Professional Guides

The Nightingale Definition of Myalgic Encephalomyelitis (ME)

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Abstract

ME is a clearly defined disease process. CFS by definition has always been a syndrome.

It essential to define clearly Myalgic Encephalomyelitis. That is what the Nightingale definition of ME sets out to do. The definition is based upon two criteria: the excellent scientific work of respected physicians and scientists who investigated the various ME epidemics; and our modern scientific testing techniques and the knowledge resulting from examining thousands of ME patients using these techniques.

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Preface

Since the Nightingale Research Foundation's publication in 1992 of its textbook, **The Clinical and Scientific Basis of Myalgic Encephalomyelitis / Chronic Fatigue Syndrome**, there has been a tendency by some individuals and organizations to assume that ME and CFS are the same illness. Over the course of two International Association of Chronic Fatigue Syndrome (IACFS, formerly the American Association of CFS) conferences, there have been suggestions that the name CFS be changed to ME, while retaining the CFS definitions as a basis for such change. This does not seem to me to be a useful initiative: it would simply add credence to the mistaken assumption that ME and CFS represent the same disease processes. They do not.

ME is a clearly defined disease process. CFS by definition has always been a syndrome.

At one of the meetings held to determine the 1994 U.S. Centers for Disease Control and Prevention (CDC) definition of CFS, in response to my question from the floor, Dr. Keiji Fukuda stated that numerous ME epidemics - he cited the Los Angeles County Hospital epidemic of 1934, the Akureyri outbreak of 1947-48 and the 1955-58 Royal Free Hospitals epidemics - were definitely not CFS epidemics. Dr. Fukuda was correct.

The Psychiatric Label

Unfortunately many physicians and some senior persons in governments, including Great Britain, Norway and to a lesser degree the USA and Canada treat CFS as a psychiatric illness. This view has been arrived by some physicians' readings of the CFS definitions from CDC. Indeed, despite clear signals in the 1994 CDC definition that CFS is not a psychiatric disease, each of the CDC definitions and their addenda referring to CFS remain open to interpretation as a psychiatric rather than a physical illness. This is not a view to which I subscribe. It is the CFS definitions themselves that give rise to this inaccuracy. Consider the following:

a) What other physical disease definitions essentially state that if you discover the patient has any physical injury or disease, then the patient does not have the illness CFS? In other words if you have CFS then it does not result in or cause any major illness. What else could CFS then be but any number of various psychiatric, social, hysterical or mendacious phenomena?

b) The various CDC administrations dealing with the subject have clearly stated that CFS is a physical, not a psychiatric disease. However, is there any other definition of any physical disease that is not provable by scientific and clinical tests? Only psychiatric diseases are not clearly verifiable by physical and technological tests.

c) What other physical disease definition requires a six month waiting period before the illness can be diagnosed? Any physician knows that to treat a disease adequately you have to be able to define the disease at its onset and treat it immediately in order to prevent chronic complications from arising. There are simply no other disease definitions that have ever been assembled similar to the CFS definitions.

d) If you are still not convinced, check the Internet for the **Diagnostic and Statistical Manual of Mental Disorder** definition of: DSMIII Somatization Disorder. You will find that there is little substantial difference to distinguish the DSMIII definition from the 1988 and 1994 CDC definitions of CFS. It is difficult to believe that the CDC medical bureaucracy is not aware of this similarity. It is thus

understandable why the insurance industry, as well as some psychiatrists and physicians, have simply concluded that CFS is somatization disorder.

I believe it essential to define clearly Myalgic Encephalomyelitis. That is what the Nightingale definition of ME sets out to do. The definition is based upon two criteria:

a) The excellent scientific work of respected physicians and scientists who investigated the various ME epidemics.

b) Our Foundation's modern scientific testing techniques and the knowledge resulting from examining thousands of ME patients using these techniques.

The proposed ME definition is designed to improve early diagnosis and treatment for the tens of thousands of patients stricken with ME It is not a new definition of CFS nor should it be conceived as a rewording of any previous CFS definition.

What follows is the primary ME definition for adults.

The Nightingale Definition of Myalgic Encephalomyelitis (ME)

Primary ME is an acute onset biphasic infectious disease process, where there is always a measurable and persistent diffuse vascular injury of the Central Nervous System in both the acute and chronic phases. Primary ME is associated with immune and other pathologies.

Primary ME is a chronic disabling, acute onset biphasic infectious disease process affecting both children and adults. There are both central and peripheral aspects to this illness.

A) The Central Nervous System (CNS) symptoms, as well as the clinical and technological abnormalities, are caused by a diffuse and measurable injury to the vascular system of the Central Nervous System. These changes in the organization of the CNS are caused by a combined infectious and immunological injury and their resulting effect on CNS metabolism and control mechanisms. Much of the variability observed in an ME patient's illness is due to the degree and extent of the CNS injury and the ability of the patient to recover from these injuries.

B) A significant number of the initial and long-term peripheral or body symptoms, as well as clinical and technological body abnormalities in the ME patient, are caused by variable changes in the peripheral and CNS vascular system. The vascular system is perhaps the largest of the body's organs and both its normal and pathological functions are in direct relationship to CNS and peripheral vascular health or injury, to CNS control mechanisms and to the difficulty of the peripheral vascular system and organs to respond to CNS neuro-endocrine and other chemical and neurological stimuli in a predictable homeostatic fashion.

C) When pain syndromes associated with ME occur, they are due to a combined injury of (i) the posterior spinal cord and / or posterior root ganglia and appendages, (ii) patho-physiological peripheral vascular changes, and (iii) CNS pain reception homeostasis mechanisms.

Depending upon the degree and extent of the ongoing CNS and peripheral vascular injuries, these patho-physiological changes in turn may give rise to both transient and in many cases permanent systemic organ changes in the patient.

As with any illness, the diagnostic criteria of ME are divided into two sections:

a) The clinical features and history of the ill patient that alert the physician to the initial diagnosis

b) The technological examinations that confirm to the physician proof of the diagnosis.

Clinical Features

The clinical features of Myalgic Encephalomyelitis are consistent with the following characteristics that can easily be documented by the physician.

1. **ME is an acute onset biphasic epidemic or endemic infectious disease:** Both Epidemic and Non-Epidemic cases are often preceded by a series of repeated minor infections in a previously well patient that would suggest either a vulnerable immune system, or an immune system subject to overwhelming stressors such as: **(a)** repetitive contact with a large number of infectious persons, **(b)** unusually long hours of exhausting physical and / or intellectual work, **(c)** physical traumas, **(d)** immediate past immunizations, **(e)** epidemic disease cases whose onset and periodicity appear to occur cyclically in a susceptible population, **(f)** the effect of travel, as in exposure to a new subset of virulent infections, or **(g)** the effects of starvation diets. (It should be noted that subsets c, d, e, f and g are all stressors associ-

ated with decreased immune adaptability **plus** an associated infection with an appropriate neurovascular infectious virus or other infectious agents. This may be due either to an immediate preexisting infectious disease or to a closely following infection, either of which may or may not be recognized.)

2. **Primary Infection Phase:** The first phase is an epidemic or endemic infectious disease generally with an incubation period of three to seven days; in most, but not all cases, an infection or infectious process is evident. (See B. Hyde and A Jain, **Clinical and Scientific Basis of ME/CFS**, Chapter 13, Nightingale Research Foundation, Ottawa, Canada, pp. 124-126)

3. **Secondary Chronic Phase:** The second and chronic phase follows closely on the first phase, usually within two to seven days; it is characterized by a measurable diffuse change in the function of the Central Nervous System. This second phase is the persisting disease that most characterizes ME

4. **The Presence or Absence of Various Pain Syndromes is highly variable:** The pain syndromes associated with the acute and chronic phases of ME may be described as **Early** and **Late** findings. **Early Findings:** (a) severe headaches of a type never previously experienced; (b) these are often associated with neck rigidity and occipital pain; (c) retro-orbital eye pain; (d) migratory muscle and arthralgia pain; (e) cutaneous hypersensitivity. **Late Findings:** (f) fibromyalgia-like pain syndromes. When occurring, these various pain syndromes may include fibromyalgia-like pain syndromes. Many of the pain features tend to decrease over time but can be activated or increased by a wide range of external and chemical stressors. (See **Clinical and Scientific Basis of ME/CFS**, Chapter 5, pp. 58-62)

Testable and Non-testable Criteria

The technological tests listed below can be used to (a) confirm the clinical diagnosis of Myalgic Encephalomyelitis and (b) to some degree gauge its severity and probability of persistence. The second and chronic phase that clearly defines ME is characterized by various measurable and clinical dysfunctions of the cortical and/or sub-cortical brain structures.

5. **Diffuse Brain Injury Observed on Brain SPECT:** If the patient's illness is not measurable using a dedicated brain SPECT scan such as a Picker 3000 or equivalent, then the patient does not have ME. For legal purposes, these changes may be confirmed by PET brain scans with appropriate software and / or QEEG. These changes can be roughly characterized as to severity and probable chronicity using the following two scales: **A:** extent of injury and **B:** degree of injury of CNS vascular function.

Extent of Injury

Type 1: One side of the cortex is involved. Those patients labeled as 1A have the best chance of recovery.

Type 2: Both sides of the cortex are involved. These patients have the least chance of spontaneous recovery.

Type 3: Both sides of the cortex, and either one or all of the following: posterior chamber organs, (the pons and cerebellum), limbic system, the sub-cortical and brainstem structures are involved. Type 3B are the most severely affected patients and the most likely to be progressive or demonstrate little or no improvement with time.

Degree of injury

Type A: Anatomical integrity is largely maintained in the Brain SPECT scan.

Type B: Anatomical integrity is not visible in the CNS SPECT scan. Type 3B are some of the most severely and chronically injured patients.

6. **Testable Neuropsychological Changes:** There are neuropsychological changes that are measurable and demonstrate short-term memory loss, cognitive dysfunctions, increased irritability, confusion, and perceptual difficulties. There is usually rapid decrease in these functions after any physical or mental activity. Neuropsychological changes must be measured in relation to estimates of prior achievement. This feature may improve over a period of years in patients with adequate financial and social support and can be made worse by chronic stressors. The neurophysiological changes are those observed by a qualified neuropsychologist with experience in examining this type of disease spectrum. (See S. Bastien in **Clinical and Scientific Basis of ME/CFS**, Chapter 51, pp. 453-460.)

7. **Testable Major Sleep Dysfunction:** This can include all forms of sleep dysfunction. All or any of the following may be present: (a) impaired sleep efficiency, (b) significant fragmented sleep architecture, (c) movement arousals if there is an associated pain syndrome, (d) absence of type 3 and 4 sleep,

(e) abnormal REM sleep pattern (f) changes in daytime alertness and (g) sleep reversals.

8. **Testable Muscle Dysfunction:** This feature may be due to vascular dysfunction or peripheral nervous or spinal dysfunction and includes both pain and rapid loss of strength of muscle function after moderate physical or mental activity. This feature tends to improve over a period of years but many patients frequently remain permanently vulnerable to new disease episodes. Few centres are equipped or funded to make these examinations.

9. **Testable Vascular Dysfunction:** This is the most obvious set of dysfunctions when looked for and is probably the cause behind a significant number of the above complaints. As noted, the primary vascular change is seen in abnormal SPECT scans and clinically most evident in patients with:

   a) **POTS:** severe postural orthostatic tachycardia syndrome. Note: This group can be confused with diabetes insipidus due to the fact that they may have polydipsia from their attempt to increase their circulating blood volume by consuming large amounts of fluids. This group can be verified by the absence of pituitary adenoma or pathology and the fact that they can sleep through the night without waking to drink fluids.

   b) **Cardiac Irregularity:** on minor positional changes or after minor physical activity, including inability of the heart to increase or decrease in speed and pump volume in response to increase or decrease in physical activity.

   c) **Raynaud's Disease:** vasoconstriction, blanching, coldness and pain of extremities. This is in part the cause for temperature dysfunctions seen in ME

   d) **Circulating Blood Volume Decrease:** this is a nuclear medicine test in which the circulating red blood cell levels can fall to below 50%, preventing adequate oxygenation to the brain, gut and muscles. This is undoubtedly a subcortical dysregulation. It is associated with serum and total blood volume measurements. Note: Body servomechanisms are genetically designed so that blood flow and oxygen to the heart are always protected. Thus blood flow to organs not necessary for short-term survival, such as the brain, the gut and muscles, can be temporarily decreased. This of course gives rise to many of the ME symptoms.

   e) **Bowel Dysfunction:** vascular dysfunction may be the most significant causal basis of the multiple bowel dysfunctions occurring in ME

   f) **Ehlers-Danlos Syndromes Group:** this is a group of illnesses with a genetic predisposition to ME or ME-like illness. In fact it probably represents a spectrum of illnesses that start with (i) Hyper-Reflexia Syndrome, moving through any of the (ii) various Ehlers-Danlos Syndromes and climaxing in (iii) Marfan Syndrome where there tends to be early death if the aortic and cardiac changes are not repaired. Ehlers-Danlos Syndromes can go undetected until what appears to be an infectious switch is turned on, usually in late teens to early thirties. Briefly, patients over the age of 16 who can (i) touch their nose with their tongue, (ii) touch their forearm with the thumb of the same extremity, (iii) touch the floor readily with the full palm should be considered suspect for further examination. See S.I. Magalini, S.C. Magalini, **Dictionary of Medical Syndromes**, pp. 251-252, Lippincott-Raven Publishers, Philadelphia, 4th Edition, 1997.

   g) **Persantine Effect in ME Patients:** Persantine is a chemical manufactured by Boehringer Ingelheim. It is employed to perform chemical cardiac stress testing when a patient cannot exercise sufficiently to stress the heart. It is a particularly safe medication but when employed with many ME patients it can cause severe muscle pain over the extremities and entire musculature. Normally this can be reversed by injection of an antidote but this does not always work in ME patients. Severe pain and fatigue can be intolerable and persist for minutes to days in some ME patients following persantine use. Persantine works by dilating both peripheral and cardiac blood vessels and causing the heart rate to increase as in a POTS patient. Obviously one major pain and fatigue factor in ME patients is caused by abnormal dilatation of peripheral blood vessels. To my knowledge, no testing of ME patients with persantine has ever been published by Boehringer Ingelheim or others. It is one of the reasons I believe that pain syndromes in ME patients are due to a pathological vascular physiology.

   h) **ME Associated Clotting Defects:** ME represents both a vasculitis and a central and peripheral change in vascular physiology. All such vascular illnesses should be potentially

treatable. We do not yet know how to treat the (i) genetic forms of vasculitis and vascular patho-physiology mentioned here, nor (ii) the probable viral triggered genetic vascular pathologies also mentioned. Nor do we know how to treat those (iii) centrally caused injuries causing the circulating blood volume defects that are demonstrated when we do the nuclear medicine circulating blood volume tests. It is important to do this test on all patients. POTS is poorly treatable and more often success in treatment presently escapes physicians' ability. Eventually, I have no doubt that these will be treatable causes of ME type disease. However there is a significant group of ME patients who are ill due to a treatable form of vasculitis and can be treated if the physician takes the time to diagnose the subgroup. These patients are the clotting defect patients. Some of these clotting defects are genetic and some appear to be genetic with an age or viral switching mechanism; although they may develop in childhood, they are more frequently noted well after puberty and before the age of 40. Many of these patients can be diagnosed by the following tests: (1) Serum viscosity test, (2) Antiphospholipid Ab., (3) Protein C defects, (4) Protein S defects, (5) Factor V Leiden defect, to name the most common that we have uncovered. However, there are others for which we also test. These conditions are all potentially treatable and when treated will allow the patient to return to normal range of activities (e.g. school, career, etc).

10. **Testable Endocrine Dysfunction:** This feature is common and tends to be a late appearance. It is most obvious in:

    a) **Pituitary-Thyroid Axis:** Changes in serum TSH, FT3, FT4, Microsomal Ab., PTH, calcium and phosphorous rarely occur until several years after illness onset. This can be followed by ultrasound of the thyroid gland, where a steady shrinking of the thyroid gland may occur in some patients with or without the development of non-serum positive Hashimoto's thyroiditis (a seeming contradiction in terms) and a significant increase in thyroid malignancy. In cases of thyroid wasting, serum positive changes tend to occur only after years and often not until the thyroid gland shrinks from the normal 13 to 21 cc. volume in an average adult female and 15 to 23 cc. volume in male patients to below a volume of 6 cc. (Mayo Clinic averages). Serum analysis of ME patients for thyroid pathology is simply not adequate. Repeat thyroid ultrasound must be performed for all ME patients to ascertain presence of dystrophic changes. It is also inadequate simply to accept the radiologist's report of a normal thyroid. The volume of each lobe and its homogenicity must be requested and documented.

The following changes, while uncommon, may also be related to an ME disease process:

b) **Pituitary-Adrenal Axis Changes:** where changes and findings are infrequent.

c) **Pituitary-Ovarian Axis Changes**

d) **Bladder Dysfunction Changes:** This dysfunction occurs frequently in the early and in chronic disease in some people. In some instances this may be due to a form of diabetes insipidus, in other cases it is related to POTS type illness where the patient is compensating for an inability to maintain vascular pressure by attempting to increase fluid volume. In other cases this may be due to interstitial cystitis or a form of polio-type-bladder particularly if the cause of the individual disease is an enterovirus. Dr. John Richardson also associated this finding with adrenal dysfunction that he measured.

Discussion

To various degrees all of the above historic findings have been observed and discussed by Doctors Alexander Gilliam, Bjorn Sigurdsson, Alberto Marinacci, Andrew Lachlan Wallis, A Melvin Ramsay (Elizabeth Dowsett who assisted in much of his later work), John Richardson, Elizabeth Bell, Alexis Shelokov, David C Poskanzer, W.H. Lyle, Sir E. Donald Acheson, Louis Leon-Sotomayor, J. Gordon Parish and many others.

In varying degrees all of the following physicians have also noted the above historical and the more recent investigational findings. They include alphabetically, Doctors Peter Behan, David Bell, Dedra Buchwald, Paul Cheney, Jay Goldstein, Seymour Grufferman, Anthony L Komaroff, Russell Lane, Ismael Mena, Harvey Moldofsky, James Mowbray, Daniel Peterson, Vance Spence and scores of others.

I have examined patients with ME since the late 1970s but only at the urging of Dr. Charles Poser of Beth Israel Hospital at Harvard and John Richardson in Newcastle-upon-Tyne did I take up the study of these unfortunate patients on a full time basis. The material in this definition is the cumulative result of my listening and interpreting the work of all of the above clinicians and my evaluation of over 3,000 ME and CFS patients since 1984. The essential concept of the indepth medical evaluation that is the basis of my work on ME and CFS since 1995 was crystallized in my discussions in Seattle Washington State in 2002 with Dr. Leonard A. Jason, Patricia A. Fennell and Renee R. Taylor. This discussion was set down as Chapter 3, "The Complexities of Diagnosis", in their book, **The Handbook of Chronic Fatigue Syndrome**, John Wiley and Sons, Hoboken, New Jersey, 2003. I would also like to thank Elizabeth Dowsett and Jane Colby whose work with children in the UK as well as their advice have been instrumental in this definition. I must also thank each and every one of the members of John Richardson's Newcastle Research Group who have provided me with so much valuable information over the years and who have all supported my continued investigations of ME patients.

What is new and different about the Nightingale ME definition?

A: A Testable Definition

The definition is set out in both a clinical diagnostic and scientifically testable fashion. This will allow the physician both an early diagnostic bedside or office understanding of the illness and a scientific and technological method to investigate and confirm the diagnosis. It is well known by all serious physicians that in order to assist the patient in a partial or full recovery the illness must be (a) prevented from occurring by either immunization or understanding and avoiding the causes, (b) diagnosed and treated immediately following onset. The Nightingale Definition assists the physician in diagnosis and early treatment.

B: A Vascular Pathophysiology

The subject of vascular pathology is not new. The fact of the children dying of a Parkinsonian-like vascular injury to the basal ganglia in Iceland during the Akureyri Epidemic is an obvious indication of the CNS vascular effects. Vasculitis has been well documented by Dr. E. Ryll in his description of the epidemic in the San Juan Mercy, Sacramento California Hospital in 1975. He described this ME epidemic as an epidemic vasculitis. In the late 1980s Drs. Jay Goldstein and Ismael Mena confirmed and proved this initial description by examining the changed brain microcirculation using brain SPECT imaging in ME patients. Following my over twenty years of examining ME and CFS patients and sixteen years of subjecting the ME and CFS patients to brain imaging techniques suggested by Goldstein and Mena, it has become obvious to me that we are dealing with both a vasculitis and a change in vascular physiology.

Numerous other physicians have supported this finding. Dr. David Bell, who rediscovered the work of Dr. David Streeten and his book, **Orthostatic Disorders of the Circulation: Mechanisms, Manifestations and Treatment**, New York: Plenum Medical, 1986, advanced this understanding of ME. The work of Dr. Vance Spence and his colleagues in Scotland have started to nail this CNS-vascular relationship down even further with a series of major research papers. The recent interpretation of the cause of Multiple Sclerosis (MS) as an injury of the microvasculization causing the injury of the schwann cells that in turn causes the demyelination injuries of MS has been added to that of paralytic poliomyelitis as an essential vascular injury. Paralytic poliomyelitis was thought to be a primary injury to the anterior horn cells of the spinal cord but is now recognized as a vasculitis injuring the circulation to the anterior horn cells. Poliomyelitis is generally a non-progressive, specific site injury, although post-polio syndrome has challenged that belief. MS is a recurrent more fulminant physiological vascular injury. ME appears to be in this same family of diseases as paralytic polio and MS. ME is definitely less fulminant than MS but more generalized. ME is less fulminant but more generalized than poliomyelitis. This relationship of ME-like illness to poliomyelitis is not new and is of course the reason that Alexander Gilliam, in his analysis of the Los Angeles County General Hospital ME epidemic in 1934, called ME atypical poliomyelitis.

C: The Lack of Mention of Fatigue

Myalgic Encephalomyelitis is not CFS. Fatigue was never a major diagnostic criterion of Myalgic Encephalomyelitis. Fatigue, loss of stamina, failure to recover rapidly following exposure to normal physical or intellectual stressors occur in most if not all progressive terminal diseases and in a very large number of chronic non-progressive or slowly progressive diseases. Fatigue and loss of stamina are simply indications that there is something wrong. They cannot be seriously measured, are generally subjective and do not assist us with the diagnosis of Myalgic Encephalomyelitis or CFS or for that matter any disease process.

D: Cause of Myalgic Encephalomyelitis

It is obvious that all cases of epidemic ME and all primary ME are secondary to infectious / autoimmune phenomena. Many ME and ME-like patients' illness

is complicated by multiple other causes. This is why a complete technological investigation has to be made on each chronically ill ME or ME-like patient. Under epidemic and primary ME there is no consensus as to the viral or infectious cause. Much of this lack of consensus may be due to the non-separation of acute onset from gradual onset patients in the ME and CFS groups of patients. Primary ME is always an acute onset illness. Doctors A. Gilliam, A. Melvin Ramsay and Elizabeth Dowsett, John Richardson of Newcastle-upon-Tyne, W.H. Lyle, Elizabeth Bell of Ruckhill Hospital, James Mowbray of St Mary's and Peter Behan all believed that the majority of primary ME patients fell ill following exposure to an enterovirus (Poliovirus, ECHO, Coxsackie and the numbered viruses are the significant viruses in this group).

I share this belief. Unfortunately, it is very difficult to recover polio and enteroviruses from live patients. Dr. James Mowbray developed a test that demonstrated enterovirus infection in many ME patients but I do not believe he qualified his patients by acute or gradual onset type of illness. In my tests in Ruckhill Hospital in Glasgow, I found confirmation of enteroviral infection only in acute onset patients and not in any gradual onset patients. Few physicians realize that almost all cases of poliovirus recovered from poliomyelitis victims came from cadavers. At the very least, these enteroviruses must be recovered from patients during their onset illness and this has rarely been done. An exception is in the case of the Newton-le-Willows Lancashire epidemic where Dr. W. H. Lyle's investigation recovered ECHO enterovirus. Recent publications by Dr. J. R. Kerr have also identified the fact that enteroviruses are one of the most likely causes of ME. If this belief is correct, many if not most of the ME illnesses could be vanquished by simply adding essential enteroviral genetic material from these enteroviruses to complement polio immunization.

I have not discussed non-infectious ME-type disease. Similar ME phenomena can occur due to diffuse Central Nervous System injuries from toxic chemical injury. I have seen this in police officers who have fallen into toxic chemical ponds in pursuit of those suspected of criminal activity. I have seen it in farmers, in hospital and industrial workers and in military personnel in contact with toxic chemicals, specifically toxic gases. I plan to explore these in a future publication as Secondary ME They do have one thing in common, and that is the diffuse CNS injury as noted on brain SPECT scans. Often these Secondary ME diseases are more severe than the Primary ME cases.

E: Caution One

One should be careful in applying the diagnostic criteria discussed under the Nightingale ME Definition without also completing a thorough investigation. ME, whether we are discussing primary or secondary forms, involves a significant diffuse injury of the Central Nervous System and an associated injury of the Immune System. This always implies the potential for secondary injuries or secondary disease or pathology caused by a dysfunctional brain and dysfunctional immune system. When the immune system is injured there is an impairment of the patient's ability to resist the development of malignancy or other important organ and systemic injuries. Due to funding limitations, we have been able to demonstrate in our work only two characteristics of this corollary injury. The first is the high incidence of thyroid cancer in ME patients. In the general public, cancer of the thyroid occurs in 1 case per 100,000. In our studies, in the case of the ME patient, thyroid cancer has an incidence of 6,000 cases per 100,000. We have already mentioned the pervasive vascular injuries. We believe that other pathological associations also occur. Failure to evaluate fully the ME patient may result in the physician missing important secondary pathology and possibly giving rise to patient death.

All ME patients as well as all chronic illness patients deserve a systematic and total body investigation. No individual should go through life, ill, disabled without knowing why he is ill. Simply offering a label, whether ME or CFS, without looking at the pathophysiology, is both unacceptable and potentially dangerous both for the patient and the patient's physician.

(See "*The Complexities of Diagnosis"* by Byron Hyde, in the **Handbook of Chronic Fatigue Syndrome**, Chapter 3)

F: Caution Two

Insurance companies regularly employ reputedly independent psychologists who demonstrate normal neuropsychological findings. This presents a grave problem in that neuropsychological testing by a truly independent neuropsychologist may be delayed for up to a year before the patient can be properly tested. The conflicting results may tend to confuse any trial judge in a legal case.

G: Depression, Anti-depressive Medications and Myalgic Encephalomyelitis

Myalgic Encephalomyelitis is not depression. Myalgic Encephalomyelitis is not hysteria. Myalgic Encephalomyelitis is not a conversion disorder nor is it a somatization disorder. Myalgic Encephalomyelitis is an acute onset diffuse injury of the brain. Psychiatrists should not ever be placed in charge of diagnosis and treatment of ME patients. It is simply not their area of expertise and

their meddling has at times caused great harm to ME patients. Also, during the 20 years that I have investigated ME patients I have yet to see a single case of real ME that has responded to psychiatric pharmacological treatment such that the patient has recovered and been able to return to work or school.

This topic is a very large subject and demands a separate publication and this is not the place for it. However I would like to note again the vascular and cardiac pathologies that one encounters in ME patients and how ME patients are often made worse by one antidepressive medication that is considered benign. One of the most common anti-depressive medications employed by psychiatrists and physicians in general for ME patients is an old pharmaceutical, Amitriptyline. Yet this medication may result in a condition referred to as Torsade de Pointes, a cardiac irregularity giving rise to resting tachycardia, QT interval prolongation and significant orthostatic hypotension. Since there is already a high frequency of these anomalies in ME patients, the use of Amitriptyline may assist sleep to some degree but may also simply worsen existing ME symptomology. I plan to return to this subject in another publication.

Definition Changes and Improvements

As with all definitions, the Nightingale Research Foundation's Definition of Myalgic Encephalomyelitis will have to be looked at by many clinicians and researchers and over the years, disagreed about, changed and improved upon. But what this definition does today is (a) separate clearly ME from CFS and (b) demonstrate that ME is an early diagnosable and provable disease - as are all true diseases, and (c) assist in the early treatment and cure of ME patients.

This Nightingale Research Foundation's Definition will be available with any updates or corrections, on the Nightingale Research Foundation's Website, www.nightingale.ca. This definition may be copied, translated, distributed by electronic or hard copy and may be included, in whole or in part in any publication without permission from the Nightingale Research Foundation or the authors, provided that this last paragraph and referral back to our website are noted.

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