CFS and the Exercise Conundrum

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The key is patience--not doing too much at once and learning not to exceed the threshold that results in "payback" symptoms…Today, 9 years after onset of CFS, I'm still encumbered by my illnesses and still disabled, but muscle pain and weakness are no longer the whole of my story. I can now lift more than folded towels and a dinner setting. I HAVE BICEPS. It has taken over 3 years to achieve "bragging rights" about new found muscular strength, although I am cognizant of the many gradient benefits all along the way, while doing my exercises... At first I did not believe that the little I could do would accomplish any improvement... Specialized exercises, done in gradients (with sufficient rest), taking a day off in between sessions, are the secrets to my success. I have lost 15 unwanted pounds. I look better and I feel better in some ways. Besides adding stamina and strength, exercise has reduced my pain. I no longer need daily pain meds. Gardening is a new hobby, made possible by new found strength and the correct balance of activity and rest. I do use my cane, a gel cushion and proper tools to make it easier.

These words were written by Linda Milne, a 64-year-old patient with disabling CFS whose life changed after she learned how to become more physically conditioned in spite of her illness.

One thing patients and medical providers agree on is that CFS is characterized by post exertional malaise, a term that often understates a "payback" that varies from escalation of widespread pain, to exhaustion requiring a recovery day in bed, to serious relapse of the entire CFS symptom complex:the cognitive dysfunction, flu-like achiness, fatigue, low grade fevers, lymph node tenderness and disturbed sleep patterns of weeks or months duration. Post-exertional malaise has always been considered a defining feature of CFS, although we are still uncertain why it occurs (Fukuda). A recent genomics paper clearly demonstrated a difference, using gene array technology, between CFS patients and controls before and after exercise (Whistler). VanNess, et al recently produced an abstract demonstrating inability of CFS patients to replicate VO2 (measured oxygen consumption) in the second of two graded cardiopulmonary exercise tests separated by only 24 hours of rest, although effort was identical as measured by RQ (VanNess). This finding may be unique to CFS. The CFS patients had almost a 20% drop in VO2 on Day 2 compared to normal, deconditioned controls who achieved the same VO2 on Day 1 and Day 2 of exercise testing. In another study, the same research team objectively demonstrated a decline in cognitive function in 20 CFS patients 30 minutes and 24 hours after a graded cardiopulmonary exercise test compared to pre-exercise levels, with no such observed change in the 20 age matched deconditioned controls (VanNess, unpublished manuscript).

A related concept is the idea that a "threshold" exists at which something pathologic happens in the body because of exercise or activity, and that exceeding the threshold causes post exertional malaise. Knowing exactly what happens at the threshold, where the threshold is, and how we can raise the threshold are questions that have proven difficult to answer, at least in some patients.

This is a not a foreign concept in medicine. A diabetic can develop life-threatening hypoglycemia from exercise. Exercise converts asymptomatic coronary artery disease to ischemia, infarction and fatal arrhythmia. Certain asthmatics develop severe bronchospasm from exercise. In each of these disorders, while potentially deadly, exercise is also an important therapeutic intervention. In each case, exercise is safe if the underlying condition is well defined and under good control, a safe level and type of exercise are prescribed, and the patient is meticulously educated regarding how to exercise and

how to recognize signs that exercise should be limited. No doctor would tell these patients that they should "just exercise and they'd feel a lot better." Our ability to safely prescribe exercise for these disorders is different than CFS because we have a much better understanding of pathophysiology, we can measure the disease severity objectively, and we have effective treatments. In the absence of adequate information about CFS, we should prescribe exercise with the same cautious and attentive approach we might use if we had inadequate clinical information and treatments for our asthmatic, diabetic or cardiac patient. We can still utilize exercise therapeutically if we respect what we do not know, and utilize what we do know from research, clinical experience and the observations of our patients.

It is common knowledge that both muscular and cardiovascular deconditioning occur from inactivity, even in healthy individuals. Pushing beyond one's current threshold or level of conditioning, by suddenly increasing either the intensity or duration of exercise, may result in fatigue, pain, stiffness and inflammation, even serious difficult-to-reverse conditions such as chronic inflammation (i.e. tennis elbow, plantar fasciitis) or stress fractures. Usually the threshold of deconditioning can be gently raised by gradual increases in the exercise stressor. Young bodies that heal more quickly have a greater capacity to recover from physical stressors or rapid escalation of exercise intensity. Advancing age and co-morbid medical conditions make it more difficult to push exercise efforts too intensely or too long without consequence, hence the "weekend warrior" who ends up limping around in widespread pain or in the Emergency Room from injury.

Patients with CFS who are unable to remain active become deconditioned, but their ability to tolerate exercise stress and raise the threshold may be impaired compared to normal individuals. Indeed, recent studies published by the CDC Computational Challenge teams suggest that CFS patients may have more difficulty than others recovering from common physical stressors, as measured by increased allostatic load (Maloney). It is possible that some stressors leave a mark or permanent injury in patients with CFS, as if their normal stress response and recovery mechanisms are dysregulated or chronically depleted.

In addition to physical deconditioning, there are many partially understood aspects of CFS, well established in the literature, that might contribute to an exercise threshold, the exceeding of which could result in pathologic injury. This might include defects of oxidative metabolism, dysregulation of the autonomic nervous system and HPA-axis (CRH, cortisol and aldosterone), presence of chronic or latent reactivating infection, dysregulated immune or inflammatory systems (cytokine production, natural killer cell function, complement activation) and other yet- to-be clarified processes. It is not difficult to imagine an exercise or activity threshold in someone with CFS after which the body experiences physiologic injury that contributes to post-exertional malaise. It is not necessary to understand this before we respect it.

Clinicians resonate with recent CDC publications supporting the idea that the CFS Case definition defines a heterogeneous group of patients (Vollmer-Conna, Aslakson). Cardiopulmonary test results of more than 200 CFS patients engaged in the Phase III Clinical trial of Ampligen show a stratification of exercise capacity (as measured by VO2, systolic blood pressure and pulse) ranging from mild to severe impairment according to AMA impairment guidelines (VanNess). This exercise tolerance heterogeneity may be the most important reason why, in spite of agreement about post-exertional

malaise, there remains a wide array of opinion in published articles about the benefits of exercise in CFS.

Factors that might contribute to heterogeneity and create a number of apparently conflicting clinical or research observations about the benefits of exercise in patients with CFS include the inherent selection bias of small studies, a variety causes of CFS, severity of illness, different stages in the natural history of CFS, age, comorbid medical conditions, weight gain, an inevitable degree of deconditioning, pre-illness state of conditioning, or prior experiences with exercise.

There is no doubt that my hundreds of patients who meet the CFS case definition exhibit a wide spectrum of exercise tolerance. On one end of the spectrum (perhaps a fibromyalgia patient with metabolic syndrome who meets the CFS Case Definition), the response to graded exercise is satisfying and clinically helpful. These patients can gradually increase their strength and aerobic capacity with proper conditioning, resulting in weight loss, better energy, improved pain and fatigue. Some even recover a higher level of function, although the fibromyalgia symptoms usually remain to some degree. On the opposite end of the exercise tolerance spectrum are certain CFS patients who invariably experience a severe relapse of symptoms after attempting to increase their physical activity, either immediately or within a few weeks. It seems that even the more healthy patients of this subset must reduce other activities in order to substitute and sustain a low level exercise regimen.

The point is that we don't need to understand all aspects of CFS or even be able to objectively subset our patients to begin sensibly utilizing physical conditioning to improve their health. From the clinical standpoint, our patient population will always be heterogeneous. There will always be a spectrum of contributing factors, including primary etiology, stage, co-morbid conditions (including obesity and deconditioning), severity of pain and secondary relapse symptoms, age, plus a variety of personal skills, resources, motivation and discipline. It is possible to adapt exercise advice compassionately and intelligently to the individual situation.

The following are some ideas about how to help your CFS patients discover how they can best improve their physical conditioning, given their particular level or type of illness.

<u>Don't call it "exercise."</u>
We all, patients and providers, have inflated perceptions about what the word exercise means. Instead of asking about exercise, try: "What are you able to do ...to keep your muscles from becoming weak? ...to keep your body moving? ...to stay strong and flexible?...to work on physical conditioning?"

<u>Discuss physical conditioning activities in every visit.</u>
Just as I review medications, current symptoms and level of function, I include a question about efforts to become better physically conditioned. Everything counts: walking up and down stairs in the home, sitting on the grass or a gel pillow and pulling a few weeds, walking the dog. Point out and commend what is being done, and think of ways to gradually push toward, but not over, the threshold and discover its nature. Confirm with patients the activities they have discovered helpful (ie, stretching helps reduce pain and stiffness; being stronger makes getting around easier).

<u>Separate physical conditioning into approachable components.</u>
1. Stretching. Stretching is well tolerated and complimented by relaxation and breathing exercises.

Start with seated or supine stretching activities, and sustain a regimen for several weeks before moving to standing activities or strength conditioning. Specific instructions are helpful and usually necessary.

2. Strength training. Progress gradually from stretching to strengthening activities. Use very low weights, light stretch bands or no equipment at all, just body weight. Strength training should initially be limited to 30-60 seconds with rest periods between, and a maximum of 3-5 intervals per session. Do not increase weight/resistance much or do prolonged repetitions. Specific instructions are imperative.

3. Cardiovascular conditioning. Aerobic upright activity is usually the least well tolerated, especially if prolonged or intense, so if done, it must be done with care. It should be brief and low intensity, such as walking to the corner and back rather than attempting to go all the way around the block. Start with only a slight increment more than current daily activities demand.

Start with small efforts, increase slowly, and find a sustainable but flexible regimen.
Physical conditioning efforts should approximate an intensity and duration that will cause no post-exertional malaise symptoms the day following the activity. "No pain, no pain," is advised by Namita Gandhi, an exercise physiologist in Oregon with both personal and professional expertise in fibromyalgia movement therapy. All fatigue, pain or cognitive symptoms should be back to baseline after a good night of sleep. The regimen should not be increased until it can clearly be sustained for weeks without consequence. Then it may be increased a small increment in duration or intensity, and observed for tolerance another 1-2 weeks, etc. There is nothing wrong with finding a tolerable, variable or constant level to maintain without graded increase, as that is the inevitable end.

Allow recovery time.
Rest between short intervals of exercise. Take at least one rest day between conditioning days. Allow more time when stressed or in a flare of symptoms. Give whatever physiologic injury may be present plenty of time to resolve before attempting further exercise.

Be cautious about upright/standing, intense or prolonged activities.
1. Upright/standing: Since people with CFS may have autonomic dysfunction, it makes sense (and works) to engage primarily in activities that minimize orthostatic intolerance (OI). OI is a general term that encompasses a variety of manifestations, including Neurally Mediated Hypotension (NMH) and Postural Orthostatic Tachycardia Syndrome (POTS).

Try to do most physical conditioning activities lying down, seated or in water. If sensitive to orthostatic stress, choose Yoga, Pilates, recumbent cycling or pool therapies rather than standing for Tai Chi, walking on a treadmill, or attempting to play soccer. Water offers a number of theoretical advantages in the setting of OI. Swimming in a horizontal position negates OI. Standing or walking in deeper water creates a hydrostatic pressure gradient, un-weights the joints and spine, and provides uniform light resistance to all movement. Cooler water may contribute positively to peripheral vasoconstriction, thus minimizing OI. Warmer water is more soothing for arthralgia, myalgia and stiffness.

Avoid becoming overheated and volume depleted. Hot tubs, hot showers, sitting too long in a hot car cause vasodilation and can result in marked OI symptoms, manifest silently as a drop in blood pressure or dramatically as a pounding or racing pulse. Frank syncope (fainting) can occur, but getting

overheated usually just lowers the threshold, prevents further activity, and can result in severe post-exertional malaise (exhaustion, headaches, cognitive decline, achiness and disturbed sleep).

Volume loading can be strategically timed to improve exercise tolerance in the face of OI. It is effective to "chug or guzzle" oral fluids in anticipation of upright activity. A 500-600 cc (medium size bottled water) bolus begins to raise blood pressure in 15 minutes, peaks in 30 minutes, and the effect is gone in 60 minutes (Shannon).

The peripheral alpha agonist, midodrine (a 10 mg dosage in most people), can compliment fluid loading. Its acts fairly quickly and the effect abruptly wanes within 4 hours due to its short half life. For severe POTS, beta blockade may also be helpful.

2. Intense: Exercising too vigorously is the most common mistake made by those who fail a trial of physical conditioning. Rapidly or dramatically exceeding the threshold results in more illness symptoms, overall a very negative experience. Assume severe underlying deconditioning and co-morbid pathology are present. I tell my patients who hire a personal trainer to begin with a program designed for "an 80 year old with a heart condition."

Staci Stevens, MS, an experienced CFS exercise physiologist in California, instructs her patients to wear a heart rate monitor with an alarm to notify them when the heart rate has climbed to a predetermined level. She measures a CFS patient's anaerobic threshold objectively during graded cardiopulmonary testing, notes their heart rate at the anaerobic threshold, and then uses that heart rate value to estimate the anaerobic threshold during physical activity. It is typically somewhere between 90-110. (Linda's was 80!) Staci counsels patients not to exceed that heart rate during physical activity. When the alarm goes off, the patient stops the activity and sits down to rest. Whether avoiding a defect in oxidative metabolism, an escalation of orthostatic hypotension, or some other mechanism, this may be one tangible way of staying below the threshold of relapse and avoiding post-exertional malaise.

3. Prolonged: Even light exercise can exceed the threshold if pursued too long. Set time limits and gradually increase them if sustainable without relapse. Respect the threshold. If increases in duration of exercise are not well tolerated, continue only shorter, less intense, sustainable regimens. Limit the time of any sustained action initially to 30-60 seconds and the whole activity to 5 minutes. Chuck Lapp, MD, in North Carolina, has shown that five minutes three times during the day are better tolerated than a 15 min block of activity, yet the results in conditioning are equivalent. It is actually better than equal, because exceeding the threshold will inevitably cause a discouraging setback and an understandable desire to abandon all efforts to continue.

<u>Be consistent.</u>
Find a range of well tolerated physical conditioning activities and doggedly stick with it, even if it seems ridiculously insignificant. Learn to pace, assess, and re-adjust the type, intensity and duration of activity day by day to stay under the relapse threshold and avoid post-exertional malaise. Observe any pattern of activity at least a week before increasing the duration or intensity. Be careful about advancing any aspect of physical conditioning unless gradual increases are well tolerated. Recognize and respect the reality that CFS patients may have a point at which, physiologically, they will become more ill from physical activity and experience a substantial set back, even if the mechanisms are not entirely clear.

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OTHER USEFUL RESOURCES:

Managing Activity and Exercise. (http://www.cdc.gov/cfs/cfstreatment.htm) (CFS > Consumers>Treatment Options)

The "Skinny" on Exercise and CFS. The CFS Research Review. Summer 2006. Vol 7, Issue 1, 8-10. A publication of the CFIDS Association of America.
