

## **CFSAC Testimony: Former Physiotherapist and Occupational Therapist Canadian/American Dual Citizen, Alberta, Canada October 11, 2010**

I am writing to your Committee with a plea for urgency. Specifically I hope to share with you the risks of mortality in ME/CFS from viral cardiomyopathy (cardio = heart; myo = muscle; pathy = disease). I am also writing with a personal sense of urgency. I have ME/CFS and biopsy-confirmed viral cardiomyopathy, and at age 48 am going into my 4<sup>th</sup> year of persistent chest pain, with no cardiology follow-up at present.

Evidence suggests that many ME/CFS patients develop viral cardiomyopathy. And a frequent presentation of Atypical Angina (chest pain, with non-obstructed coronary arteries) in ME/CFS patients, abundantly documented on patient forums, is being routinely ignored in N. American emergency departments. I know, because it has happened to me repeatedly. Just a sampling of the many chest pain threads from just one forum:

- <http://www.forums.aboutmecfs.org/showthread.php?7923-My-aching-heart&highlight=chest+pain>
- <http://www.forums.aboutmecfs.org/showthread.php?5629-Is-it-our-heart-virus&highlight=chest+pain>
- <http://www.forums.aboutmecfs.org/showthread.php?6345-Left-arm-tingling-short-of-breath-feeling-sick&highlight=chest+pain>

A key challenge is that viral heart disease eludes standard, "in-the-box" cardiology testing. You may be aware of the inequities in cardiac care between men and women. The status quo is that patients – mostly middle-aged women – presenting with Atypical Angina, arrive in emergency, only to be told their atypical chest pain is "all in their head". A history of ME/CFS virtually guarantees their concerns will be dismissed. And this is also happening to male ME/CFS patients with atypical angina. Meanwhile research is accumulating to support the grim reality that many of patients with Atypical Angina and ME/CFS –male and female- die from viral heart disease. In fact some 40% of patients presenting with persistent chest pain – who don't have blocked coronary arteries – experience a major cardiovascular event within 5 years (see enclosed NHLBI's Women's Ischaemia Syndrome Evaluation – WISE - study references). ME/CFS urgently requires fast-tracked funding to research these cardiac risks.

**Introduction:** I'm a former Rehabilitation Medicine professional and MBA with an 11-year case of persistent Parvovirus B19 and ME/CFS. I had a classic flu-like onset after an episode of "Fifth Disease" at our childrens' preschool. Shortly after I got the memorable hit-by-a-truck-unable-to-move 'flu, followed by distal, transient polyarthritic symptoms... and ME/CFS. About half a decade ago, I was too debilitated to continue working and lost my own company.

In year 9 I realized that I had ME/CFS, but like many, was told that I was depressed, unmotivated, getting old. I pushed through the exhaustion and malaise and sorely regret the vacuum of guidance on the dangers of overexertion in ME/CFS. A dutiful Physio, I pushed my body, trying to exercise my way back to vitality. Formerly a jock, I'm mostly housebound – indeed mostly bedbound lately. I have the RNase-L deficiency; my NK cell function is 3 (normal is 8-170); and I meet all the stringent Canadian Criteria for ME/CFS.

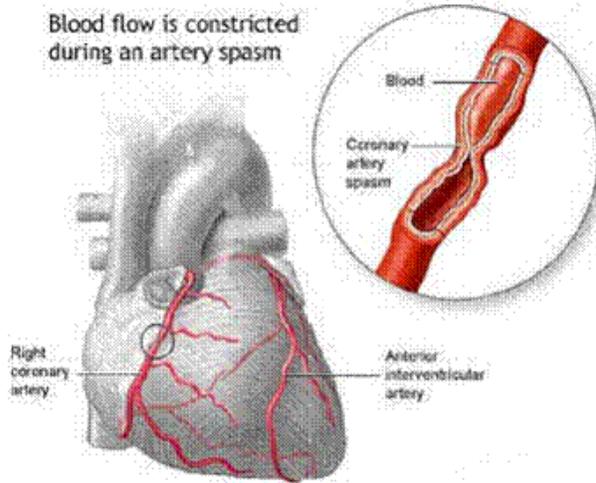
### **The tip of the iceberg: Heart Complications associated with ME/CFS infections:**

Three years ago, my debilitating ME/CFS became more complicated. I developed stroke and TIA symptoms: L) sided facial droop, foot drop, severe sequencing, word-finding and orientation problems. Readily recognized, given my rehab med background.

And then I developed Atypical Angina: ischaemic heart pain, in the absence of "blocked" coronary arteries. My recent complication of PVB19 viral heart disease, ignored by Canadian emergency departments and cardiologists, was diagnosed by endomyocardial biopsy (EMB), quantitative polymerase chain reaction, and immunohistochemistry in Germany – on the recommendation of the leading cardiologist specialist on heart biopsies at the Mayo Clinic. In the face of raging cardiac symptoms – and a refusal from emergency to refer me for cardiology follow-up in Canada, we remortgaged our home and put our trust in my clinical

symptoms. Indeed, I have a “textbook” history of chronic PVB19 that fits the descriptions and Table in Kerr’s 2003 article on Parvovirus B19 and ME/CFS (<http://www.cfids-cab.org/cfs-inform/Virus/kerr.etal03.pdf> . And I was proven right by my heart biopsy results. Not only do I have active PVB19 infection in my heart, they also found antibodies against the inner lining of my blood vessels (the endothelium), and against my heart muscle itself. Think of a hangnail: red, swollen, inflamed – that’s what’s happening in my blood vessels, intermittently

blocking off flow of blood to my vital organs, including my heart. I was told that I was the first North American patient to receive diagnosis for PVB19 viral cardiomyopathy in Germany – although this is a routine practice for Germans presenting with atypical angina and suspected viral myocarditis. My German team was aghast that I was also told *not* to come back to emerg in Canada. “*What happens to the other patients?*” What, indeed. North Americans with Atypical Angina (aka “Syndrome X”) are slipping through the cracks. For persistent PVB19 causes endothelial inflammation – coronary arterial spasm and/or impairment of the microcirculation causing ischaemia - and left untreated it kills.



**Other ME/CFS viruses implicated:** The Germans are also finding pathology connected with other classic ME/CFS viruses, such as HHV-6, EBV, CMV. (See PubMed “virus & myocarditis”: <http://www.ncbi.nlm.nih.gov/sites/pubmed>). Given potential XMRV/MLV causation in ME/CFS, this constellation of opportunistic viral heart infections should be no surprise.

Is viral cardiomyopathy a natural progression of ME/CFS? Thanks to sensitive PCR and immunohistochemistry techniques, and the world’s best safety record in potentially risky EMB’s, the Germans have determined that the most common cardiotropic virus is not Cocksackie-B virus, but PVB19. And they are finding *active* PVB19 in 30-50% of the biopsies they conduct in these atypical angina cases. This is interestingly in line with the 40%+ WISE patients who have a major cardiovascular event within 5 years of persistent chest pain. The next question of course is: how many of these patients have XMRV/MLV’s? After all, early studies on primates have shown reservoirs of XMRV in the heart itself.

Based on the German epidemiology – and they are only seeing the tip of the iceberg – there are likely *tens of thousands* of Americans dying of “idiopathic cardiomyopathy” – undiagnosed viral myocarditis that is treatable. Kristin Loomis, head of the Human-Herpes 6 Foundation – together with Dr Dharam Ablashi (co-discoverer of the HHV-6 virus) echo this concern about ME/CFS and undiagnosed viral cardiomyopathy:

*“One of the most intriguing new ideas to come along in ME/CFS is the idea that subsets of these patients actually have subacute, chronic viral myocarditis. In the US, cardiologists stopped doing myocardial biopsies 25 years ago on the theory that there was nothing one could find that was treatable. In Germany, however, cardiologists continued to do biopsies and treat viral myocarditis aggressively. Three top German cardiology groups have recently reported that Parvovirus B-19 is the most common pathogen in myocarditis, followed by HHV-6... Most of these patients have very few symptoms (except fatigue) until the disease has progressed to a late stage. Martin Lerner, in the US has also been suggesting the same process EBV/CMV myocarditis in ME/CFS for over ten years, but has not had the “smoking gun” biopsy/ immunohistochemistry data to prove it.”*

<http://www.mecfsforums.com/index.php/topic,1159.0.html>

**How bad is this epidemic of viral cardiomyopathy in ME/CFS patients?:** “We don’t know”, although the Germans are certainly closer to the truth. And because viral

cardiomyopathy is not readily detected on routine clinical testing, these patients – already discredited for having ME/CFS – and many of whom are middle-aged women with metabolic syndrome – are further dismissed as hypochondriacs. It's not surprising that ME/CFS patients with heart disease have been identified in Dr L. Jason's research to die earlier than the norm.

*"The fact that approximately 20% of the sample died of heart failure is of importance given the growing evidence of cardiac problems among patients with CFS... If one examines national rates of death for these conditions, the ages of death for these three conditions among the patients with CFS are considerable earlier... the average age of heart failure is 83.1 (CDC, 2003, versus an average age of 58.7 years for the CFS sample). What this suggests is that those from this memorial list who did die of cancer, suicide, and heart failure were considerable younger than what would have been expected from the general population, which means that CFS might have increased the risk of death for at least this sample."*

But the tide is turning in North American cardiology circles. Cardiologist Dr Jeffrey Towbin has found PVB19 to be the #1 cardiotropic virus in his former lab, and by gaining the attention of the heart transplant community, may gain traction for the ME/CFS cardiac community ([http://www.bcm.edu/pediatrics//index.cfm?Realm=99992426&This\\_Template=Home\\_Page\\_Text](http://www.bcm.edu/pediatrics//index.cfm?Realm=99992426&This_Template=Home_Page_Text)):

*"In 1986, the identification of Coxsackievirus B in the hearts of patients with myocarditis or dilated cardiomyopathy was reported. Subsequently, Dr. Jeffrey Towbin identified adenovirus as another virus that is commonly found in the hearts of patients with these diseases, as well as a cause of organ rejection in patients with lung and/or heart transplants. More recently, we have shown that the predominant virus causing myocarditis and heart transplant rejection has again changed with parvovirus B19 now being most common."*

Dr T.J. Anderson, in Calgary, Canada is an example of a cardiologist who recognizes the significance of atypical angina. In a presentation entitled, "**Angina in Women with Normal Coronary Arteries: Not as Benign as we Thought**", he essentially describes my case (<http://acclakelouise.com/downloads/presentations/2007/Anderson2.pdf>). But what really jumped out at me is his description in Slide 9, of women with atypical angina:

#### **"Atypical Angina in Women**

- Since late 80s recognition of vasomotor abnormalities labeled microvascular angina, Syndrome X, endothelial dysfunction
- Abnormalities of:
  - Epicardial Ach(acetylcholine) mediated dilation (constriction)
  - Attenuation of Ach mediated increase in CBF (coronary blood flow)
  - Attenuation of CFR (coronary flow rate)
  - Abnormal metabolism by CMR-spectroscopy and PET
  - Net lactate production
  - Documented ischemia in about 50% of cases
  - Abnormal pain perception
  - Associated conditions such as migraine headache, Raynaud's, and chronic pain conditions
  - Peripheral endothelial dysfunction
  - Overlap with metabolic syndrome"

**I believe this describes patients with ME/CFS:** abnormalities in metabolism, problems with lactate, Raynaud's (I have Raynaud's-like symptoms; and ME/CFS patients are noted for losing their fingerprints); chronic pain (ME/CFS/FM); neurologically and vascular-induced headaches; metabolic syndrome, and abnormalities nitric oxide metabolism.

**A non-invasive alternative to the EMB? And a way to further legitimize ME/CFS?:** We are facing a critical roadblock in the emergency departments and cardiology offices across North America... patients with Atypical Angina – and possibly ME/CFS - urgently need endothelial-specific testing, yet continue to get useless (and expensive) routine cardiac diagnostics. But non-invasive, safe measures of endothelial function do exist and are used by rheumatologists & cardiologists (eg. to assess digital perfusion in Raynaud's phenomenon; and Itamar Medical's EndoPat for cardiac function (<http://www.itamar-medical.com/Index.asp>).

Atypical Angina may be a hallmark of progressive ME/CFS that is slipping through the cracks in America. Another reason to urgently investigate ME/CFS and atypical angina is the finding by Johnson et al (*European Heart Journal* 2006;27:1408,

<http://www.ncbi.nlm.nih.gov/pubmed/16720691> ) from the WISE study, that persistent chest pain in women with no coronary artery disease predicts serious adverse outcomes.

“Among women undergoing coronary angiography for suspected myocardial ischaemia, PChP (persistent chest pain) in women with no obstructive CAD (coronary artery disease) predicted adverse CV (cardiovascular) outcomes.”...Among women without CAD (coronary artery disease), those with PChP (persistent chest pain) had more than twice the rate of composite CV(cardiovascular) events (P=0.03), that included non-fatal **myocardial infarctions** (P=0.11), **strokes** (P=0.03), **congestive heart failure** (P=0.38), and **CV deaths** (P=0.73), compared with those without PChP.”

In our risk-averse culture in North America, where EMB's are perhaps understandably avoided, might the Endopat or similar endothelial technologies provide validation to ME/CFS patients with atypical angina? And might this accelerate validation of ME/CFS pathology – and our access to meaningful therapeutics? If we can legitimize the cardiac issues in many ME/CFS, this might shorten the vital time to treatment for many. Isn't it time for the heavy investment by the NHLBI in the WISE study to be translated into the ME/CFS population?

***The significance of the WISE Study to ME/CFS research:*** The WISE Study has spawned a flurry of follow-up papers, particularly through the NHLBI which further illuminate the dangers of untreated persistent chest pain. Just a few examples:

**1) Coronary Microvascular Reactivity to Adenosine Predicts Adverse Outcome in Women Evaluated for Suspected Ischemia**, Results From the National Heart, Lung and Blood Institute WISE (Women's Ischemia Syndrome Evaluation) Study, *J Am Coll Cardiol*, 2010; 55:2825-2832, doi: 10.1016/j.jacc.2010.01.054. From: <http://content.onlinejacc.org/cgi/content/abstract/55/25/2825>

**“Conclusions:** Among women with suspected ischemia and atherosclerosis risk factors, coronary microvascular reactivity to adenosine significantly improves prediction of major adverse outcomes over angiographic CAD severity and CAD risk factors. These findings suggest that coronary microvessels represent novel targets for diagnostic and therapeutic strategies to predict and limit adverse outcomes in women.”

*My note: We need endothelial diagnostics for the many ME/CFS patients with atypical angina!*

**2) Adverse Cardiovascular Outcomes in Women With Nonobstructive Coronary Artery Disease**, *Arch Intern Med*. 2009; 169(9):843-850. From: <http://archinte.ama-assn.org/cgi/content/abstract/169/9/843>

**Results** ...the 5-year annualized cardiovascular event rate being 25.3% in women with nonobstructive CAD, 13.9% in WISE women with normal coronary arteries, and 6.5% in asymptomatic women (P = .003).

**Conclusion** Women with symptoms and signs suggestive of ischemia but without obstructive CAD are at elevated risk for cardiovascular events compared with asymptomatic community-based women.

*My note: The 5-year annualized cardiovascular event rate for women who have persistent chest pain but don't have blocked arteries is HIGH at almost 40%! Worse, over 13% of these women are asymptomatic true silently-ticking time bombs! We URGENTLY need to be testing ME/CFS patients, men/women, with/without persistent chest pain with endothelial-specific tests*

**3) Digital Assessment of Endothelial Function and Ischemic Heart Disease in Women**, *J Am Coll Cardiol*, 2010; 55:1688-1696, doi:10.1016/j.jacc.2009.10.073. From: <http://content.onlinejacc.org/cgi/content/abstract/55/16/1688>

**Conclusions:** RH-PAT (digital reactive hyperemia peripheral arterial tonometry) indexes were significantly attenuated in women with IHD (Ischaemic Heart Disease). Digital RH-PAT can predict patients with IHD, especially NOCAD (Non-Obstructive Coronary Artery Disease) before angiography. RH-PAT is potentially useful for identifying high-risk women for IHD.

*My note: There are easy ways to do endothelial testing. Digital – measuring the finger's blood flow – is about as easy as it gets! Rheumatologists routinely assess digital perfusion patients with Raynaud's patients. Such non-invasive tests can also serve as cost-effective triage to identify patients needing further cardiac testing/care..*

#### 4) Self-Rated Versus Objective Health Indicators as Predictors of Major Cardiovascular

**Events:** The NHLBI-Sponsored Women's Ischemia Syndrome Evaluation, *Psychosomatic Medicine* 72:549-555 (2010) . From: <http://www.psychosomaticmedicine.org/cgi/content/abstract/72/6/549>

**Conclusions:** Among women with suspected myocardial ischemia, self-rated health predicted major CVD events independent of demographic factors, CVD risk factors, and angiogram-defined disease severity. However, functional impairment seemed to explain much of the self-rated health association. These results support the clinical utility of self-rated health scores in women and encourage a multidimensional approach to conceptualizing these measures.

*My note: Listen to the patient! If they are exhausted by trivial daily activities, this is a red flag for cardiovascular disease events. Recall Dr Anderson's: "Angina in Women with Normal Coronary Arteries: Not as Benign as we Thought". These patients had "abnormal pain perception; associated conditions such as migraine headache, Raynaud's, and chronic pain conditions (think ME/CFS/FM). Consider Dr Kerr's work on PVB19 and ME/CFS: Raynaud's is a frequent finding. Think Dr deMeirleir's work on the gut – many of his ME/CFS patients have active PVB19 infections. All of this suggests many of the WISE patients may be ME/CFS patients with endothelial dysfunction, with mortal risk from viral heart disease. We urgently need the NHLBI to revisit their WISE participants, using appropriate, sensitive criteria (eg. XMRV/MLV testing; rigorous Canadian Criteria ME/CFS) to study this red flag – AND to strengthen the vital WISE conclusions. And this requires funding!*

#### 5) Depressive Symptom Dimensions and Cardiovascular Prognosis Among Women With Suspected Myocardial Ischemia, *Arch Gen Psychiatry*. 2009;66(5):499-507. From: <http://archpsyc.ama-assn.org/cgi/content/abstract/66/5/499>

**Conclusions** In a sample of women with suspected myocardial ischemia, somatic but not cognitive/affective depressive symptoms were associated with an increased risk of cardiovascular-related mortality and events. These results support the need to research dimensions of depression in CVD populations and have implications for understanding the connection between depression and CVD.

*My note: On the contrary, these results support the need to differentiate ME/XMRV/MLV patients from depressive CFS. It is an international joke that the CDC can't differentiate sedentary, depressed patients from M.E. patients with neuro-immunological dysfunction. If women are reporting somatic complaints, and these are associated with an increased risk of cardiovascular-related mortality – but unrelated to cognitive/affective depressive symptoms, might not something be amiss with the diagnosis of depression – and indeed with the diagnosis of "CFS"?*

#### 6) Psychotropic medication use and risk of adverse cardiovascular events in women with suspected coronary artery disease: outcomes from the Women's Ischemia Syndrome Evaluation (WISE) study, *Heart* 2009; 95: 1901-1906 doi: 10.1136/hrt.2009.176040.

From: <http://heart.bmj.com/content/95/23/1901.abstract>

**Conclusions:** These data suggest that factors related to psychotropic medication such as depression refractory to treatment, or medication use itself, are associated with adverse CV events in women with suspected myocardial ischaemia.

*My note: "Depression refractory to treatment may well be a euphemism for mis-diagnosed depression... or ME/CFS. This warrants a differential diagnosis to establish whether these patients are depressed, or whether they have the neuro-immune, possibly retroviral -mediated disease ME/CFS.*

#### **Cardiac involvement by opportunistic viruses: Even more reason to urgently investigate XMRV/MLV's in ME/CFS:**

The stakes for ME/CFS are far higher than imagined. It's not just the disproportionate number of long-term ME/CFS patients developing lymphomas. Or the devastation of living with post-exertional malaise and other ME/CFS symptoms. Evidence suggests viral cardiomyopathy is a profound driver of morbidity & mortality in this ME/CFS population. These patients are at mortal peril because they are being routinely ignored by physicians. The silver lining is that cardiac pathology – if detected soon – might help us not only treat our cardiac complications, but also underscore a need for a sense of urgency for ME/CFS funding. Your Committee can do something about that! Please treat this devastating disease with the urgency it requires.

*This has been an abbreviated version of my testimony. Further details, research references, and Appendix on diagnosis and treatment of viral cardiomyopathy are available from me.*