits do not have clear, unchanging boundaries. Jane says, “When I’m housebound, [PEM] can be brought on by talking too much on the phone, being animated, being at the computer. When I’m feeling better, it can be brought on by walking too far.”

Pacing is an approach to self-management that helps patients “remain as active as possible while avoiding overexertion.”⁴⁶ Patients limit their energy expenditure to the energy they have available, engaging in activities and rest as needed. There is no single pacing strategy. Rather, a combination of practices can be applied by an individual in pursuit of the goal: to be as active as possible without experiencing PEM.

A few research studies have tested the efficacy of pacing, but the diversity of techniques and programs makes cross-study comparisons difficult. Patients enrolled in a multi-component program experienced significant improvement in fatigue, self-efficacy, and anxiety compared to controls.⁴⁷ A cognitive therapy treatment that emphasized pacing techniques produced better outcomes for patients in several areas, including PEM, than several other non-pharmacologic treatments.⁴⁸

Dr. Leonard Jason has written extensively about the Energy Envelope Theory “which recommends that patients with ME/CFS pace their activity according to their available energy resources.”⁴⁹ Patients were asked to rate their perceived energy (amount of energy available) and expended energy (total energy exerted). Expended energy can exceed perceived energy, especially when patients push themselves over their limits. Patients who exceeded their Energy Envelope limits experienced higher levels of symptoms, especially PEM.⁵⁰ Patients who stayed within their energy envelopes were more likely to experience improvements over time.⁵¹

Dr. Bruce Campbell is a pioneer of pacing in CFS, and offers courses and free materials through CFIDS & Fibromyalgia Self-Help Program, a non-profit organization (<http://www.cfidselfhelp.org>). The goal of pacing is to live within one’s limits, and “move gradually toward consistency in both activity and rest.”⁵² By moving away from

the push-crash cycle so common in CFS patients, Campbell says that patients experience more predictability and control, while also giving their bodies a respite from PEM.

Pacing, according to Dr. Campbell, is a multi-layered process of adaptation. People can gain control by finding and staying within limits in four areas: physical activity, mental activity, social activity and physical sensitivities. Instead of one energy envelope, Campbell says that every type of activity (such as standing, talking, driving, or using a computer) has its own envelope or limit. “Chronic illness has different rules than acute illness,” Campbell says. CFS cannot be pushed through or overcome because “the body will always win, and exact a punitive price for small mistakes.” Just as overdrawing a checking account by \$2 can result in disproportionate bank fees, Campbell notes that exceeding one’s energy limits by one hour could lead to a week or more of suffering and PEM.

Pacing offers a wide variety of practices and behaviors that can help patients learn to better manage their limitations and avoid that suffering. Pacing strategies include reducing activity level, taking daily planned rests, setting activity limits, switching among tasks, and keeping detailed records. Campbell points out that, “Pacing also includes making mental adjustments based on acceptance that life has changed. Acceptance is not resignation, but rather an acknowledgment of the need to live a different kind of life. Pacing is not a single action or strategy, but rather a way of living with CFS.”

The first and most important strategy recommended by Dr. Campbell is pre-emptive rest according to a planned schedule rather than in reaction to symptoms.⁵³ Rest breaks are integrated into a person’s daily routine, regardless of how the patient is feeling. By taking scheduled rest, lying down with eyes closed, patients have found that they can avoid PEM while still accomplishing the same tasks. The length and timing of rest breaks will vary from person to person, although severely ill patients may need many brief rests throughout the day (e.g. 15 minutes of rest every hour or two).

Pacing strategies can be customized and applied by patients at every point along the illness severity continuum. Moderately ill patients can use pacing strategies to manage activities like errands, household chores, and travel. The most severely ill and bedbound patients can benefit from the same techniques modified to their own circumstances. Activities of daily living (such as showering, dressing, or sitting upright for a brief period) can be managed with pacing techniques.⁵⁴ Dr. Campbell thinks pacing may be even more important for bedbound patients “because their cushion is so small and thus their vulnerability to PEM is greater.”

It is not uncommon for patients to be overwhelmed by the complexity of pacing management. Rather than a linear process with a single end point, Campbell believes that pacing is a cyclical learning process. People with CFS, like people with diabetes and other chronic illnesses, must engage in a lifetime process of adjustment and change. Campbell emphasizes that each person needs a highly individual approach based on his or her own health and life circumstances. He encourages patients to choose their own starting points by asking, “what is the next thing I can do to improve my health?”

Power Over Post-exertional Malaise

PEM is a disabling symptom for many CFS patients. There is no objective way to measure it, and no way to treat it once it occurs. But to some extent, it is possible for people with CFS to prevent PEM. Pacing can help patients avoid both overexertion and under-exertion, and may reduce the frequency and severity of PEM. Patients can choose from a wide variety of techniques and practices to create their own customized pacing program.

Pacing is not a cure for PEM, or for CFS. While some patients may be able to expand their energy envelope, other patients may not. The multiple body system impairments involved in CFS may create hard ceilings for activity capacity.⁵⁵ But pacing, and being able to prevent PEM to some degree, gives CFS patients some power over the illness. If a patient can predict the consequences of an activity, that patient is empowered to make informed choices.

Research has not yet discovered what causes PEM or how to treat it. It is up to people with CFS to apply their own strategies to minimize PEM and the suffering it causes. Although the medical system cannot yet offer much help to people with CFS, pacing to prevent PEM is one way that people with CFS can help themselves.

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¹ Some patients believe that PEM is an offensive term or, at best, an insufficient one. The term is used here because it has become ubiquitous in definitions and discussions of CFS.

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