

# TOP 10 TESTS for MYALGIC ENCEPHALOMYELITIS & CFS LABELED PATIENTS

by Steven Du Pre

Though the CDC steadfastly says there are no tests for M. E./CFS, there are in fact a number of non-routine tests that delineate Myalgic Encephalomyelitis clearly and can be used for diagnostic or disability purposes. Evidence-based diagnostic tests are superior to questionnaires based on subjective symptoms or shoddy criteria like the Fukuda definition or Reeves wrongheaded empirical definition. The tests listed below also, through the work of scientists & clinicians, firmly contradict the falsehood that CDC claims there are no tests for this disease.

To the credit of the [2003 M.E./CFS Consensus Criteria](#), they list some of the tests that can delineate the disease. (You can also view and print a brief summary of these tests [here](#).)

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## TOP 10 TESTS for MYALGIC ENCEPHALOMYELITIS & "CFS" LABELED PATIENTS:

### TEST #1: Cardio-Pulmonary Exercise Testing with measurement of VO2 max, anaerobic threshold, and maximal heart rate and respiration.

This test is mentioned in the book Disability and CFS: Clinical, Legal and Patient Perspectives with this comment by Dr. Daniel Peterson: "One objective and reproducible technique for determining and measuring functional disability that should be used consistently is Cardio-Pulmonary Exercise Testing with measurement of VO2 max, anaerobic threshold, and maximal heart rate and respiration. The test is well established, sedentary and ill norms are published and the technology is relatively inexpensive and quite available. Approximately 1700 patients [as in 1997] have been tested over the past 10 years and the test is now used on the initial visit to screen patients, to direct rehabilitation, and adjunctively to determine disability."

#### [Diminished Cardiopulmonary Capacity During Post-Exertional Malaise](#)

(Abstract) J. Mark VanNess PhD, Christopher R. Snell PhD, Staci R. Stevens

AOL: <http://www.cfids-cab.org/rc/VanNess.pdf>">Here</a

"Conclusion

In the absence of a second exercise test, the lack of any significant differences for the first test would appear to suggest no functional impairment in CFS patients. However, the results from the second test indicate the presence of a CFS related post-exertional malaise. It might be concluded then that a single exercise test is insufficient to demonstrate functional impairment in CFS patients. A second test may be necessary to document the atypical recovery response and protracted malaise unique to CFS."

#### [Legal and Scientific Considerations of the Exercise Stress Test](#)

Ciccolla, Stevens, Snell, Van Ness, ©2007 The Haworth Press

"This article examines the legal and scientific basis on which an exercise stress test can provide medically acceptable evidence of disability for the CFS patient." This research group's excellent work proves the post-exertional disability that ME & CFS patients suffer, much worse on average than heart failure and COPD patients."

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## **TEST #2: Brain neuro SPECT & PET scans and MRI brain scan**

The CDC statement against using SPECT & MRI scans in the diagnosis of CFS is inaccurate, as shown by the many studies referred to below. It is also dangerous for physicians to be misguided in this way by the CDC.

(Quote from CDC web site

<http://www.cdc.gov/cfs/cfsscreening.htm>)

"Magnetic resonance imaging scan: single-photon emission computed tomography: Some CFS researchers have observed apparent differences in the cranial blood flow between CFS patients and controls. These studies remain unconfirmed, and imaging tests should not be performed as a diagnostic technique for CFS."

Evidence From recent 2007 IACFS/M. E. conference: New methods in viral studies using refined technology show further abnormalities in subsets of ME/CFS patients. Increased use of instruments like MRI, SPECT/SPET, PET and fMRI show some of the abnormalities in functioning that patients with ME/CFS experience on a daily basis but these may not have practical application if a patient cannot have this testing done. A number of abnormalities with reduced responsiveness on fMRI is an essential feature of ME/CFS.

Brain imaging shows that, amongst other abnormalities, ME/CFS patients have reduced blood flow to the brain (especially to areas that are involved in autonomic nervous system functioning and in sleep, concentration and pain, including the pre-frontal cortices, the anterior cingulate and the cerebellum); altered patterns of brain activation; reduced grey matter volume; altered serotonergic neurotransmission and reduced acetyl-carnitine uptake.

A collaboration of researchers from Spain, Belgium and Australia used SPET scanning to observe patterns of brain activity; they found that the brain abnormalities correlated with abnormal immune results.

Patients with ME/CFS require more brain regions to perform tasks, ie. they have to work harder to achieve the same results as healthy controls.

One particular area of the brain - the Wernicke area, essential for understanding and formulating coherent speech-showed evidence of reduced activity after exercise.

Proton resonance spectroscopy showed greatly increased levels of brain metabolites (lactate levels were 300% higher than in controls).

According to Dr Tae Park from South Korea, the unexplained bright spots on MRI scans of some ME/CFS patients are evidence of an "arteriolar vasculopathy" or a blood vessel disease. He believes ME/CFS is a "systemic micro-vascular inflammatory process" - a process that would affect not only the brain or the heart or the muscles, but potentially every organ system in the body. Dr Park found not only capillary inflammation and perivascular cuffing (the accumulation of immune cells that surround injured blood vessels), but that all the ME/CFS patients in his study demonstrated remarkably reduced renal blood flow. Dr Park noted that diabetics with renal vascular disease also complain of profound fatigue.

Dr Hiro Kuratsune from Japan gave a summary of what is known about brain function in ME/CFS. It has been known for over a decade that frontal and temporal lobe blood flow is

reduced in ME/CFS, and that exercise exacerbates this reduced blood flow for up to 72 hours. The new evidence is that elevated elastase and RNase-L levels correlate with reduced blood flow. It is known that the MRI is abnormal in the majority of people with ME/CFS due to numerous T2 weighted hypertintense foci, with evidence of demyelination. Patients with more brain abnormalities tend to be more physically impaired.

The remarkable similarity in the brain images of patients with ME/CFS and multiple sclerosis was noted.

Dr Gudrun Lange from New Jersey, USA, stated what can be said with certainty about the central nervous system findings in ME/CFS:

- 1) the major cognitive problem seen is in information processing
- 2) studies showing reduced cerebral blood flow are starting to show consistency
- 3) there is a problem with serotonergic neurotransmission in the hippocampus and anterior cingulate regions
- 4) there are spinal fluid abnormalities
- 5) fMRI studies are showing altered patterns of brain activation.

(See references at the end of this article for more Neuroimaging evidence for ME/CFS diagnosis.)

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### **TEST #3: Mitochondrial Dysfunction**

(2 possible tests):

- 1). The magnetic resonance spectroscopy(MRS) brain scan is almost informative of the brain scans for ME/CFS. It indicates mitochondrial dysfunction. Check [www.co-cure.com](http://www.co-cure.com) in the archives for more info on MRS, and google Dr Cheney's MRS scan data for his patients. More info from a Dr. Cheney patient at this website:  
<http://users.adelphia.net/~sherry423/GuaiWhey/fmmito.htm>

\*\*\*MRS scanning has found abnormally high lactic acid spikes near around the hippocampus in PWME brains which indicates mitochondrial dysfunction, a central feature being found in just about all cases through the UK's BioLab testing. An MRI is good for ruling out gross abnormalities such as tumors and obvious areas of brain damage while the SPECT can help verify hypoperfusion in the brain.

- 2). Dr. Myhill in UK has a lab that screens for mitochondrial dysfunction: [Mitochondrial Function Profile test - practical information for non-UK residents](#)

From 2007 IACFS/M. E. Conference:

Dr Jonathan Kerr from London stated that his gene expression studies are finding three main abnormalities in ME/CFS patients: these involve the immune system, mitochondrial function and G-protein signaling. There are seven genes upregulated in ME/CFS - those associated with apoptosis, pesticides, mitochondrial function, demyelination and viral binding sites. Kerr mentioned three genes in particular: gelsolin, which is involved in apoptosis and amyloidosis; one that is upregulated by organophosphates, and a mitochondrial gene involved in the demyelination of nerves.

Also, **Mitochondrial abnormalities in the postviral fatigue syndrome.**

Behan WM, More IA, Behan PO Department of Pathology, University of Glasgow, Scotland. Acta Neuropathol 1991;83(1):61-5

“We have examined the muscle biopsies of 50 patients who had postviral fatigue syndrome (PFS) for from 1 to 17 years. We found mild to severe atrophy of type II fibres in 39 biopsies, with a mild to moderate excess of lipid. On ultrastructural examination, 35 of these specimens showed branching and fusion of mitochondrial cristae. Mitochondrial degeneration was obvious in 40 of the biopsies with swelling, vacuolation, myelin figures and secondary lysosomes. These abnormalities were in obvious contrast to control biopsies, where even mild changes were rarely detected. The findings described here provide the first evidence that PFS may be due to a mitochondrial disorder precipitated by a virus infection.”

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#### **TEST #4: TH1/TH2 imbalance**

TH1/TH2 Cytokine Production

Immune testing availability:

Neuroimmunology Labs at the company Neuroscience in Wisconsin. Their toll-free number is: 888-342-7272

Also, [Redlabs](#) appears to be offering some of this in Reno.

Th1/Th2 Imbalance – There are two general branches (Th1/Th2) of the immune system. Some patients appear to have an over activation of the anti-inflammatory (Th2) branch and an under activation of the pro-inflammatory (Th1) branch of the immune system. This could cause increased rates of allergy and sensitivity on the one hand and difficulty fighting off pathogens on the other. Further explanation from Dr. Cheney: [Balance the Th1/Th2 Immune System](#)

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#### **TEST #5: Natural Killer Cell Function (Activity) testing**

Immune testing availability:

Neuroimmunology Labs at the company Neuroscience in Wisconsin. Their toll-free number is: 888-342-7272

Also, [Redlabs](#) appears to be offering some of this in Reno.

Natural Killer (NK) and T-cell Dysfunction – NK and T-cells are two other components of the immune response to pathogens. A set of chronic fatigue syndrome (ME/CFS) patients have been shown to have reduced NK cell numbers and poor NK and T-cell functioning. These problems also could interfere with the ability of the immune system to find infected cells and kill them. Intriguingly some researchers believe that chronic immune activation due to an underlying chronicinfection has caused these cells to 'burn out'.

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#### **TEST #6: abnormalities of the 2-5A pathway (RNase-L ratio):**

37kDa 25A RNase L immunoassay: protein, activity, PKR cleavage, & elastase activity assays testing at [Redlabs USA](#) & [Redlabs Belgium](#)

Impaired Cellular Immune Response – Two abnormalities in the responses cells have to infection in the 'interferon pathway' have been documented. An antiviral enzyme in this pathway called the

RNase L has been shown to be fragmented in many patients. A subset of chronic fatigue syndrome (ME/CFS) patients also display increased activity of another enzyme called protein-kinase R (PKR) that is involved in killing cells infected with pathogens. These problems suggest the immune systems of chronic fatigue syndrome (ME/CFS) patients could have troubles finding pathogens and killing the cells they've infected. (Note: Immune function Test #s 4-6 are objective markers of pathophysiology and severity)

From January 2007 International Conference on ME/CFS summary of immunological abnormalities:

Anthony Komaroff (Professor of Medicine, Harvard) summarized the immune abnormalities that have been demonstrated in ME/CFS. These include activated CD8 (T cells); poorly functioning Natural Killer cells; novel findings -seen only in ME/CFS -- of abnormalities of the 2-5A pathway (RNase-L ratio); cytokine abnormalities (pro-inflammatory dysregulation); increased TGF, and 27 times more circulating immune complexes than in controls.

(More Immune Function references at the end of this article)

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### **TEST #7: Virology**

Viral antibodies, including Coxsackie B; bacteria, including HHV6; mycoplasma, [Wisconsin Viral Research Group](#)

Dr Dharam Ablashi from Santa Barbara, USA, showed that RNase-L was found to correlate with HHV-6 infection in ME/CFS and that RNase-L protein is a marker for active infection. Info on HHV-6 testing at [The HHV-6 Foundation](#).

Some patients clearly have a persistence of virus in their brain.

Enterovirus infections have previously been reported in UK studies but have not been much explored by US researchers. Enteroviruses are a genus of RNA viruses that includes echovirus, coxsackie virus and poliovirus. In a recent US study by John Chia from California of 108 patients with ME/CFS who underwent gastric biopsies, 100 revealed chronic inflammation and 80% were positive for VP1 (enteroviral capsid protein - first used by Professor James Mowbray et al in the UK in 1988). Enteroviral RNA was detected in 33% of patients."Use of valganciclovir in patients with elevated antibody titers against Human Herpesvirus-6 (HHV-6) and Epstein Barr Virus (EBV) who were experiencing central nervous system dysfunction including long-standing fatigue.

**Journal of Clinical Virology 37 Suppl. 1** (2006) S33–S38 Andreas M. Kogelnik a, Kristin Loomis b, Mette Hoegh-Petersen c, Fernando Rosso a,c, Courtney Hischer b, Jose G. Montoya a,c,\*

\*Stanford University School of Medicine, Stanford, CA, USA

\*HHV-6 Foundation, Santa Barbara, CA, USA

\*Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA

Symptoms observed in ME/CFS are compatible with a viral aetiology.

Many infectious agents have been cited as implicated in ME/CFS including EBV, Lyme, parvovirus, enteroviruses, Q fever, RRV, mycoplasma and HHV-6.

Over the last ten years there has been increasing evidence that infection is most likely to be a prime cause of ME/CFS.

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### **TEST #8: Heart Function**

(at least 2 possible tests)

1). Impedance Cardiography (available at many teaching hospitals)

[Chadwick Medical Associates](#)

[CardioDynamics](#)

[Abnormal Impedance Cardiography Predicts Symptom Severity in Chronic Fatigue Syndrome](#) - (Peckerman procedure: 10 minutes lying down followed by 5 minutes standing up)

[Abnormal Heart Pumping After Exercise Linked to Chronic Fatigue Syndrome](#)

Peckerman Q&A:

<http://www.cfids.org/archives/2003rr/2003-rr2-article01.asp>

2). 24 Hour Holter Monitoring: repetitively oscillating Twave inversions and/or Twave flats during 24hour monitoring. Note: this pattern may not be reported or subsumed under nonspecific Twave changes. More information at [The Treatment Center for Chronic Fatigue Syndrome](#)

[The Cardiac Insufficiency Hypothesis](#) is explained at the M.E. Society of America website.

\*\*Important note:

If the doctor insists on a regular exercise stress test, then these 2 studies below should be referenced, which show that a stress test must be followed the next day with another one to show the extreme disability.

### [Legal and Scientific Considerations of the Exercise Stress Test](#)

J of Chronic Fatigue Syndrome, Vol 14, No. 2, 2007, pp. 61-75 Margaret Ciccolella EdD, JD, Staci R. Stevens MA, Christopher R. Snell PhD, Mark Van Ness PhD

ABSTRACT. This article examines the legal and scientific bases on which an exercise stress test can provide medically acceptable evidence of disability for the Chronic Fatigue Syndrome (CFS) patient. To qualify for disability benefits, a claimant must establish the existence of a serious medically determinable impairment (MDI) that causes the inability to work. The single stress test has been used to objectively establish whether a claimant can engage in "substantial gainful employment" and is an important determinant of the award or denial of benefits. A review of case law indicates problems associated with a single test protocol that may be remedied by a "test-retest" protocol. The results of a preliminary study employing this approach indicate that the test-retest protocol addresses problems inherent in a single test and therefore provides an assessment of CFS related disability consistent with both medical & legal considerations is available in PDF at

[AOL: <http://www.cfids-cab.org/rc/Ciccolella.pdf> >Here</a>]

[Diminished Cardiopulmonary Capacity During Post-Exertional Malaise](#)

Journal of Chronic Fatigue Syndrome, Vol. 14, No. 2, 2007, pp. 77-85 J. Mark VanNess PhD, Christopher R. Snell PhD, Staci R. Stevens

[AOL: <http://www.cfids-cab.org/rc/VaNess.pdf>>Here</a>]

\*\*Also, in the whole area of neuro-cardiology is the tilt table testing since Dr. Charles Lapp says in his recommendations for people with this disease, up to 97% demonstrate vasovagal syncope (neurally mediated hypotension) on tilt table testing. [Canadian Consensus document](#) (p. 6 in the pamphlet, p. 13 in the PDF file under the title Autonomic Manifestations describes this orthostatic intolerance. Here's the first paragraph of a very good explanation from the document which includes some other very important information regarding circulation problems in the M.E./CFS:

6. Autonomic Manifestations

Chronic Orthostatic Intolerance (COI), the inability to sustain upright activity (standing, sitting or walking), is very common and may be an important component in ME/CFS. Upon limited standing, the patient experiences overwhelming exhaustion, an urgency to lie down, confusion, malaise, and worsening of other symptoms. Sitting and light walking are tolerated better than standing still, but no upright activity is tolerated well. Lying down helps alleviate symptoms. Tilt-table testing may be helpful in diagnosis but some patients may have a normal tilt-table test and still have severe COI. Quiet standing in the office allows for observation and monitoring the blood pressure and pulse. NOTE: This just only be done with extreme CAUTION with someone standing beside the patient at all times in order to support him/her if s/he begins to feel weak!

(Note: the in-office tilt table testing described in this paragraph are made more specific by Dr. Mary Schweitzer in a detailed description below the references at the end of this post after the references) Additionally, most of us are aware that Dr Paul Cheney found evidence of diastolic (cardiac) dysfunction in ME/CFS, with evidence of another cardiac abnormality (patent foramen ovale, or PFO). This results in hypoxia (low oxygen levels relative to metabolic needs). Cheney stated that the cardiac index of ME/CFS patients is so severe that it falls between the value of patients with myocardial infarction (heart attack) and those in shock. On September 9, 2006, Paul Cheney, MD, PhD, presented a seminar titled "CFS: The Heart of the Matter." This outstanding seminar contains important, fascinating and unique material that will eventually be published. There is an overview of chronic fatigue syndrome, an in-depth look at the cardiovascular issues in CFS, a new model of the illness, and a full update on Dr. Cheney's latest study, including the treatment protocol [available on DVD](#) from the DFW Support Group.

Also, helpful is this testing showing impaired blood flow: Hypercoagulability - flow cytometry fibrinogen, thrombin/anti-thrombin complexes.

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**TEST #9: Neurocognitive testing & sleep studies**

Neurocognitive:

To ascertain neurological abnormalities in brain neuro SPECT scan, disability representative may have a licensed psychologist perform a battery of 6 neurocognitive tests to test mental performance. Cognitive performance: decreased processing speed, working memory, information learning, etc.

## Sleep Studies:

Testable Major Sleep Dysfunction: This can include all forms of sleep dysfunctions. All or any of the following may be present: (a) impaired sleep efficiency, (b) significant fragmented sleep architecture, (c) movement arousals, particularly if there is an associated pain syndrome, (d) absence or significant decrease of type 3 and 4 sleep, (e) abnormal REM sleep pattern (f) changes in daytime alertness and (g) sleep reversals.

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## TEST #10: Endocrine testing

CT scans may show reduced adrenal gland size; thyroid hormone levels with attention to bioavailability of T3 & those with reduced level should be checked for selenium as it regulates conversion of T4 to T3; reduced HPA function (see this article):

[Diagnosis and Treatment of Hypothalamic-Pituitary-Adrenal \(HPA\) Axis Dysfunction in Patients with Chronic Fatigue Syndrome \(CFS\) and Fibromyalgia \(FM\)](#), J of Chronic Fatigue Syndrome, Vol. 14, No. 3, 2007, pp. 59-88, by Kent Holtorf MD  
[AOL: <a href="http://www.cfids-cab.org/rc/Holtorf.pdf">Here</a>]

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These Top 10 Tests also would be appropriate considering Dr. Ramsey's 1986 definition & criteria:

"A syndrome initiated by a virus infection (TESTS #4, 5, 6, 7), commonly in the form of a respiratory or gastrointestinal illness with significant headache, malaise and dizziness (TEST #8) sometimes accompanied by lymphadenopathy or rash. Insidious or more dramatic onsets following neurological (TEST #2), cardiac (TESTS #1, 8) or endocrine (TEST #10) disability are also recognised.

“Characteristic features include:

- (1) A multisystem disease, primarily neurological with variable involvement of liver, cardiac and skeletal muscle, lymphoid and endocrine organs.
- (2) Neurological disturbance - an unpredictable state of central nervous system exhaustion following mental or physical exertion which may be delayed and require several days for recovery; an unique neuro-endocrine profile which differs from depression in that the hypothalamic/pituitary/adrenal response to stress is deficient; dysfunction of the autonomic and sensory nervous systems; cognitive problems (TEST #9).
- (3) Musculo-skeletal dysfunction (TEST #3) in a proportion of patients (related to sensory disturbance or to the late metabolic and auto immune effects of infection)
- (4) A characteristically chronic relapsing course"

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The above list and additional references support the obvious fact that Reeves' "do not give these tests" list on the CDC website is the height of ignorance and chutzpah. CDC website states (in the material for professionals to read):

<http://www.cdc.gov/cfs/cfsdiagnosisHCP.htm>

"No diagnostic tests for infectious agents, such as Epstein-Barr virus, enteroviruses, retroviruses,

human herpesvirus 6, Candida albicans, and Mycoplasma incognita, are diagnostic for CFS and as such should not be used (except to identify an illness that would exclude a CFS diagnosis, such as mononucleosis). In addition, no immunologic tests, including cell profiling tests such as measurements of natural killer cell (NK) number or function, cytokine tests (e.g., interleukin-1, interleukin-6, or interferon), or cell marker tests (e.g., CD25 or CD16), have ever been shown to have value for diagnosing CFS. Other tests that must be regarded as experimental for making the diagnosis of CFS include the tilt table test for NMH, and imaging techniques such as MRI, PET-scan, or SPECT-scan. Reports of a pathway marker for CFS as well as a urine marker for CFS are undergoing further study; however, neither is considered useful for diagnosis at this time."

In light of this, there is a need to focus on and publicize biomarkers, treatments resulting from biomarkers, and peer-reviewed published research long ignored by CDC, which would result in doctors confidence in the diagnosis of Myalgic Encephalomyelitis and the return to the name Myalgic Encephalomyelitis or another suitable medical name for that ICD code.

Dr. Jonathan Kerr in his gene studies included patients who had been diagnosed with M.E., and they generally already met the Fukuda definition because it's so much looser even though his research only mentions CFS-Fukuda.

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Poetry website: <http://www.angelfire.com/poetry/soareagle/index.html>

"By words the mind is winged." Aristophanes

[National Alliance for Myalgic Encephalomyelitis](#)

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#### Additional References & Poor man's tilt table testing description

#### Neuroimaging References:

Neurological Dysfunction in Chronic Fatigue Syndrome, Journal of Chronic Fatigue Syndrome (The Haworth Medical Press, an imprint of The Haworth Press, Inc.) Vol. 6, No. 3/4, 2000, pp. 51-68. Abhijit Chaudhuri, DM, MD, MRCP; Peter O. Behan, DSc, MD, FACP, FRCP

"SPECT Imaging of the Brain: Comparison of Findings in Patients with Chronic Fatigue Syndrome, AIDS Dementia Complex, and Major Unipolar Depression," Richard B. Schwartz, Anthony L. Komaroff, Basem M. Garada, Marcy Gleit, Teresa H. Doolittle, David W. Bates, Russell G. Vasily, B. Leonard Holman; American Journal of Roentgenology, Vol 162, 943-951, Copyright © 1994 by American Roentgen Ray Society.

Summary: "This study shows that CFS (ME) shares some similarities on SPECT imaging with AIDS Dementia Complex - acute changes in radionuclide uptake in the younger population may be caused by inflammatory processes at the cellular or micro vascular level .... the findings in CFS (ME) face are consistent with the hypothesis that CFS (ME) ... results from a viral infection of neurons, glia or vasculature ....viral infection can provoke neurological dysfunction by interfering with intra-cellular mechanisms or membrane transport systems .... or by cerebral hypoperfusion due to vasculitis".

It has been known for some time that CFS patients have abnormal blood flow in their brains; that is, some areas of the brain are not getting as much blood as they should. Dr. Ismael Mena has studied M. E./CFS patients' brains using SPECT scans at the University of California-Los Angeles, where he is a professor of radiology (Ismael Mena, M.D., "Study of Cerebral Perfusion by NeuroSPECT in Patients with Chronic Fatigue Syndrome," The Cambridge Symposium on Myalgic Encephalomyelitis, 1990; 1: 21-22.)

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Brain positron emission tomography (PET) in chronic fatigue syndrome: preliminary data Tirelli U et al. *Am J Med* 1998;105: (3A):54S-58S

Brain MRI abnormalities exist in a subset of patients with chronic fatigue syndrome. Lange G, DeLuca J, Maldjian JA, Lee H, Tiersky LA, Natelson BH. *J Neurol Sci.* 1999 Dec 1;171(1):3-7.

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Evidence for the Presence of Immune Dysfunction in Chronic Fatigue Syndrome. Benjamin H. Natelson, Mohammad H. Haghghi, and Nicholas M. Ponzio. Departments of Neurosciences, Pathology, University of Medicine and Dentistry—New Jersey Medical School, Department of Psychology, Rutgers University, Newark, New Jersey Clinical and Diagnostic Laboratory Immunology, July 2002, p. 747-752, Vol. 9, No. 4, 1071-412X/02/\$04.00+0 DOI: 10.1128/CDLI.9.4.747-752.2002 [2002](https://doi.org/10.1128/CDLI.9.4.747-752.2002), [American Society for Microbiology](https://doi.org/10.1128/CDLI.9.4.747-752.2002)

Low NK syndrome and its relationship to chronic fatigue syndrome. Aoki T, Miyakoshi H,

Usuda Y, Herberman RB. *Clinical Immunology and Immunopathology* 1993; 69(3): 253-65.

A chronic illness characterized by fatigue, neurologic and immunologic disorders, and active human herpesvirus type 6 infection. Buchwald D, Cheney PR, Peterson DL, Henry B, Wormsley SB, Geiger A, Ablashi DV, Salahuddin SZ, Saxinger C, Biddle R, et al. *Annals of Internal Medicine* 1992; 116(2): 103-13. Immunologic abnormalities associated with chronic fatigue syndrome. Barker E, Fujimura SF, Fadem MB, Landay AL, Levy JA. *Clinical Infectious Diseases* 1994; 18(Supp 1): S136-41. A comprehensive immunological analysis in chronic fatigue syndrome. Gupta S, Vayuvegula B. *Scandinavian Journal of Immunology* 1991; 33: 319-327. Abstract: A detailed analysis of cell-mediated and antibody-mediated immunity was performed in 20 CDC-defined patients with chronic fatigue syndrome (CFS) and 20 age- and sex-matched healthy controls. CD3+, CD4+, CD8+, and CD20+lymphocytes were comparable in two groups. Natural killer cells as defined by CD16, CD56 and CD57 antigens were significantly reduced in CFS. A significant increase in the proportions of CD4+ ICAM 1+ T cells was observed in CFS. Monocytes from CFS displayed increased density (as determined by mean fluorescence channel numbers) of intercellular adhesion molecule 1 (ICAM-1) and lymphocyte function associated antigen 1 (LFA-1), but showed decreased enhancing response to recombinant interferon-gamma in vitro. The lymphocyte DNA synthesis in response to phytohaemaglobulin (PHA), Concanavalin A (Con A) and pokeweed mitogen (PWM) was normal but the response to soluble antigens was significantly reduced. Serum IgM, IgG, IgA, and IgG subclasses were normal. In vivo specific antibody response to pneumococcus vaccine was depressed in CFS. Forty percent of patients showed titres of anti-human herpes virus 6 (anti-HHV-6) antibody higher than that in the controls (greater than or equal to 1/80). These data suggest immunological dysfunction in patients with chronic fatigue syndrome. The significance of these observations is discussed. Immunological abnormalities in patients with chronic fatigue syndrome. Tirelli U, Marotta G, Improta S, Pinto A. *Scandinavian Journal of Immunology* 1994; 40(6): 601-8. Low NK syndrome and its relationship to chronic fatigue syndrome. Aoki T, Miyakoshi H, Usuda Y, Herberman RB. *Clinical Immunology and Immunopathology* 1993; 69(3): 253-65.

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Description of poor man's tilt table testing procedure(courtesy of Dr. Mary Schweitzer):

You lie still and rest for 15 minutes to 20 minutes. Then they take your blood pressure and pulse. Then you sit up for about 10 minutes (same thing). Then you stand and lean slightly against a wall - do NOT flex your muscles or struggle or talk.

Be calm. (Have somebody there who can catch you if there is trouble)!

After ten minutes they should do the blood pressure and pulse again.

Keep leaning. DO NOT FLEX ANY MUSCLES OR TALK.

After another ten minutes, take them again.

If at any time you start to feel sweaty or hot or nauseous or basically super-M.E., they need to do the bp and pulse right away and get you lying down. Congratulations.

For Neurally Mediated Hypotension (NMH), you have to have a 20-25 mm drop in

systolic blood pressure (the higher number).

If your pulse suddenly rises at least 30 bpm (beats per minute), then you have Postural Orthostatic Tachycardia Syndrome (POTS).

Dr. Rowe believes they are both really the same thing - with either, if you don't get down, you're going to pass out. And the treatment for both is the same. Rowe published the first article on the relationship between CFS and autonomic nervous system dysfunction (NMH/POTS) in JAMA in the fall of 1995. (Note: See abstract below.)

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**What is neurally mediated hypotension?**

Neurally mediated hypotension is also known by the following names: the fainting reflex, neurocardiogenic syncope, vasodepressor syncope, the vaso-vagal reflex, and autonomic dysfunction. Hypotension is the formal medical term for low blood pressure, and syncope is the term for fainting. Neurally mediated hypotension occurs when there is an abnormal reflex interaction between the heart and the brain, both of which usually are structurally normal.

Dr. Cheney's treatment for NMH:

[http://www.immunesupport.com/library/showarticle.cfm/ID/3499/e/1/T/CFIDS\\_FM/](http://www.immunesupport.com/library/showarticle.cfm/ID/3499/e/1/T/CFIDS_FM/)

**What is Postural orthostatic tachycardia syndrome?**

Postural orthostatic tachycardia syndrome (or POTS) is a condition of [orthostatic intolerance](#) in which a change from the [supine position](#) to an upright position causes an abnormally large increase in heart rate, often, but not always accompanied by a fall in blood pressure. Patients with POTS also have problems in maintaining homeostasis when changing position ie moving from one chair to another or reaching above their heads. The syndrome was identified as such by Schondorf and Low in [1993](#). Similar symptoms were collectively described as "[idiopathic hypovolemia](#)" by Fouad in [1986](#). A comprehensive historical account is given by Grubb (2002).

Symptoms include an abnormally large increase in heart rate upon standing, [lightheadedness](#), extreme [fatigue](#), [nausea](#), [headache](#), [chest pain](#), [exercise intolerance](#) and impaired concentration. Patients may exhibit mild [hypotension](#) while standing, but most do not experience [fainting](#). Patients with POTS may frequently be misdiagnosed as having [panic attacks](#), [chronic fatigue syndrome](#) or chronic [anxiety disorder](#) (Grubb, 2002). POTS patients are usually significantly debilitated by their symptoms.

POTS is often difficult to diagnose. A routine physical examination and standard blood tests usually will not indicate POTS. A [tilt table test](#) is vital to diagnosing POTS although all symptoms must be considered before a final diagnosis is made. A test to rule out [pheochromocytoma](#) is usually performed. Other tests such as multi-site photoplethysmography a measure of how well the blood vessels constrict can also be useful. A blood test may be performed to verify abnormally high levels of [norepinephrine](#) usually present in POTS patients (Raj, 2006).

**The Relationship Between Neurally Mediated Hypotension**

**and the Chronic Fatigue Syndrome** Issam Bou-Holaigah, MD; Peter Rowe, MD; Jean Kan, MD; Hugh Calkins, MD

**OBJECTIVE:** To compare the clinical symptoms and response evoked by upright tilt-table testing in healthy individuals and in a sample of those satisfying strict criteria for chronic fatigue syndrome.

**DESIGN:** Case-comparison study with mean (SD) follow-up of 24 (5) weeks.

**SETTING:** Tertiary care hospital.

**PATIENTS AND OTHER PARTICIPANTS:** A sample of 23 patients with chronic fatigue syndrome (five men and 18 woman; mean age, 34 years), each of whom fulfilled the strict diagnostic criteria of the Centers for Disease Control and Prevention, was recruited from regional chronic fatigue support groups and from the investigators' clinical practices. There were 14 healthy controls (four men and 10 women; mean age, 36 years).

**INTERVENTIONS:** Each subject completed a symptom questionnaire and underwent a three-stage upright tilt-table test (stage 1, 45 minutes at 70° tilt; stage 2, 15 minutes at 70° tilt with 1 to 2 g/min of isoproterenol; and stage 3, 10 minutes at 70° with 3 to 4 g/min of isoproterenol). Patients were offered therapy with fludrocortisone,  $\beta$ -adrenergic blocking agents, and disopyramide, alone or in combination, directed at neurally mediated hypotension.

**MAIN OUTCOME MEASURES:** Response to upright tilt and scores on symptom questionnaires prior to and during follow-up.

**RESULTS:** An abnormal response to upright tilt was observed in 22 of 23 patients with chronic fatigue syndrome vs four of 14 controls ( $P<.001$ ). Seventy percent of chronic fatigue syndrome patients, but no controls, had an abnormal response during stage 1 ( $P<.001$ ). Nine patients reported complete or nearly complete resolution of chronic fatigue syndrome symptoms after therapy directed at neurally mediated hypotension.

**CONCLUSIONS:** We conclude that chronic fatigue syndrome is associated with neurally mediated hypotension and that its symptoms may be improved in a subset of patients by therapy directed at this abnormal cardiovascular reflex. JAMA, September 27, 1995 - Volume 274, No. 12

[Diagnosis: Orthostatic Intolerance \(OI\)](#)

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