

Phoenix Rising: An ME/CFS Newsletter
by Cort Johnson (January 2009)

“Cracking the Foundations – the Pacific Fatigue Lab and ME/CFS”

(<http://aboutmecfs.org/News/PRJan09Pacific.aspx>)

A New Dawn for ME/CFS? Could a small lab in the Central Valley of California shake the CFS research field with a quake of epic proportions? Change how the disease is viewed? How it’s defined? Legitimize the disease once and for all? It’s possible that given enough resources the Pacific Fatigue Lab at the University of the Pacific in Stockton, California may do all of these.



Run by three exercise physiologists, Dr. Christopher Snell (Ph.D), Dr. Mark Van Ness (Ph.D) and Staci Stevens (M.A.), a former grad student and now a researcher with chronic fatigue syndrome (ME/CFS), the lab focuses on a very basic and still very misunderstood aspect of CFS – why patients have so much trouble with exercise.

Staci Stevens, the founding Executive Director of the Pacific Fatigue Lab explained. “Many researchers look at ME/CFS patients when they’re at rest- at baseline. But as any ME/CFS patient knows, the real problems occur when their systems are under stress due to too much activity. We’re taking a close look the physiology of CFS patients as they undertake the most stressful activity of all – exercise.”



Since oxygen plays a key role in energy production, exercise physiologists use oxygen consumption during exercise to tell how much energy a person’s body is capable of producing. Having people pedal a stationary bicycle until they can pedal no more tells researchers how much air their lungs can take in (Ventilation Max) and therefore how much oxygen they use to produce energy (VO₂ Max) at their peak level of effort. Since oxygen plays a key role in the energy production process this test effectively tells researchers how much energy is being produced.

Given the fatigue and post-exertional problems often noted in ME/CFS one would think aerobic exercise tests would have played a key role in legitimizing this disease, but instead they’ve given

rise to further skepticism. The ability of many patients to pass them has added to confusion about a disease characterized by the word fatigue. How could CFS patients be *so* fatigued if they're able to generate normal amounts of energy?

A New Approach. The Pacific Fatigue Lab researchers realized, however, that while researchers may have been asking the right questions they were asking them in the wrong way. Many ME/CFS patients can, after all, get through a single 'workout' or a single day or single afternoon at work okay only to 'crash' afterwards. Until now, though, no one's taken a close look at the ME/CFS patient's ability to produce energy when they're in a crash – an odd oversight in a disease whose symptoms are so tied to activity. (Indeed, study after study is showing that many variables which test out normal or near normal when ME/CFS patients are at rest are abnormal when their systems are put under stress). With the Pacific Fatigue Lab doing a new exercise testing regime, two exercise tests two days in a row and other tests (now known as the Stevens' Protocol) they've given the post-exertional problems ME/CFS patients have reported for so many years a chance to show up – and they have.

Their results are both profound and disturbing. About half of the ME/CFS patients they've tested do, in fact, 'fail' or significantly under perform in the first single exercise test – they cannot generate normal amounts of energy even when they're 'rested'. It's the rest of the patients that are so intriguing, though. When you give these patients a second test a day later many of them will fail as well--and fail spectacularly.

The amount of impairment the Lab see's can be astonishing - some patients suffer as much as a 50% drop in their ability to produce energy the next day. Ms. Stevens spoke of a twenty-something man whose next day exercise tests were worse than those of a normal 85 year old. In a hospital setting his cardiopulmonary exercise profile would suggest he had heart failure.

According to modern medical science this shouldn't occur. For decades researchers have shown that human beings, under virtually all conditions and in a variety of disease states, can take an exercise test to exhaustion, recover and return the next day and score the same the next day. It doesn't matter if she/he has heart failure or end-stage kidney disease – again and again researchers have shown that the human body – even in extremely poor health - has an amazing ability to quickly return to a baseline level of energy. That is until now.

But it's not just that chronic fatigue syndrome (ME/CFS) patients are failing these tests, it's also the unique *way* they're failing them that's raising eyebrows. Decades of research have shown if you take a female of W age and have her do X amount of exercise at Y heart rate she will exhibit Z levels of oxygen consumption. Researchers have believed these algorithms are set in stone but they're not holding up in chronic fatigue syndrome (ME/CFS) patients. That they're not suggests that something has gone awry in the basic physiological processes the body uses to produce energy in this disease.



Even after 20 years in the field Staci Stevens' excitement was palpable. The implications of her findings are profound not just for ME/CFS patients but for the field of exercise physiology. She

said “We are charting waters that have never been charted before. It’s an exciting time to be involved in CFS research!”

Revolutionary Findings - The lab’s findings are so unusual that their peers sometimes can’t believe what they’re hearing. Since decades of research have indicated there’s no need to do repeat exercise tests, they are simply not done. Until recently the Pacific Fatigue Lab may be the only lab in the world that regularly does them.

I asked Staci Stevens how her colleagues across the country were reacting to this data – were they excited? She said some of them say, “It’s just not possible, they think we must have imputed the data wrong but others are enthralled”. She said one colleague on the east coast who’s doing the tests said that after 30 years in the field, “I’d never seen anything like this”.

A Quick Road To Legitimacy? – Their findings undermine long held beliefs not only about chronic fatigue syndrome (ME/CFS) but about exercise physiology as well. Overturning paradigms is not easy but the Pacific Fatigue Lab has an ace in the hole in this regard. Many ME/CFS researchers and patients have looked to the future for technological breakthroughs that will legitimize the disease once and for all. The new technologies coming to bear on ME/CFS are exciting but new technologies take time, sometimes long periods of time, to be assimilated and accepted.

There’s nothing new, however, about the technology the Lab is using; in fact it’s boringly well established. The aerobic exercise tests they do form an essential part of every cardiologist’s and pulmonologist’s tool kit. Once the Pacific Fatigue Lab’s test results are replicated and make it into the broader research community acceptance should come relatively quickly. In fact if one were to chart the quickest road to legitimacy for this disease it would very much look like the path the Pacific Fatigue Lab has embarked on - charting gross abnormalities in well accepted, well established tests. If the Pacific Fatigue Lab’s findings hold up, the news couldn’t be better for chronic fatigue syndrome (ME/CFS) patients.

Redefining Chronic Fatigue Syndrome (ME/CFS) – The Pacific Fatigue Lab’s results should also clarify one of the key questions concerning the disease: whether researchers have been mixing apples and oranges in their studies. For decades researchers have worried that the disease’s vague definition allows people with different illnesses to participate in research studies. The most pressing question concerns whether ‘post-exertional malaise’ (PEM), which signifies dramatically worsening symptoms after physical or mental exertion, uniquely identifies this disorder or is simply one symptom among many.

One side, lead by the producers of the Canadian Consensus Definition of ME/CFS, believes that post-exertional malaise (PEM) is a hallmark symptom that reflects unique physiological processes. They believe that allowing people without this problem to participate in chronic fatigue syndrome (ME/CFS) studies may have greatly hampered efforts to understand this disease.

The other side, exemplified in the Center for Disease Control’s (CDC) empirical definition of 2005, believes that post-exertional malaise (PEM) is one of many symptoms present in the disease. They argue that the most important feature of the disease is unexplained degrees of ‘unwellness’ that interfere significantly with people’s work, personal, social, etc. activities. They believe some different process is at work.

The Pacific Fatigue Lab's results suggest that the Canadian Consensus group is correct; during either the first or second exercise test a large subset of patients demonstrates significant physiological abnormalities in their ability to produce energy. Another subset of patients does not. The Lab's findings suggest that these two groups should be separated in research studies.

Ms. Stevens could not say, however, how big the PEM subset is. The Lab has derived most of its data from three groups of patients – research subjects in the test/ re-test studies, those attempting to get disability and participants in the Ampligen trials. Many of the people they screen do exhibit PEM on the exercise tests but others do not. It will take statistically rigorous studies to determine how prevalent the post-exertional malaise group is.

Demonstrating that this subset does exist and can be differentiated by standard physiological tests would go a long way toward breaking up the CFS label, revamping the definition of the disease, focusing researchers in on key abnormalities, and, of course, creating a new name.

Answering the subset question would be tremendously valuable but the Stevens' Protocol could also have an enormous impact on another very broad and butter issue: disability.

A Comprehensive Disability Evaluation – CDC studies indicate that the average annual financial costs of CFS (@\$25,000/year) impose an economic burden that many families cannot sustain for long. Getting disability can be the difference between absolute poverty and at least a minimum amount of financial comfort and medical attention. Without clear diagnostic or functional tests, however, getting disability has been a challenge.



Chronic fatigue syndrome (ME/CFS) patients don't win their disability cases because they have ME/CFS, they win when they can demonstrate they cannot function well enough to work. Fortunately, measuring functioning is what the Pacific Fatigue Lab is all about. The simplicity of the exercise tests is their grace; patients who cannot produce sufficient amounts of energy cannot be expected to function – it's as simple as that. Aerobic exercise tests have the added advantage of a long history; they've been used to demonstrate disability in heart patients and others for decades. The Steven's Protocol has the potential to produce a clarity that has been strikingly missing in this arena.

The Pacific Fatigue Lab offers perhaps the most extensive disability evaluation in the country. The exercise tests don't take long – 8-10 minutes with a slow windup period. – and they can have brutal after-effects– but, if successful, they are time well spent. (The Pacific Fatigue Lab will not allow severely disabled patients or those with moderate to high cardiovascular risk to take the tests. If the first test shows disability the next test is not needed).

They're not cheap, but even at \$2,000 a pop, they present a good value for those who can afford it. (Single exercise tests typically run from \$800-\$1200 at a hospital. Some insurance companies will reimburse for the testing though billing insurance is the responsibility of the client). The Stevens' Protocol 8-12 minute aerobic exercise tests, resting pulmonary function tests measuring lung function, bioelectrical impedance exams measuring hydration, acoustic nasal rhinometry measuring sympathetic nervous system functioning, reaction time testing evaluating cognitive processing time, and a seven page written evaluation. Not every patient who does the disability evaluation gets a diagnosis of 'disabled,' but for those who do it can be financial lifesaver.

The Stevens' Protocol has the potential to rewrite the disability rules for ME/CFS. The CFIDS Association of America has already asked the Social Security Administration to take them into account but they're behind the game; the Fatigue Lab has already notched its first of several wins in the long term disability field. In fact, their first win holds a place of honor in a frame on the wall of their office.

That's a lot of promise for a small lab but we're not done yet. The Pacific Fatigue Lab also uses the results of their exercise studies to build ME/CFS patients a unique rehabilitation program.

Education. With all the many ramifications of the Lab's work, it's the day to day process of educating students about ME/CFS that may be the most fulfilling for Staci. She, Dr. VanNess and Dr. Snell all incorporate their latest findings into their classes; 'Here is a normal exercise stress test' they say and 'here is a CFS patient's' test. The students are enthralled and they should be; they are being exposed to cutting edge data that the textbooks say shouldn't be happening. It's exciting to be a young (or old) student on the cusp of research that has the possibility of overturning accepted paradigms. Ms. Stevens laughed and said "They love working with CFS patients. They're always asking to see the results on the last patient".

When these students leave the University of the Pacific they'll be ambassadors for this disease and spread the word about the unusual findings. Currently the PFL has four graduate students and a handful of undergraduates working with them.



They also provide hope for a field that is not attracting many new faces. In fact, the lack of young researchers may be the biggest long-term problem the research field faces. The researchers that got engaged in the field when it was new and not subject to so much controversy will be retiring in the not so distant future. Ms. Stevens lamented the lack of young faces at the Symposium on Viruses in CFS in Baltimore in May, 2008.

The chronic fatigue syndrome (ME/CFS) research world is catching onto the implications of the Pacific Fatigue Lab's work. A repeat exercise study by Ellie Stein in Canada recently opened and one is reportedly underway in Europe. Ms. Stevens readily acknowledged that replicating results has been difficult in ME/CFS, but she's confident that their results will hold up. She's done 1,000's of single cardiopulmonary exercise tests on chronic fatigue syndrome (ME/CFS) over the years and close to a hundred with the Stevens' Protocol at the Pacific Fatigue Lab. Whether in Stockton, Stanford, Incline Village or Ithaca, New York they see the same general pattern again and again, a unique metabolic dysfunction that characterizes and objectifies the most mystifying symptom in the disease, post exertional malaise.

(Research, education, treatment...does this sound familiar? Advocates have been asking for the federal government to produce Centers of Excellence that combine research, treatment and education. The Pacific Fatigue Lab is a COE in miniature.) My that does have a nice ring to it ☺

Opportunity – The Pacific Fatigue Lab is a remarkable accomplishment – a testament to one grad student's persistence – and a small coterie of advisors and mentors who made her passion

their own. University affiliated chronic fatigue syndrome facilities are almost non-existent. Aside from the Whittemore-Peterson Neuro-Immune Institute in Reno, Nevada (which won't open its doors on the university campus for another two years) there may be no other University sponsored Chronic Fatigue Syndrome lab in the country. Special thanks must go to the Sport Sciences Department Chair Dr. Christopher Snell and to the University of the Pacific for having the vision to recognize the opportunity the Lab presents and backing it despite of the controversy still surrounding this disease.



The opportunities the Lab presents for this disease are staggering. Yet the contrast between the opportunity present and the resources available is a little heartbreaking.

The Pacific Fatigue Lab is entirely volunteer run by three people who are trying to analyze their data, get grants and publish on their off-time. Somehow, they've managed to create a beautiful lab but they're still missing key ingredients. Their papers have mostly been published in less well known journals, they don't have a website to get the word out, and they don't have a strong funding base. Indeed the theme of overworked (and unpaid) researchers trying to make do on a shoestring is a constant one in the ME/CFS research community.

I asked Staci Stevens about doing heart rate variability (HRV) studies. Given their ability to provide data on how the autonomic nervous system is functioning –which appears to be a key player in the disease – HRV studies seem like a perfect fit for the lab. She said 'I'd love to do HRV but we don't have the funding'. Staci noted that "This doesn't need to be rocket science. We could go a long way just by focusing on some simple areas that the research community has basically ignored" One gets the idea that there are many things the Pacific Fatigue Lab could do to advance the science of ME/CFS if they just had a bit more money.

But there's only so much money and so much time in the day. The Pacific Fatigue Lab has been able to produce what it has through two private grants from the CFIDS Association of America and from funds it gathers from doing its comprehensive disability studies and firefighter fitness testing on the side. Currently the Lab's researchers are focused on analyzing the results from the Stanford Montoya Valcyte study and the data from their latest repeat exercise study plus a new study, all while they're teaching full loads

The Next Level. One wonders what these researchers could achieve if they had more time and money to focus on a subject that they're obviously so passionate about.

I asked Staci how much money would it take to move the Lab to next level? She said 'For sixty thousand dollars we could hire a Ph.D in exercise physiology to write grants, run the studies and write up the data. There are plenty of people who would love to get a job to do that'. Hiring a full time clinical testing supervisor who could take over the grunt work of data input would allow them to focus more on the big picture. Monetarily speaking this is chicken feed in the medical world; they're not far at all from creating a lab that could start turning out study after study.

Ms. Stevens was reluctant to delve into the thorny issue of federal financing for CFS research but it was clear that she felt that whatever semblance of a spigot that had once been turned on has been mostly turned off. The loss of the Cooperative Research Centers at the NIH in 2002 was a severe blow. The Pacific Fatigue Lab's efforts to get an NIH grant failed. When I asked if the

Centers for Disease Control had shown an interest in her work she said ‘Interest and funding are two different matters and they are struggling with funding as well.’ One would think that somewhere in a community of 1,000,000 patients a way could be found to assist them in their work.

Advocacy. When the federal system fails to assist people in need one must turn to advocates to put pressure on the government. Ms. Stevens agreed that advocacy was critical but noted that the problems with exhaustion chronic fatigue syndrome (ME/CFS) patients faced made them ill-equipped for advocacy. Still she noted that when she served on the federal advisory committee for CFS (CFSAC) they typically had less than 5 patients show up for the meetings – and they tended to be the same five patients - not a strong signal to the government to move on these issues.



The Future - The Pacific Fatigue Lab is creating a body of work that has the potential to revolutionize the medical community’s understanding of this disease. The possibilities are impressive; legitimize ME/CFS, rewrite the disease’s disability rules, create viable subsets, focus the attention of the research community on the post-exertional period to determine how this disease is defined and guide both non-pharmacological and pharmacological treatment to improve quality of life for patients.

How well it will be able to achieve these goals will in good part depend on the resources it has and how well it can get the word out about its findings. Indeed the Lab is still mostly a secret in the ME/CFS community. Ms. Stevens said that as they’ve been accumulating data and analyzing it that “We’ve been kind of underground” but she also felt it was about time for them to come out. Chronic fatigue syndrome (ME/CFS) patients can only hope they come out in a big way indeed.

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Contribute to the Pacific Fatigue Lab through the Workwell Foundation; a non-profit foundation created by Staci Stevens to advance research into chronic fatigue syndrome (ME/CFS). Phone: (209)599-7194. email: staci@workwellfoundation.org

Support the Lab! - Having a University support an ME/CFS laboratory is a rare thing. In fact, aside from the Whittemore-Peterson Institute there doesn’t appear to be another University laboratory devoted to ME/CFS in the U.S. The University of the Pacific deserves our heartfelt thanks for their leadership in this area. Let’s help out the PFL in their work. Please e-mail the people below and say Thank You!

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