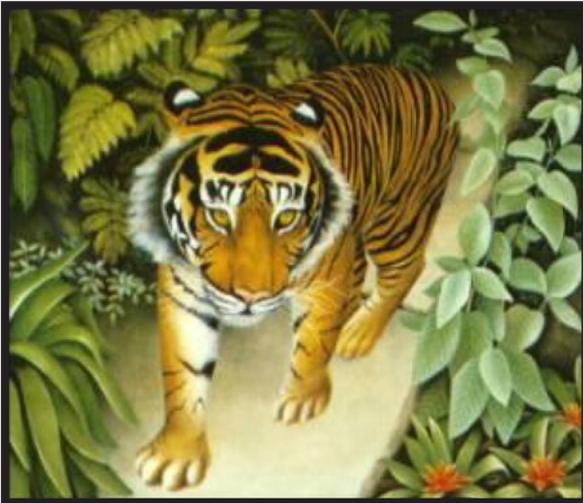


The Nightingale Research Foundation Definition of Myalgic Encephalomyelitis (M.E.)



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(3) A very limited number of: **The Clinical and Scientific Basis of M.E./CFS** can be purchased for \$100 US dollars or 100 euros. This includes the scandalous mailing costs. This book can be downloaded **free** of charge from the Nightingale web site, but it is a very large, heavy 724 page book.

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The Nightingale Research Foundation
Definition of
Myalgic Encephalomyelitis (M.E.)

Definitions, Abbreviations and Acronyms

EV = Enterovirus: (incubation period circa 3-7 days) (illness beginning most frequently in late summer and autumn in the north temperate world) (these infections first enter the body through the gastric portal, hence the name: entero. Enteroviruses cause paralytic polio, other paralytic enteroviral diseases, type I diabetes, major gastric diseases.

Genome = The complete set of genes or genetic material which defines a micro-organism.

M.E. = Myalgic Encephalomyelitis: a complex epidemic and sporadic biphasic disease state caused by a chronic enteroviral infection, which injures the GIT system and the upper CNS brain function. CNS dysfunction, in turn, causes generalized body dysfunctions.

CFS = Chronic Fatigue Syndrome: CFS is not a disease. It is a non-specific group of poorly investigated chronically disabling and major illnesses, diseases and pathologies.

EBV = Epstein Barr Virus is the primary cause of Mononucleosis (Glandular Fever in the UK): This is an easily diagnosed viral illness that due to its circa 40 day incubation period does not cause epidemic diseases. Unlike Enteroviral infections there is no specific season when it is more common.

CNS = Central Nervous System: (brain, brain stem, spinal cord and appendages).

MRI = Magnetic Resonance Imaging: Used as brain imaging technology. This technique visualizes anatomy not function. Routine MRI cannot demonstrate most physiological brain dysfunction.

SPECT = Single Photon Emission Computed Tomography: This technique visualizes physiological function or vascularization, not anatomy. SPECT can document major brain dysfunction.

HMPAO = A nucleotide (Hexa-Methyl-Propylene-Amine-Oxime) used in SPECT imaging and the essential product for brain mapping employing Segami Oasis Neurogram software.

Dysautonomia = a malfunction of the autonomic nervous system seen in many severe M.E. patients, specifically Insula hypoperfusion. (Several brain areas are responsible for normal blood pressure, efficient body and CNS circulation, and normal heart rate.)

POTS = Postural Orthostatic Tachycardia Syndrome: (This is a variety of dysautonomia.)

Insular Lobe = a hidden lobe covered by the operculum (the junction of the temporal, parietal, frontal lobes). The insular lobe is the brain area significantly responsible for autonomic control. Hypoperfusion of the operculum is consistently found in patients with Dysautonomia.

GIT = Gastrointestinal Tract: (oesophagus, stomach, small and large intestines)

CDC = Centers for Disease Control and Prevention: (Atlanta, Marietta Georgia)

NIH = National Institutes of Health (Bethesda, Maryland) One of the worlds foremost medical research centres, an agency of the USA Department of Health.

To the reader,

The following information explains how physicians can diagnose clinically & test scientifically for Myalgic Encephalomyelitis (M.E.). But, first a word about M.E. and **Enteroviral (EV)** infections

M.E. is not Chronic Fatigue Syndrome (CFS). Primary M.E. is an epidemic and sporadic illness caused by many E.V.s. The best known E.V.s are Polio 1, 2 & 3 but the genomes of the approximately 100 different E.V.s are identical to the polio genome except for a 5% difference in the 5' (prime) untranslated area. **Most interesting is that the first-year symptoms of M.E. are identical to Dr. Ivar Wickman's description of the Polio symptoms** in the 1905 Stockholm-area polio epidemic, which maimed and killed over 1031 patients. The principal differences between polio and M.E. is that E.V.s injure primarily the upper CNS:

- a. **E.V.s** injure the CNS, primarily above the spinal cord; whereas **Polio E.V.s** injure the spinal cord, brainstem, & to a lesser extent the brain itself.
- b. Certain **E.V.s** have always caused paralysis but not usually as frequently nor as severely as polio 1 & 3, although many of these **E.V.s** can cause muscle weakness as in M.E. In addition, **E.V.s** cause a large number of other serious and often fatal illnesses, both in children and adults.
- c. Polio immunization researchers didn't know about E.V. until after the first successful Salk polio vaccine. In effect, they built the polio-immunization on the basis of the 5' prime area (at the left of the following diagram). If they had built the immunization on the basis of the VP3 section of the genome below, were it possible, there would be no M.E. today, nor would there be any paralytic polio either.



Above is the structure of all EV genomes, including M.E. & polio.

There are many causes of viral and chemical brain injury but classical or primary M.E. is only caused by Enteroviruses (E.V.). Today, it is likely that in most cases, Lansing Polio 2 virus would be considered to be an M.E. virus since it causes significantly less flaccid paralysis than polio 1 & 3. Many of the same **E.V.s** that cause M.E. can also cause flaccid paralysis simulating polio. Example, **E.V.s 68 &**

70 and at least another 10 **E.V.s**. In effect, they might all be called polio today and there is no immunization for them.

Primary post-E.V. M.E. is the typical M.E. described in this booklet caused by enteroviruses.

Secondary sporadic M.E. can be associated with any CNS (neurotropic) injuring or infectious agent. Childhood infections in adults (usually adults over 20 yrs.) such as varicella (chicken pox), measles, EBV, can cause death or chronic brain dysfunction, which can provoke the so-called CFS-type patients. But EBV can never cause rapidly-spreading epidemics.

Chronic Fatigue Syndrome (CFS): in our experience the diagnosis of CFS only means the investigating physicians have not thoroughly investigated the patient. We routinely find in US, Canadian and European CFS patients diagnosed by physicians in their country, a variety of missed diseases. These include: toxic & chemical injuries, genetic injuries, cardio and cardio-vascular injuries, collagen diseases, adverse medication reaction, mitochondrial disease, adverse immunization caused illness, Ehlers-Danlos Syndrome, rarely MS, missed thyroid malignancy and thyroid diseases. CFS in general implies a serious missed disease. I have found up to 20 significant pathologies in a single CFS patient, none of them caught by any physician. Yet they are diagnosed as CFS. Fibromyalgia is also a legitimate symptom in over 10 different classically-accepted illnesses. See our book: **Missed Diagnoses at Lulu.com**. I believe CFS is not a disease or a syndrome, but is a mixed group of undiagnosed significant illnesses.

The CDC 1988 CFS publication, based on the summer 1984 Lake Tahoe epidemic, was a classic enterovirus epidemic & not an EBV infection. The authors of the 1988 CDC definition quoted EBV research publications almost exclusively, believing this to be an Epstein Barr epidemic. They also appear to have crafted the CFS diagnostic criteria to fit their EBV prejudice. One rarely ever found swollen cervical glands in M.E. patients. The CFS authors should have known, EBV, with an incubation period of 40 days, can never have caused the rapidly spreading epidemic across Nevada & North America. Also, EBV does not have a late summer early autumn peak. Late summer and autumn is enterovirus territory.

The so-called **Oxford Guidelines** were created primarily by a large group of UK psychiatrists, in attempt to receive NIH funds. However, they crafted their CFS definition as a psychiatric illness. This intentional prejudice has been disastrous for many M.E. patients in the UK, as it succeeded in the psychiatric-ization of this epidemic post-infectious CNS-injuring illness. The dangerous practices of CBT,

GET and PACE treatment do not result in recovery in true M.E. brain-injured patients any more than if CBT had been used to treat paralyzed polio patients. In our experience, CBT & GET are often employed to nullify disability pensions since true M.E. patients cannot continue such treatments without further damage.

Today, many UK, NA & European patients are routinely dismissed, rarely correctly investigated and too often placed on a psychiatric treatment, or hospitalized against their will due to the Oxford & CDC definitions. They base their diagnosis upon the fallacious concept: a patient with only symptoms and no physical or positive test findings is a psychiatric patient. This is why correct tests for M.E. must be performed as described in this booklet.

I am in turn critical of the **New England Journal of Medicine**, one of the world's best medical journals, for making the late Dr. Stephen Straus one of the three secret peer reviewers of CFS and M.E. papers. His blocking of the Dr. Dan Peterson et al Lake Tahoe paper destroyed any honest understanding of this tragic epidemic. No medical journal should place a peer reviewer on their board who has a financial stranglehold on publications as had Straus, the chair for CFS funding at NIH. I am also critical of the CDC & NIH, having given no serious funding to investigate chronic patients of this 1984 Tahoe epidemic, North American illness, which has resulted in the chronic disability of tens of thousands of Americans and Canadians.

This Nightingale M.E. definition is particularly important to physicians since the cause of primary M.E. is related only to chronic enteroviral infections, close cousins of paralytic poliomyelitis. At the August European 2016 meeting on picornaviruses & enteroviruses in Switzerland, several new anti-enteroviral medications were discussed, including: Pirodavisir, Vapendavisir, Pocapavisir, Plecoaril & Rupintrivir. Although at an early stage, some have shown success in animal models. Help may yet be on the way for chronically-disabled M.E. patients. Prevention is always better than treatment. Prevention can only occur with a new enterovirus immunization which would not only stop M.E. and polio from occurring, but would prevent many type 1 diabetes and many deaths in millions of children world wide who die every year due to EV diarrhea and pneumonia.

Byron M. Hyde M.D.

THE NIGHTINGALE RESEARCH FOUNDATION

Precise Diagnostic Criteria for Myalgic Encephalomyelitis (M.E.)

This definition of M.E. is distinct and exclusive of the various Chronic Fatigue Syndrome definitions. It is based upon over 30 years of patient investigation and M.E. literature. This definition proposes M.E. and CFS should be considered as separate entities.

Proposal: Myalgic Encephalomyelitis (M.E.), distinct from CFS is the result of an acute and chronic Enteroviral (E.V.) post-encephalitic injury, a close genomic cousin to the three recognized polioviruses. M.E. is diagnosed by **(a)** the clinical history and at least **(b)** two reproducible scientific tests, which are: **(i)** proof of enteroviral infection & **(ii)** appropriate diagnostic brain SPECT mapping with **Segami Oasis Neurogram software**. Also these two tests are sufficient to make a diagnosis and to reduce diagnostic costs. This is unlike the CDC definition, which requires a six-month wait before a physician can diagnose CFS disease. As in any true disease, both of these tests become positive within the first week of M.E. illness. The **(a)** localization, **(b)** degree, & **(c)** variability of SPECT brain injuries accord with the patient's clinical symptoms and disability.

Contributors:

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The following are the simple and accurate diagnostic criteria for disabling M.E. and can be utilized in arriving at both a clinical diagnosis and for all scientific research papers.

1. The patient conforms to the clinical history of M.E. as described.
2. Proof of E.V. infection at onset or from gastric or GIT biopsy in chronic patients.
3. HMPAO brain SPECT (**Single-Photon Emission Computed Tomography**) demonstrating significant hypo-perfusion (up to 4 standard deviations below the normal mean) in at least the left temporal lobe and cingulate gyri employing **Segami Oasis Neurogram software** in all M.E. patients.
4. Increased M.E. disability is associated with an increased and irregular brain hypoperfusion of both cerebral hemispheres, midbrain and basal ganglia injuries. Motor difficulty is associated with hypoperfusion of the motor cortex as seen in the following typical brain map of a chronic M.E. patient. Dysautonomia in M.E. is associated with insular lobe hypoperfusion (Operculum) in all of our patients employing Segami software.
5. Multiple tests can confirm M.E. disability (eg. Keller, B cardiopulmonary exercise test). These 2 tests confirm M.E. illness itself. Depending upon degree of E.V. brain area injury, dysautonomia, & ongoing muscle weakness can occur.

The Clinical History

M.E. is a biphasic illness: The acute & chronic symptoms are identical to the onset symptoms in poliomyelitis patients as described by Wickman* in 1905, only lacking paralysis. As in polio & most enteroviral (E.V.) infections, M.E. tends to onset in late summer and autumn. As in Polio, the incubation period is usually from 3-7 days in humans, possibly depending on viral lode. M.E. is seen in both sexes and at any age, including children, but tends to be most frequently a post-pubertal illness with circa 80% occurring in females, suggesting an autoimmune role (asymptomatic carriers who then infect others may create the appearance of a longer incubation period).

First Phase, The Acute Illness: The first phase symptoms can be minor or missed, resembling (a) an upper respiratory illness, (b) a significant flu-like illness with headaches, malaise and/or gastric upset, or (c) the first evidence of disease can be the severe second-stage symptoms. Elevated temperature

might occur but normal or slightly subnormal temperatures are usual. Patients may complain of feeling feverish or having chills and sweats. M.E. is rarely taken seriously at onset & mistaken as influenza, EBV or a short term illness. It is essential for the investigating physician to order E.V. tests to make this diagnosis.

Second Phase: Chronic Illness: The severe second phase is diagnostic of the illness and in cluster and epidemic situations tends to begin anywhere from day 1 to day 10 following the initial onset phase. Physical signs tend to be limited. The symptoms of the second phase are divided into two parts:

1. Second Phase, Part One: The second phase can include the symptoms of the first phase plus:

a. Apparently inexplicable severe crippling exhaustion: The patient experiences overwhelming physical lassitude, and may appear semi-conscious and not wanting to move, often due to pain.

b. Pain: Pain may be described as either mild or severe, persisting, transitory or fleeting. There tends to be persisting malaise & migratory pain and infrequently polyarthritis. Pain may include severe headaches and retro-orbital eye pain, visible muscle spasms, chest and abdominal pain. Headaches can be severe as seen in encephalopathy. Many pain syndromes and their intensity tend to decrease over time. Narcotic use can cause persistence and addiction. Their use is cautioned. Narcotic withdrawal can cause increased pain.

c. Paresthesias: (pins & needles) in extremities often occurs, causing physicians to consider multiple sclerosis, but CNS-MRI rarely demonstrate any significant abnormalities. Lumbar puncture in first two weeks may show (a) oligoclonal banding suggesting neuronal injury, (b) increased pressure and sometimes (c) leuco-cytosis. **Dr. Charles Poser*

d. Fear: The patient often feels so ill they believe they are dying. A sense of impending doom may prevail. If the patient is sufficiently conscious, anxiety can be a common early complaint. Compassion and physician understanding help. Anti-anxiolytics, anti-depressives and increased activity are often worse than the condition.

e. Lack of Physical Signs: Unless (a) EV tests are ordered at onset or (b) EV GIT mucosa tests are examined in chronic patients or (c) appropriate brain SPECT mapping is requested, the most startling finding is the

almost total lack of significant physical signs or positive routine tests commensurate with the patient's severe symptomatic complaints & disability. Temperature increase, cervical glands, neurological signs are absent or infrequent. Inappropriate, routine lab tests tend to be negative. Due to largely negative physical findings the physician may consider the patient's illness hysterical or anxiety-based. MRI, X-Ray, CT scans and routine blood tests are poor diagnostic tools for a scientific diagnosis of M.E. but are important to exclude other major diseases.

2. Second Phase, Part Two: The severely disabling and chronic aspects of M.E. tend to be recognized once the early acute complaints become subdued or the new norm. This phase tends to manifest itself over the next two or more weeks and occurs when the patient attempts to mobilize themselves or return to normal pre-illness activity, school or work. Any return to even a reduced physical or intellectual activity can be seriously problematic. The acute disability may persist for months. Major activity at this time has infrequently resulted in deaths. The patient becomes aware of major disabling, persisting and disquieting intellectual and physical changes which can include:

Neurological Associated Symptoms: These may become permanent but are more significant in early illness.

a. Many CNS difficulties may occur: (a) short term memory impairments or dysfunctions, (b) mathematical or dyscalculia difficulties, (c) difficulty remembering written material just read, (d) anomia, (e) facial agnosia, (f) word dysfunction. Ataxia, near syncope or syncope, confusion & disorientation are common; (Bastien, S*)

b. Auditory, inner ear changes can occur frequently. Presbycusis, auditory pain, balance difficulties and the inability to appreciate music, due to acquired tone deafness may occur;

c. Particularly during the first weeks or months, visual abnormalities & distortions can occur regularly, including tunnel vision, spatial perception & distance judgment difficulties, visual agnosia, loss of night vision, colour perception, retro-optical pain, mild to severe light intolerance is frequent. Rarely, these can become permanent.

d. Persisting (a) Reynaud's-like sensory changes in the extremities, peripheral coldness (b) menopausal-like sweats can occur in both men and women, (c) the inability to maintain a normal body temperature, are all frequent findings. These neurological complaints can falsely suggest Vit B12 deficiency or M.S.

e. Inability to return to a normal physical state after minor physical activity is diagnostic. Post-activity disability can continue for days. Forced activity in our experience has resulted in death & in permanent house bound invalids. The young patient (16-60 years) describe themselves as becoming overnight, an ill 80-90- year person;

f. Major sleep dysfunctions, sleep reversals, hypersomnia and failure of restorative sleep become the norm. At onset, sleep can be associated with terrifying dreams;

g. Bladder dysfunction and interstitial cystitis commonly seen in polio and simulating bladder infection, also polyuria, interstitial cystitis and nocturia are frequent in women;

h. Tachycardia, hypotension, dysautonomia, POTS or hypertension can occur on minor activity & are often mistakenly dismissed by physicians as a result of inactivity:

For an additional list of M.E. signs & symptoms see: The Clinical & Scientific Basis of M.E. & CFS. Library of Congress 92-064489 & ISBN 0-9695662-0-4)

*For multiple and sometimes treatable causes of fibromyalgia and CFS, see: **Missed Diagnoses: Lulu.com***

Muscular Dysfunction:

a. After even minor activity, unusual persisting muscle weakness, malaise, inability to easily climb stairs without stopping occurs. A normal walking distance can cause patient days of muscle weakness and pain. Muscle spasms may occur early in illness.

b. Significant intercostal muscle pain, pleurodynia and spasm are common in the first years of illness and are often mistaken by the patient as cardiac symptoms.

Psychological Symptoms:

a. Psychological despair and reactive depression set in, particularly if the patient does not have support or **disability pension access**. The symptoms can be so severe, the fear the doctors are missing some terminal illness is a common patient sentiment. This becomes more evident when the

patient's physicians, due to unfamiliarity, are unable to find anything to explain the patient's now chronic illness and their inability to return to the normal activity expected. **Why?** The illness has been mistakenly diagnosed as a typical short-term viral infection or influenza.

b. A sense of abandonment often occurs when friends and family members begin to drift away, and physicians begin to talk of a psychological diagnoses, depression and suggest antipsychotic medications, which if taken, often make the patient worse and if abruptly stopped by the patient due to side effects or lack of funds, has provoked many suicides.

Gastroenterological, GIT Symptoms and Dysfunctions:

a. Pain, uncomfortable change of bowel habitus often occurs both at onset and in chronicity. Autoimmune bowel illnesses have been seen. **Beware:** M.E. patients may have unrelated GIT illnesses not associated with M.E. such as bowel malignancy and ulcers. The physician must be aware of more traditional illnesses.

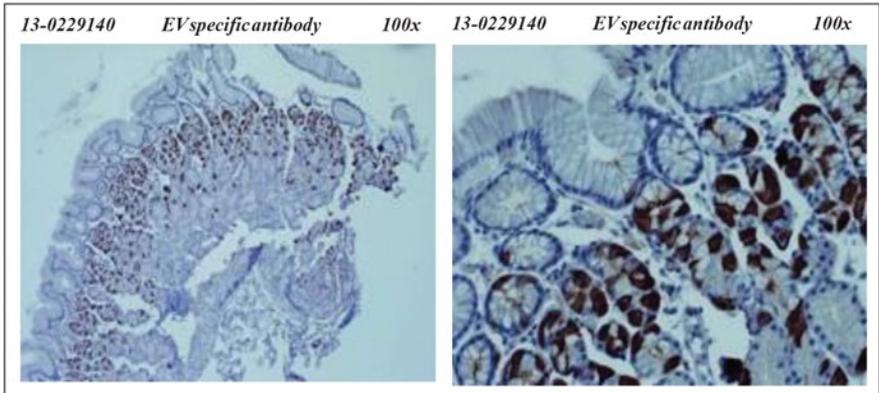
Conclusion: *Any neuropsychology or neurology resident, if given these, acute onset, post-viral neurological findings on an examination would be expected to place M.E. encephalopathy in the differential diagnosis.*

Enteroviral (EV) Testing:

General Preamble: The proof of EV infection has previously always been difficult since there are over 100 different enteroviruses and often, E.V. tests are unavailable locally. E.V. infection can be identified by many ways today, including:

1. Rising titres to specific enteroviruses at onset,
2. Mobray* and Yousef Monoclonal antibody test,
3. ELISA antibody test for enterovirus, Bell*,
4. Chia's* Gastric mucosa test,
5. Various stool tests for enterovirus.
6. PCR testing.

John Chia's test has several advantages. Since a large number of M.E. patients complain of gastric difficulties they frequently have had an endoscopy examination where mucosal biopsies are taken and kept unstained for years in paraffin blocks. These are readily obtained unstained on microscopic slides and in Canada at no cost to the patient. The presence of un-typed enterovirus can be identified from these gastric mucosa sections.

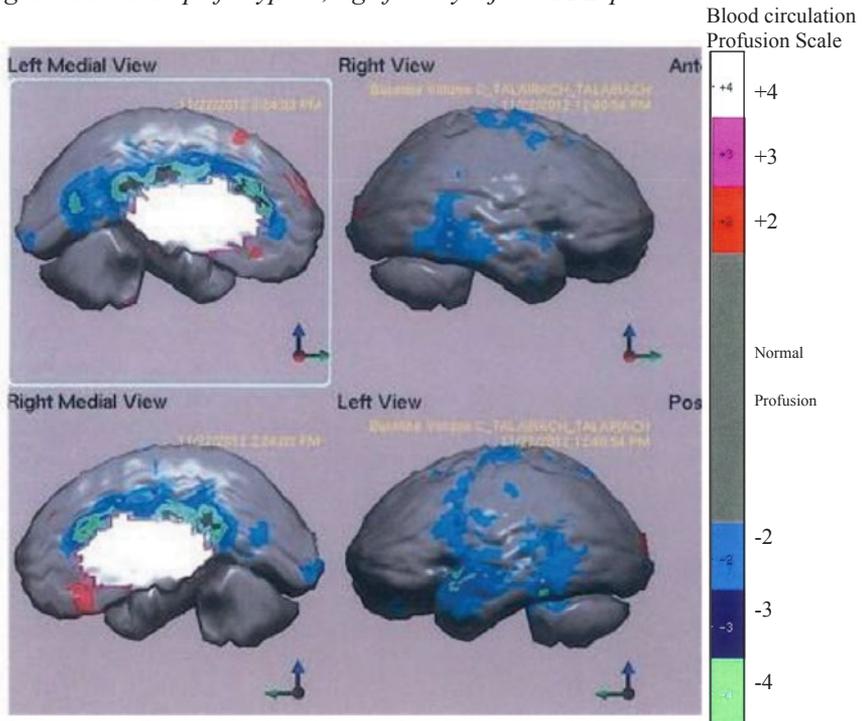


The dark speckled areas are typical microscopic images of chronic E.V. infestation of the M.E. patient's gastric mucosa supplied by Dr. John Chia.

Functional Brain Mapping with HMPAO SPECT & Segami Oasis Neurogram software

The following M.E. patient brain map is a Tc99m-HMPAO brain perfusion SPECT obtained with NeuroGam software by Dr. Sonia Neubauer, Clinica Las Condes, Santiago, Chile on a classical M.E. patient of Dr. Hyde. This OASIS software was developed by Dr. Ismael Mena & Segami Corp., USA, in comparison with age-related, healthy, drug, alcohol, tobacco, caffeine free controls.

SPECT brain scans of Canadian & USA patients were performed by Dr. Neubauer in Chile, some by Dr. Marc Freeman at Mount Sinai and Mississauga Hospitals in Toronto and Dr. Jean Leveille in Sorel Quebec and the DICOM data sent to Dr. Neubauer to obtain the 3D normal database comparison brain maps. The following is the brain map of a typical, significantly injured M.E. patient.



Note: In the 3D SPECT brain map above, colour coding documents the standard deviations of hypoperfusion below normal. The gray field is the normal perfusion within 2 standard deviations of the mean: **blue**: minus 2; **dark blue**: minus 3; **green**: minus 4 standard deviations of hypoperfusion below normal. Decreased perfusion represents progressively decreased vascularization & cognitive function. Two day, post-physical or post-intellectual activity scans show further decreased SPECT brain perfusion & associated CNS disabilities consistent with patients' complaints.

The above M.E. brain SPECT demonstrates significant 3 and 4 standard deviations hypoperfusion injury of:

- a. **the temporal lobes**, including Brodmann's areas 38 and 22, more marked on the left side, one of the brain's primary intellectual control, receiving and transmitting centres.

b. the posterior cingulate area of the limbic system, (Brodmann's area 23 and 31)

c. the damaged cingulate lobe of the limbic system, (Brodmann's area 24, 32, 33)

d. the operculum area covering the insular cortex. The Insula plays an essential role in homeostatic functions. In our experience, this area is always hypo-perfused in M.E. patients with autonomic dysfunctions (& POTS). The physician is mistaken if he believes exercise, CBT, GET or PACE theory will help insula injury patients. Nor does it help the patient to stay forever in bed due to fear. Depending upon the patient's severity of illness, a gradual, patient regulated increase in activity is necessary, both for the body and the soul.

SPECT hypoperfusion findings are variable in each patient but consistent with their symptoms. The most disabled M.E. patients demonstrated the most severe bilateral brain SPECT functional abnormalities. All patients with significant muscle dysfunction had hypoperfusion in the motor cortex, (Brodmann's 4 of the posterior frontal lobe). EV infection causing localized myositis has also been demonstrated. (Leonard C. Archard)

Severity of the M.E.

a. As in all diseases, M.E. patients differ as to severity.

b. The severity of the disease-state is in part directly related to the increasing degree & extent of bilateral involvement of the brain,

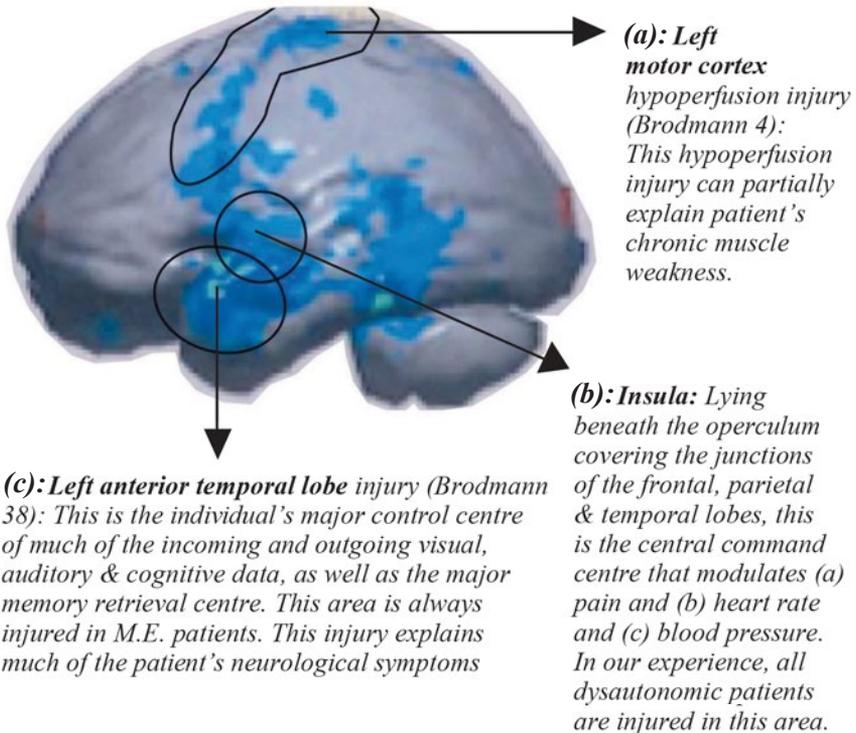
c. Patients with dysautonomia and/or POTS dysfunctions invariably demonstrated hypoperfusion in the operculum area overlying the insular cortex as in the above patient, suggesting an insular cortex injury in our dysautonomia patients.

d. Patients with pre-existing or newly-discovered (a) Ehlers-Danlos Hypermobility Syndrome, (b) Collagen diseases, and those who have fallen ill immediately (within hours or 7 days) upon receiving (c) Recombinant Hepatitis B immunization are among the most disabled patients we have seen.

e. Deaths have occurred during epidemics & infrequently in sporadic cases. These deaths are usually attributed to other brain injuries.

How to Read & Understand This Oasis Brain SPECTMap

This is a brain map of a significantly disabled M.E. patient. The degree & area of injuries explains patient symptoms.

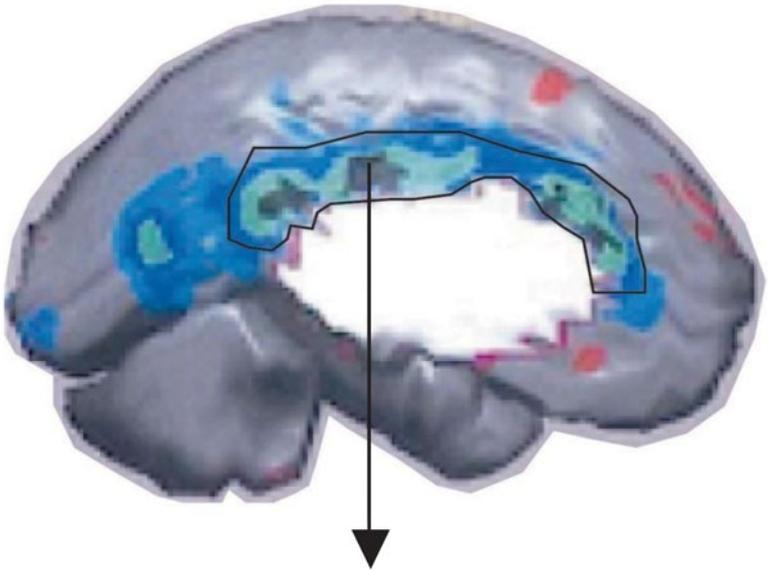


There is marked increase of hypoperfusion in several brain areas in M.E. patients 24-48 hours after significant increased physical or intellectual activity as first noted by Mena* in 1990. It can take a week or more for the brain maps to return to the usual abnormal state explaining patients' slow recovery following physical and intellectual stressors.

(d): The anterior-superior cerebellum: There is a -2 standard deviation below normal hypoperfusion. This area is responsible for balance.

In 1990, Dr. Jay Goldstein stated M.E. is a Limbic System Encephalopathy.

**Left Interior Medial View
Demonstrates Limbic Injury of the Cingulate Gyrus.**



*The severely injured & hypoperfused green and blue band represents the left cingulate gyrus of the limbic system. The posterior cingulate (to the left) is directly associated with Brodmann 38 of the anterior left temporal lobe. All data (auditory & visual information) recovered in Brodmann 38 is relayed to the left posterior cingulate to co-ordinate information with the right hemisphere and to command body functions through lower brain command centres. **This part of the limbic system is always injured in M.E. patients.** (The corpus callosum is not seen but lies immediately below the cingulate gyrus.) The white area is an artifact, where the left and right cortex & corpus callosum are technologically bisected.)*

Discussion of Physiological Changes in this Brain Perfusion SPECT

a. Anterior Temporal Lobe Injury: hypoperfusion involving the left anterior temporal pole (Brodmann 38). It is these temporal (& cingulate) lobe injuries that both define & explain many M.E. disabilities. The anterior temporal area is the major brain area responsible for retrieving & processing all intellectual & memory data, including: (a) information-gathering from memory storage banks in the cerebrum, (b) all visual & auditory information & memory transmission, learning & processing from the brain & certain external receptors, pass through this essential information center of the brain, (c) speech comprehension, naming of items, word retrieval, voice identification, (d) humour, irony, music appreciation is mediated through this and the posterior temporal region. When the left temporal lobe is injured there is a disruption of learning, data transfer and cognition. In all of our M.E. patients, the temporal lobe is always injured. Data retrieved in Brodmann 38 is processed through the posterior cingulate gyrus. **Overriding these defects is possible but severely energy-costly. It is our belief that only at great energy expenditure can the patient, for short periods, override these physiological deficits. However, this increased energy expenditure is the cause of temporary or long-term exhaustion, typical of the M.E. patient.**

b. Insular Cortex Injury: In this patient's brain map, there is hypoperfusion of the operculum, (the anterior sylvian fissure area of the temporal, frontal and parietal lobe junction). (The operculum overlies the insular cortex.) The insular lobe is a major area responsible for homeostasis and other autonomic, sympathetic and parasympathetic nervous system functions including heart and vascular regulation. This may be the CNS area largely responsible for much of the vascular and autonomic dysfunction of M.E. patients. In our experience, POTS and cardiovascular irregularity are typical findings in some significantly injured M.E. patients. They consistently have severe hypoperfusion in the operculum area.

c. The Cingulate Lobe of the Limbic System: There is significant hypoperfusion of the left posterior cingulate gyrus (Brodmann 23, 31), as well as the left anterior cingulate lobe (Brodmann area 33, 24) of the limbic system in this and all M.E. patients. However, in this patient there is also hypoperfusion in both left and right cingulate (limbic system).

The posterior cingulate is an area involving learning, memory retrieval, recall, learning complex motor skills, visual processing, emotions, consciousness, sleep and alertness functions. The posterior cingulate, in our experience, is directly related to the anterior temporal lobe (Brodmann 38) discussed above. It is believed to be an important area in regulating important cognitive data and retrieving autobiographical information. The **anterior cingulate** (Brodmann 33, 24) shares many of the same intellectual and memory tasks as the posterior cingulate but also pain endurance, visuospatial attention, multi-tasking, and auditory attention. There is generally injury in both cingulate areas.

d. Although significant hypoperfusion is always present in the left temporal and cingulate lobes of the limbic system in M.E. patients as noted by Goldstein* in 1990, in this severely disabled M.E. patient there is bilateral cingulate hypoperfusion. In addition there is hypoperfusion of the left motor cortex. (Brodmann 4)

* * *

Other Laboratory Findings Found in M.E.: The following laboratory findings give understanding to the noted first and second phase illness but are not always found. Findings can vary depending upon the time after illness when the tests were taken. The following findings are not essential in making the laboratory diagnosis of M.E. but support a disability diagnosis.

a. Lumbar puncture: Positive oligoclonal banding & increased pressure & leukocytosis in first weeks. (Poser) (Suggesting CNS neuronal injury). This requires a lumbar puncture and is rarely done since the physicians tend to mistake the initial weeks of illness as a transitory influenza-like illness. (A small gauge needle must be used due to potential increased spinal fluid pressure.)

b. SPECT: Basal ganglia hypoperfusion injuries. These findings can be seen in early & ongoing persisting chronic illness. (Mena; Hyde). Two of our M.E. patients have gone on to develop Parkinson's disease which may be co-incident, but this also occurred three years later in children, who then died as a result of the Akureyri M.E. epidemic in Iceland.

c. Neuropsychological Abnormalities: There are measurable neuropsychological abnormalities on neuropsychological studies (Bastien*).

d. Circulating Blood Volume: There is a significant decrease in circulating blood volume in most patients. (seen in SPECT blood testing.)

e. Decrease in number and activity of **Natural Killer Cells** in early weeks of illness.

f. Cardio-Vascular Exercise Dysfunction in comparing resting and post activity exercise findings. (See Keller, B. Ithica)

g. Sleep Function Studies in early years tend to be significantly abnormal with decreased or absent type 3 (previously 3 & 4).

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Major Contributors to This Presentation

L. Memeo & G. Timpanaro supplied 20 gastric mucosa specimens, 10 patients with gastric malignancy, and 10 from healthy obese patients. No evidence of EV were found in normal gastric mucosa by **J. Chia**, who also documented chronic enteroviral infection of the gastric mucosa of all 20 of Hyde's M.E. patients. Acute EV identification in these M.E. patients was also made by (i) the Gov. of Ontario, Health Services and by (ii) DN Galbraith and Carron Nain, previously of Ruchill Hospital, Glasgow. **Sonia Neubauer Grunberg and Ismael Mena:** supplied the resting and post-activity brain SPECT maps and a normal database comparison using NeuroGam Oasis (Segami Corp.) software demonstrating gross perfusion abnormalities of 2, 3 and 4 standard deviations below normal in the affected lobes. **B. Hyde** supplied: (a) History based upon 20 M.E. patients, (16 females and 4 males); (b) in-depth exhaustive family and personal histories, and laboratory, chemical, brain MRI and SPECT & vascular assessments, to rule out non-related illnesses. The neuropsychological brain map interpretations, & significance of the hypoperfusion brain injuries were correlated with neuropsychological studies & technological assistance by Drs. Bastien, S; Sweeney, J; Mariani, M; Persinger, M; & Keller, B.

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Byron M. Hyde M.D.

Byron M. Hyde MD

General Treatment Advice

In any disease or illness, all effective treatments depend upon an indisputable, reproducible scientific diagnoses. This booklet provides these criteria. This definition allows research scientists and pharmaceutical companies to research effective treatment modalities.

The various broad symptom-based CFS definitions are all non-specific and common to many chronic illnesses. There have been over 50 treatments suggested for CFS since it appeared as a working case diagnosis in 1988. The sheer number is a clear indication that there is no effective treatment for any of the various CFS diseases. Some of the many CFS diseases are treatable if the diagnostic cause is found. CFS is not a disease. It is many different and sometimes treatable diseases.

Clues to Diagnosis: (1) Proof of an enteroviral infection. (2) In the north-temperate latitudes, M.E. & enteroviral infections tend to begin in late summer and early autumn. (3) 80% of patients are women. (4) Students, teachers and health care workers are among the most common groups injured. (4) Immediate post immunization illness (within one week) can be a trigger. Immunizations decrease immune response for 1-3 weeks, particularly if they are already infected or leaving on a trip to a third world country.

Epstein Barr Virus: Unlike M.E., EBV infectious mono (glandular fever in the UK) is associated with: (i) A blood picture resembling malignancy. (ii) Throat has a putrid thick white coating. (iii) Enormous cervical glands. (iv) Often a branny chest rash. Youths usually recover in 3 to 24 months. Those in their thirties can die or have major brain injury. Late pregnancy + EBV can cause death. It is impossible to mistake EBV mono.

M.E. is a Polio Analog: Ivar Wickman described M.E. in his 1905 epidemiological study of the Stockholm polio epidemic as superior polio as opposed to spinal and bulbar polio. Paralysis and death occur in bulbar and spinal polio due to catastrophic blood vessel injuries supplying the anterior horn cells, which in turn cause permanent nerve injury to muscles. There is no muscle connection in brain neurons, only weakness occurs. If the vascular supply to the neurons is injured as in classical paralytic polio, this might be treatable.

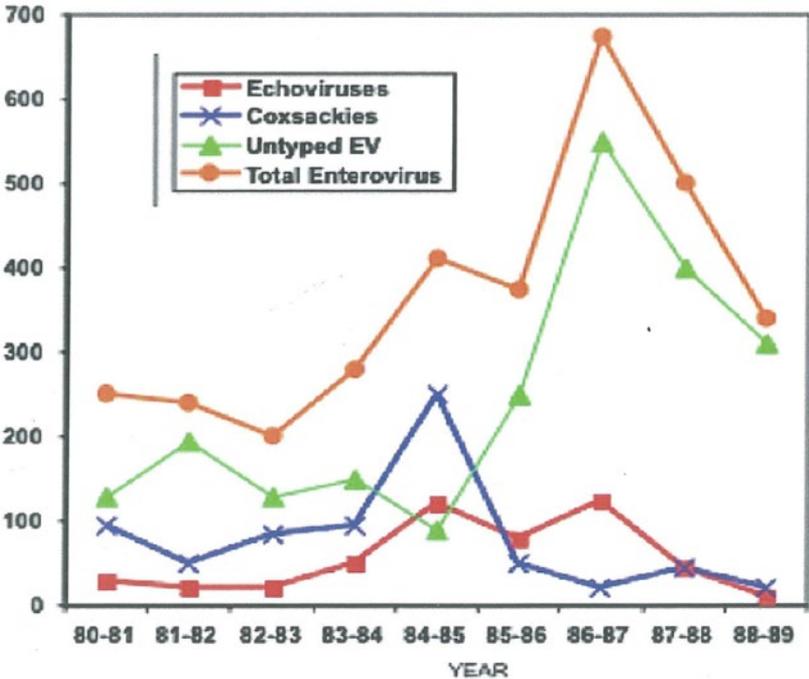
Initial Disease Severity: (1) Depending upon the degree of upper CNS injury the patient's illness varies. (2) Those with minor CNS injury tend to recover better. (3) Those with major CNS injury as indicated in the brain SPECTs tend to recover only partially or not at all. (4) Total bed rest is essential during the first two or three months. (5) Then from 3-6 months, a very slow return to modest activity, if possible. It may take years to recover reasonable functionality. Even mild injuries never fully recover all CNS facilities. Major injuries may never recover pre-illness abilities. (6) The younger the patient the better the chance of recovery. (7) M.E. is additive in patients with collagen diseases, asthma, genetic associations (Ehlers Danlos Syndrome) or other chronic illnesses. (8) Avoidance of physical and emotional stress is essential during the first year.

Specific Anti-Enterovirus Anti-Viral Medications: Because motor neurons are not destroyed, and paralysis has not occurred, the development of enterovirus-specific antivirals in the future may provide a reasonable treatment modality. As in the initial statement, several anti-EV medications are being tested in animal models.

Protect the Patient: (1) immediate short-term disability pensions if available must be provided. Stress makes M.E. illness physiologically worse and retards any recovery, if any recovery is to occur. A general, non-specific enterovirus immunization would prevent M.E.

Ontario Government Viral Services

Enteroviral Findings for the Period 1980-1990



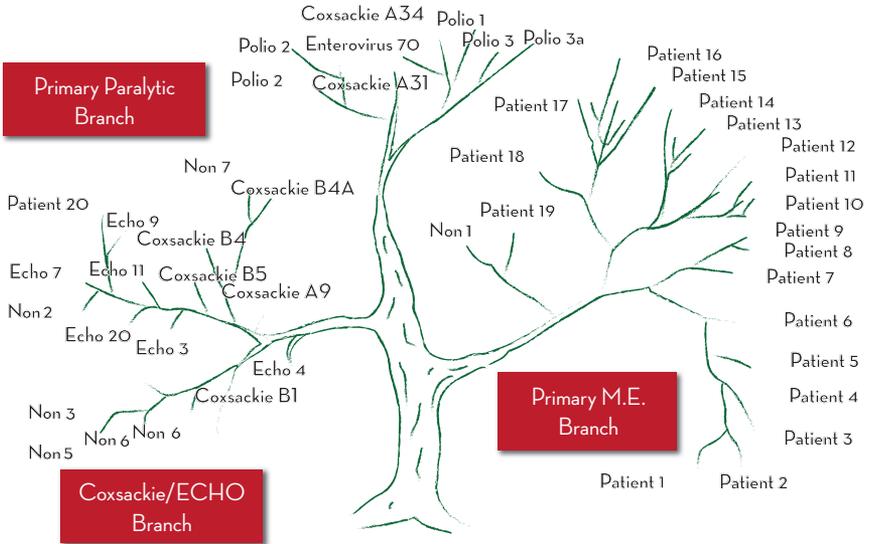
An ongoing M.E. epidemic, of chronic post-infectious disease, occurred across the USA and Canada that became apparent in the late summer and autumn of 1984 and continued on until the early 1990s. The Lake Tahoe epidemic was a typical enterovirus provoked illness that occurred in 1984.

The cause of the epidemic in Ontario was recorded by the Ontario Government Health Services as seen in the above graph. A variation of this graph was first published in the 1992 publication, *The Clinical and Scientific Basis of M.E. and CFS*. There was no increased activity of EBV-generated mononucleosis or fatigue syndrome during this period.

The Personal Computer Revolution: What became very different about this severe and disabling epidemic, was the knowledge of its presence was taken out of the hands of the American National Institute of Health, and Centers for Disease Control and Health Canada by the rise of the personal computer that allowed the disabled individuals and their families to communicate the presence of this illness to the world. These disabled individuals have not gone away. In effect, this is the chart of the continental North American M.E. epidemic that struck Lake Tahoe, North Carolina Symphony, Lyndonville NYS and the various Canadian and European M.E. epidemics. It would appear that the various North American epidemics from 1984 are all enteroviral based epidemics.

Enterovirus Family Tree

Location of majority M.E. Enterovirus positive cases are
in a newly-discovered branch of the Enteroviral tree
DN Galbraith, C Naim, GB Clements, Ruchill Hospital, Glasgow



ECHO-21 Like Enterovirus

Beginning in 1984 and extending into the 1990s, the Nightingale Research Foundation took quarterly blood samples of over 70 disabled individuals with post-infectious M.E. along with about 30 controls. My daughter and I carried these samples to the Ruchill Hospital in Glasgow Scotland, where they were examined by the virologists Drs. Daniel Galbraith and Carron Nain.

Ruchill was then the viral investigation laboratory for all of Scotland and was run by the senior virologist, the late Dr. Eleanor Bell. The above tree is consistent with the findings of the Ontario Government Health Services except where the Ontario Government was able to identify the E.Vs. in this epidemic, but not always the subtype. Ruchill was able to identify a significant number of E.V. subtypes as noted in this tree from 20 different Canadian and US patient samples.

On the basis of this study we were able to conclude that many different enteroviruses are capable of causing M.E. No other active viruses were noted.



**The Nightingale Research Foundation
Ottawa, Canada
<http://www.nightingale.ca>**

We chose the Tiger, a natural killer, as our logo because one of the first scientific benchmarks of M.E. and CFS was the fact that patients lacked active natural killer cells, an essential part of the immune system.

We chose Nightingale as our name in honour of Florence Nightingale who fell ill with an infectious disease during her service in the Crimean War. Despite her severe disability, she went on to reform both public health and health care, helping to bring medicine and especially the care and treatment of the ill patient into the Twentieth Century.

You may purchase copies of this printed M.E. definition booklet from: office@nightingale.ca (see inside front cover) or obtain it free of charge online later in 2017.

www.nightingale.ca

Nightingale depends upon and greatly appreciates your charitable donations.