

A Researcher's Review of the IOM Report: *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness*
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March 17, 2015

On February 10, 2015, the Institute of Medicine (IOM) released a report on Chronic Fatigue Syndrome (ME/CFS) entitled, *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness* (ISBN 978-0-309-31689-7). The report is significant not only because of its content but because of its source, the IOM, one of the National Academies that serve as advisers to the United States government on matters of science, engineering and medicine under the authority of Congressional Charter granted in 1863. The specific function of the IOM is to identify issues of medical care, research and education and bring them to the attention of the federal government.

Members of the IOM Committee who authored this report are to be commended for their dedication to their work. Their compilation and analysis of ME/CFS research is unparalleled. Their conclusions that ME/CFS research is inadequate, and patients are mis-diagnosed and under-diagnosed, and, in consequence, are either inappropriately treated or not treated at all, are strong arguments for change in federal policy and support. More impressive than the actual report, is the Committee's desire to be helpful to the afflicted patient population. A prestigious committee, composed of ME/CFS experts and respected scientists naïve to the controversies and difficulties surrounding the diagnosis and treatment of ME/CFS, came to consensus and the conclusion that the ME/CFS patient community is a community in dire need of new federal policy, increased research attention, and greater and more compassionate medical assistance.

The IOM report has been released in a time of heightened drama and confusion about the illness. Chronic Fatigue Syndrome (CFS), Chronic Fatigue Immune Dysfunction Syndrome (CFIDS), Myalgic encephalomyelitis (ME), Myalgic encephalopathy (ME), CFS/ME, and ME/CFS are all names previously given to a set of symptoms believed to represent the same illness and, therefore, correctly classified as a syndrome. Now, the IOM report recommends that the syndrome be renamed and called, "Systemic Exertion Intolerance Disease (SEID)." The U.S. government, which renamed the illness in 2011, has known about and attempted to advance knowledge of the illness for the past thirty years. Yet despite its efforts in research, medical education, and patient care, the etiology of the illness remains unknown, there is no effective treatment for diagnosed patients, and the majority of patients suffering from the syndrome go undiagnosed. The authors of the IOM report believe that there may be as many as 2.5 million patients suffering with this syndrome in the United States and that the majority of them have not been diagnosed. There is such a paucity of medical education regarding the syndrome that the majority of physicians in this country cannot diagnose or treat it. And the few physicians capable of treating these patients do not have any definitive therapy or medication to offer.

If ever a medical condition were in need of being brought to the attention of the federal government by dint of an IOM report, this illness, rebranded *ME/CFS* by the National Institutes of Health in 2011, ranks high. The IOM did not undertake the study of, or a report on, ME/CFS on its own volition. The IOM's study and report are contract work sponsored by, "the Office on Women's Health within the

Department of Health and Human Services (HHS), the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration, the Agency for Healthcare Research and Quality, and the Social Security Administration.” (CONTEXT FOR THIS STUDY, SUMMARY, the IOM Report, 2015) As such, *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness* is not an independent inquiry into all areas of ME/CFS endeavor, but rather a study of specific areas of the ME/CFS quagmire. The IOM was tasked to: (1) identify the evidence for various clinical diagnostic criteria for ME/CFS, (2) develop (new) diagnostic criteria for clinical use, (3) recommend whether new terminology for ME/CFS should be adopted, and (4) develop an outreach strategy for disseminating the new (ME/CFS) criteria nationwide to healthcare professionals. And no more.

In view of the IOM’s charge, the ensuing study, and the resultant report, it is imperative that both the United States Government and the public understand that the IOM’s report is a well-reasoned list of opinions and recommendations prepared for its sponsors and is not the accepted policy of the federal government or any other sector of the United States. In and of itself, the IOM report does not determine the future course of federal policy or direction for ME/CFS research, patient care, and drug development. Rather, the intent of the IOM report is to serve as impetus for further and future discussion of federal policy which would fulfill the IOM Committee’s concluding hope, “of providing a firm foundation for future improvement in diagnosis and treatment.” As Dr. Ellen Clayton, Chair of the Authoring Committee of the report has stated, the document gives, “the ME/CFS Community the ammunition it needs for a movement in the historic sense of the word.”

On the surface, the IOM Report appears to be a long-awaited gift to the ME/CFS Community. On closer inspection, elements of harm may be contained therein. The report is flawed by both what it says and what it does not say.

Flawed statements in the report include:

1. **The Committee’s recommended new name for the illness. A new name should not have been proposed and the name proposed does not satisfy its goal:** The Committee was asked to determine if a name change was warranted. The Committee was not asked to propose the new name. The recommendation to change the name of the illness to SEID (Systemic Exertion Intolerance Disease) exceeds its charge.

The Committee’s choice of words for the new name of the illness is unfortunate. The Committee made known its intentions for the name in the February 10th video accompanying the release of the report. But its intentions are not successfully executed in the name chosen for five reasons:

- (1) Inclusion of the word “disease” in the Committee’s proposed new name is not scientifically accurate for ME/CFS. Misapplication of the term “disease” in a proposed new name weakens the credibility of the illness in the minds of those who question its existence. While knowledgeable people may sympathize with the Committee’s desire to de-trivialize the name of the illness, a new name for ME/CFS needs to respect the traditions and rules of classification of illnesses into diseases and syndromes. Particularly if the

Committee decided to exceed its charge by developing a new name for the illness, it should have created a name that is both scientifically accurate as well as indicative of its severity. ME/CFS satisfies the criteria of being classified as a “syndrome” – a unique constellation of symptoms, but it does not satisfy the criteria of being classified as a “disease” because the same, specific triggering agent or event does not initiate the illness in all patients diagnosed as having it.

Medline Plus defines a disease as: an impairment of the normal state of the living animal... or one of its parts that interrupts or modifies the performance of the vital functions, is typically manifested by distinguishing signs and symptoms, and is a response to environmental factors (as malnutrition, industrial hazards, or climate), to specific infective agents (as worms, bacteria, or viruses), to inherent defects of the organism (as genetic anomalies), or to combinations of these factors. <http://www.merriam-webster.com/medlineplus/disease>

Medline Plus defines a syndrome as: a group of signs and symptoms that occur together and characterize a particular abnormality. <http://www.merriam-webster.com/medlineplus/syndrome>

- (2) A further consequence of wrongfully inserting the word “disease” into the illness’s name is the implication that the etiology of the illness is known. A known etiology suggests that further research into the etiology of ME/CFS is unnecessary. Inserting the word “disease” into the illness’s name misleads the general public as to the status of the etiology of ME/CFS and may prejudice the public and scientific community against the importance of research into the etiology of ME/CFS thereby reducing funding opportunities for such research.
- (3) The Committee’s use of the word “exertion” is also unfortunate. “Exertion” is usually understood as being limited to physical activity. The intent of the Committee’s use of the word “exertion” is made clear in its February 10th video. The Committee intended the word “exertion” to cover activity in three domains: physical, cognitive, and emotional. The Committee intended to use an inclusive term that indicated the exacerbation of symptoms in all three domains but did not do so.

WebMD, as well as *Merriam-Webster*, do not define *exertion*. *WebMD* refers those seeking a definition for *exertion* to *perceived exertion* and the *Borg Scale of Perceived Exertion with Exercise*: The “Borg Scale for Rating of Perceived Exertion: is a useful way of checking the intensity of your exercise program. The scale is also helpful when you are trying to manage a limited amount of energy to complete your daily actions.”
<http://www.webmd.com/lung/copd/borg-scale-of-perceived-exertion-with-exercise>

- (4) “Systemic” is the third poor word choice in the proposed new name for the illness. “Systemic” has two meanings in medicine. “Systemic” may refer to the entire body as in the term, “systemic infection,” which refers to an infection throughout the body. But, “systemic” may also refer to any of the body’s organ “systems,” as in an upper respiratory system infection. By using the term “systemic exertion,” one is referring, grammatically, to the body system involved in physical exertion which would be the neuromuscular system. Thus,

Systemic Exertion Intolerance Disease refers to the fatigue brought on by physical exertion or exercise, and that fatigue occurs in the neuromuscular system. Evidence that this limitation or specificity of organ system in renaming the illness was not the Committee's intent is provided in the presentation video. The Chair of the Authoring Committee, Dr. Ellen Clayton, refers to ME/CFS as being a "multi-system" illness brought on by activity in any of the three domains. Thus, a more appropriate name, based upon the Committee's intent as conveyed in the presentation video, and terminology used in the video, would be, "Multisystem Activity Intolerance Disorder" with an acronym of MAID or M-SAID.

- (5) An informal consultation among ME/CFS experts in the U.K., Australia, and New Zealand, suggests that were the United States to adopt the name Systemic Exertion Intolerance Disease, the international community would continue calling the illness ME/CFS. These experts expressed the further concern that by adopting a new name for the illness which did not contain the words "chronic fatigue syndrome," or "myalgic encephalomyelitis," indexing and retrieving the biomedical literature on the illness would become more difficult.

2. **New criteria for diagnosing the illness should not have been recommended without evidence of their validity:** Concern over implementing the proposed, new, diagnostic criteria has been articulated and published by Dr. Leonard Jason elsewhere. There is concern that the criteria may be too broad and may include patients that clearly do not have the illness. Inclusion of patients with other illnesses will have negative impact on research into the etiology of the illness and on the evaluation of, and subsequent identification of, effective treatments. In an informal consultation among ME/CFS experts in the U.K., Australia, and New Zealand, there was consensus that the adoption of the IOM's proposed diagnostic criteria would complicate the evaluation of clinical trials. The use of a new set of criteria for accepting patients into studies, when older studies have used different criteria, will make the comparison of old and new studies more difficult if not impossible.

Lacking from the report is discussion of the following topics:

1. **The proposed, new diagnostic criteria may result in an ICD code reclassification of ME/CFS from a neurological disorder to a mental disorder.** Currently, ME/CFS is classified in the ICD-10 and ICD-10-CM under code G93.3: *Other Disorders of Brain; Diseases of the Nervous System; Post viral fatigue syndrome*. The ICD-10 is the 10th revision of the International Statistical Classification of Diseases and Related Health Problems published by the World Health Organization. The ICD-10-CM (Classification Modified) is that version of the ICD-10 to be used in the United States. ICD classifications are the basis of Medicare reimbursement and are used to process nearly every medical claim in the United States. How an illness is coded in the ICD will determine the extent of medical insurance coverage for that illness, and, in effect, how that illness is treated. According to the CDC, which contributes to the decisions of

where illnesses are placed in the ICD, Chronic Fatigue Syndrome, and its synonymous names, can remain under code G93.3. However, implementing the IOM report's new set of diagnostic criteria for Chronic Fatigue Syndrome may jeopardize that classification of Chronic Fatigue Syndrome as a post-viral syndrome of the nervous system. There is nothing in the proposed set of new diagnostic criteria to suggest a neurological basis for the illness. Rather, the proposed criteria rely heavily, if not exclusively, upon the patient's report of changes in his/her activity patterns. Conceivably the proposed criteria may provoke the decision to return Chronic Fatigue Syndrome to the vague, patient complaint category of *Syndrome, fatigue, reference code 300.5, a Neurasthenia condition* which is classified as a mental disorder. Thus, while well intentioned, the IOM Committee's proposed new diagnostic criteria may well result in moving Chronic Fatigue Syndrome from a neurologically based illness to a somatoform or mental disorder. Movement of Chronic Fatigue Syndrome from a neurological coding to a mental disorder coding will impact the ability of patients to receive benefits for a real, medical condition. This would be contrary to the intent of the authors of the IOM report of convincing the healthcare community and the general public that ME/CFS is a serious and real disease. It would also be contrary to the authors' intent of having ME/CFS treated as a real, medical condition.

- 2. The preferential incidence of ME/CFS in females suggests endocrinological underpinnings of the illness that warrant investigation:** The report gives little attention to the ratio of illness expression in women and men. The report does not indicate that the cause of gender disparity found in ME/CFS is an area of insufficient research nor does it make the recommendation that research funding should be increased to investigate this gender disparity. The literature suggests that the ratio of women:men succumbing to this illness is somewhere between 3:1 to 4:1 in the adult population. And while the report mentions a variable ratio of gender disparity among female:male children (estimated between 2:1 to 6:1), there is no discussion of changes in illness incidence with the hormonal changes associated with the onset of puberty. The ability of the illness to be triggered and perpetuated preferentially in females implies endocrinological underpinnings of the illness. The triggering and perpetuating mechanisms of ME/CFS will not be completely explained or understood until the role of the endocrine system in the incidence and perpetuation of the illness is revealed.
- 3. Cluster outbreaks assumed to represent one illness:** There have been reports of multiple, cluster outbreaks of illnesses which appear to be ME/CFS. The IOM report enumerates these studies, but does not verify that these illnesses are, indeed, one illness. Given the advances in biomedical science, should there not be an epidemiological characterization of these reports sufficiently rigorous to determine whether all of the reported cluster outbreaks represent the same illness? Alternatively, what epidemiological parameters should we use to determine if these outbreaks represent different illnesses? Is the conclusion that the reported cluster outbreaks represent the same illness a premature conclusion that could/should be altered by a more careful examination of the epidemiological evidence and an application of more

contemporary or rigorous epidemiological criteria? Such studies would either support the current assumption that ME/CFS is a worldwide, highly variable illness, or provide evidence that ME/CFS is a generic category of similar illnesses.

- 4. Despite multiple triggers, varying symptoms, and varying illness duration, ME/CFS is assumed to be a single illness:** The failure to identify a unique etiology of ME/CFS despite repeated attempts, the documentation of different triggers precipitating what we choose to characterize as the same illness, and the highly variable case presentation of that illness, all suggest that we are not dealing with a single illness. Rather than being a specific illness, should the name be considered a generic term akin to the term, “cancer”? If what we call ME/CFS is, in fact, a series of related illnesses, are we impeding progress in the treatment of these illnesses, impeding our understanding their etiologies, and impeding our ability to eventually cure them, by treating them as if they were one illness? The convergence of ME/CFS and Lyme disease serves as an example: 209 patients who satisfied the International Case Definition for CFS, who exhibited clinically significant fatigue for > 6 months, and were seronegative for Lyme disease, were treated with antimicrobials pursuant to Lyme disease protocols. 62 percent of patients achieved a 50 percent improvement in clinical status while an additional 26 percent reported subjective improvement. In total, 88 percent of the patients studied improved suggesting to the author that the improved patients had seronegative Lyme disease rather than ME/CFS. [Shor, S., (2011). Retrospective Analysis of a Cohort of Internationally Case Defined Chronic Fatigue Syndrome Patients In A Lyme Endemic Area. *Bulletin of the IACFS/ME* **18(4)**:109-123.] If the author is correct, and we have difficulty in distinguishing between some Lyme disease and some ME/CFS patients, then what assurance do we have that all the patients we currently characterize as having ME/CFS actually have the identical illness? Greater precision needs to be developed for defining the illness and diagnosing the people who have it. This issue was recently aired publicly. On February 16, 2015, guest host Anthony Brooks, on National Public Radio’s “On Point” presented a broadcast entitled, “The New Science of Exhaustion,” in response to the IOM report. Dr. Daniel Neides, Medical Director of the Wellness Institute of the Cleveland Clinic stated that ME/CFS as currently characterized could very well be more than one disorder. If we are making the mistakes of characterizing multiple illnesses as one, attempting to study multiple illnesses as one, attempting to treat multiple illnesses as one, then we are impeding our understanding of these illnesses and our ability to successfully treat the individuals who suffer from these illnesses.
- 5. Bias against ME/CFS impedes patient care, and the development of new ME/CFS knowledge.** Doubt of the pathophysiological underpinnings of ME/CFS, and the false belief by many that it is a mental condition, impede patient care, drug development, and our ability to advance ME/CFS research. “Elephants in the Room,” a presentation at the NIH-sponsored, State of the Knowledge Workshop *Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) Research*, highlights some of the prejudices, who holds them, and their negative consequences on patient care, ME/CFS

knowledge, and research (http://orwh.od.nih.gov/research/me-cfs/pdfs/ORWH_SKW_Report.pdf and <http://immunedysfunction.org/images/Elephants%20in%20the%20Room%20As%20Delivered.pdf>).

Measures to discourage the continuance of ME/CFS disparities have yet to be enacted. The continuance of these disparities, without so much as an attempt at countermeasures, encourages the notion that the acts creating these disparities are acceptable. If it is the hope or expectation that the disparities will dissipate without corrective measures, history indicates otherwise. The United States government has needed to accelerate the decline of bias and discrimination by creating policies, and in some cases passing federal laws, that prohibit these offensive behaviors, and by establishing penalties for the continuance of these now banned, and in some cases now illegal, behaviors.

History shows that the DHHS has made repeated attempts to accelerate the acceptance of ME/CFS as an illness, and to accelerate ME/CFS research: In 1994, the National Institute of Allergy and Infectious Diseases announced the establishment of Chronic Fatigue Syndrome Cooperative Research Centers to foster ME/CFS research; In 1997, the DHHS established the Chronic Fatigue Syndrome Coordinating Committee (CFSCC) to advise the Department of policies which would accelerate progress on ME/CFS issues; In 2001, the Centers for Disease Control established the Train-the-Trainer Program for Chronic Fatigue Syndrome to dispense ME/CFS medical education to healthcare providers; In 2003, the DHHS established the Chronic Fatigue Syndrome Advisory Committee to advise the Department on matters which would accelerate ME/CFS research and patient care; In 2004, the Centers for Disease Control launched its Chronic Fatigue Syndrome Awareness Campaign not only to make healthcare providers aware of ME/CFS, but the general public as well; In 2012, the Centers for Disease Control launched its online, continuing medical education, Chronic Fatigue Syndrome course: *Chronic Fatigue Syndrome: The Challenges of Primary Care* in an effort to involve more physicians in the diagnosis and treatment of ME/CFS.

The information has been disseminated. The information has not been absorbed.

The IOM Report recommends that DHHS develops a toolkit for screening and diagnosing ME/CFS patients in a wide array of clinical settings. Were this recommendation to be implemented, it would be the Department's fourth dissemination of ME/CFS diagnosis information. Clearly the effort needs to be made, again. For the effort to succeed, however, something needs to be done to enhance the material's reception. Now is the time to acknowledge that ME/CFS bias exists and to act to overcome it.

Prognosis:

The IOM report contributes to our understanding of ME/CFS by virtue of its literature review, its analysis, and its opinion with, "fresh," eyes. However, as a, "for hire," work satisfying specific charges by

its sponsors, it is by necessity selective in its coverage of ME/CFS. As such, it cannot serve as an overview of all of the domains in need of consideration for the determination of the most appropriate path forward for ME/CFS research and patient care. The report was written to develop a series of recommendations to assist in the development of policies that will guide future ME/CFS research, education and patient support. The IOM report needs to be placed in the broader ME/CFS environment. Additional input regarding the historical, medical, social and research environment of ME/CFS needs to be received by the Department of Health and Human Services prior to the development of new ME/CFS policies and initiatives. That input should be provided by responsible ME/CFS researchers, clinicians, healthcare educators, patient advocacy organizations, patients, social scientists and social services organizations. Only then can the correct path forward for ME/CFS be projected.

About The Author

Kenneth J. Friedman, Ph.D. is a retired Associate Professor of Pharmacology and Physiology of the New Jersey Medical School in Newark, NJ. He is a *Master Educator* of his University and is the recipient of an *Excellence In Teaching* award from the Foundation of UMDNJ. His students awarded him two *Golden Apples* for being one of their best teachers and two *Excellence in Physiology* awards for being their best Medical Physiology teacher. He retired when the University of Medicine and Dentistry of NJ, forbade him from continuing any work related to Chronic Fatigue Syndrome in their workplace because it was “not professional.” To retain his position at the University, Dr. Friedman would have needed to perform all of his CFS work at home, at night, on weekends, and on official holidays.

At the time of his retirement, Dr. Friedman’s Chronic Fatigue Syndrome work included: (1) authoring the lead chapter and co-writing two clinical chapters of the *Consensus Manual for the Primary Care and Management of Chronic Fatigue Syndrome* (2) being an invited, trained trainer of the CDC’s Chronic Fatigue Syndrome Continuing Medical Education Course, and delivering continuing medical education courses to physicians and other healthcare professionals throughout the United States, (3) developing his own continuing medical education course for Chronic Fatigue Syndrome, approved by the American Academy of Family Physicians, and delivering that continuing medical education program when the CDC discontinued the Trained Trainer program, (4) serving a full term as a member of the Chronic Fatigue Syndrome Advisory Committee and, in that capacity, advising two U.S Secretaries of Health on matters related to Chronic Fatigue Syndrome, (5) establishing the first medical student scholarship in the United States to stimulate Chronic Fatigue Syndrome medical education at the New Jersey Medical School, (6) assisting in the establishing of medical student Chronic Fatigue Syndrome scholarship programs in two additional states modeled after the one he initially established and (7) serving as Chair of the Medical Education Committee and as a Board member of the New Jersey Chronic Fatigue Syndrome Association, as well as (8) a Board member of the Vermont Chronic Fatigue Immune Deficiency Syndrome Association.

Retirement from UMDNJ permitted Dr. Friedman to participate as an invited speaker at the National Institutes of Health’s, Chronic Fatigue Syndrome, State of Knowledge Workshop held in 2011. He served as a Board member and Treasurer of the International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (the IACFS/ME) for the maximum amount of time permitted by its Constitution. He is an author of the monograph *ME/CFS: A Primer For Clinical Practitioners*, conducted the art contest for the artwork which adorns its cover, and worked with a patient to create the monograph’s index. Originally published in 2012, Dr. Friedman participated in the *Primer’s* revision

published in 2014. Dr. Friedman currently serves as an author, and as a member of the Authoring Steering Committee of *the Pediatric and Adolescent ME/CFS Primer*, expected to be published in 2016. He continues to serve as a Board member and Chair of the Medical Education Committee of the New Jersey Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Association (NJME/CFSA). This year, Dr. Friedman is overseeing the expansion of the scholarship program to include physicians who are completing medical residencies in New Jersey. Dr. Friedman continues to serve as a Board member of ImmuneDysfunction.org. In addition, Dr. Friedman currently serves on two working groups of the Chronic Fatigue Syndrome Advisory Committee