Public Comment
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Some important quotes regarding the neurological disease myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS):

1. Name: Myalgic encephalomyelitis, a name that originated in the 1950s, is the most accurate and appropriate name because it reflects the underlying multi-system pathophysiology of the disease. ***Our panel strongly recommends that only the name 'myalgic encephalomyelitis' be used to identify patients meeting the ICC because distinctive disease entity should have one name.*** *Patients diagnosed using broader or other criteria for CFS or its hybrids (Oxford, Reeves, London, Fukuda, CCC, etc.) should be reassessed with the ICC.* ***Those who fulfill the criteria have ME; those who do not would remain in the more encompassing CFS classification****.*

2. ***Remove patients who satisfy the ICC from the broader category of CFS.*** *The purpose of diagnosis is to provide clarity. The criterial symptoms, such as the distinctive abnormal responses to exertion can differentiate ME patients from those who are depressed or have other fatiguing conditions.* ***Not only is it common sense to extricate ME patients from the assortment of conditions assembled under the CFS umbrella, it is compliant with the WHO classification rule that a disease cannot be classified under more than one rubric....***

3. Research on ME: The logical way to advance science is to select a relatively homogeneous patient set that can be studied to identify biopathological mechanisms, biomarkers and disease process specific to that patient set, as well as comparing it to other patient sets.... Research on other fatiguing illnesses, such as cancer and multiple sclerosis (MS), is done on patients who have those diseases. ***There is a current, urgent need for ME research using patients who actually have ME.*** [Emphasis added]

– Myalgic Encephalomyelitis – Adult & Paediatric: International Consensus Primer for Medical Practitioners (Carruthers, 2012)

I felt for some time, Keiji, that those who have CFS are at a certain point along a continuum of illness in which fatigue is either the most dominant symptom or the most clearly articulated by virtue of impressions on the part of the patient or physician that such a complaint is important. ***I predict that fatigue itself will remain the subject of considerable interest, but the notion of a discrete form of fatiguing illness will evaporate****. We would, then, be left with Chronic Fatigue that can be distinguished as Idiopathic or Secondary to an identifiable medical or psychiatric disorder.* ***I consider this a desirable outcome.*** [Emphasis added]

– NIH official Stephen Straus in an undated letter to CDC epidemiologist Keiji Fukuda before the 1994 Fukuda et al. redefinition of chronic fatigue syndrome (Straus, undated)

We propose a conceptual framework to guide the development of studies relevant to the chronic fatigue syndrome. In this framework, in which the ***chronic fatigue syndrome is considered a subset of prolonged fatigue*** *(>1 month), epidemiologic studies of populations defined by prolonged or chronic fatigue can be used to search for illness patterns consistent with the chronic fatigue syndrome.*

Prolonged fatigue is defined as self-reported, persistent fatigue *lasting 1 month or longer. Chronic fatigue is defined as self-reported persistent or relapsing fatigue lasting 6 or more consecutive months.*

Diagnosis of the chronic fatigue syndrome can be made only after alternative medical and psychiatric causes of chronic fatiguing illness have been excluded*. No pathognomonic signs or diagnostic tests for this condition have been validated in scientific studies; moreover, no definitive treatments for it exist.*

[N]one of the provisions in these guidelines*, especially the definition of idiopathic chronic fatigue and subgroups of the chronic fatigue syndrome,* ***establish new clinical entities.*** *Rather, these definitions were designed to facilitate comparative studies.* [Emphasis added]

– Fukuda K, Straus SE, Hickie I et al. Chronic fatigue syndrome: a comprehensive approach to its definition and study. (Fukuda, 1994)

Fatigue is a totally undefinable concept. Fatigue is impossible to measure or quantify. Fatigue is so non-specific that it can be a common element in any acute or chronic disease and many psychiatric diseases. Worse, it redirects the medical and public attention to the totally undefinable fatigue and away from the obvious Central Nervous System changes in these patients. Much worse, it makes fun of a serious illness since most people and most physicians tend to equate fatigue with laziness, work avoidance, something that a bit of effort will chase away. It has turned out to be a damning indictment to all M.E. patients.

– Dr. Byron Hyde in a 2006 speech delivered in London

The recent Stanford brain imaging study (Zeineh, 2014), which found profound brain abnormalities in CFS-labelled subjects, is consistent with the neurological disease myalgic encephalomyelitis (ME) and shows the problem with the continued use the 1994 Fukuda "International" CFS case definition (Fukuda, 1994) to select research subjects for biomedical research. When the Fukuda CFS definition is used, results can only be applied to an undetermined subset of CFS patients which is never delineated.

The ME IC Primer (Carruthers, 2012), on the other hand, already lists brain abnormalities similar to those found in the Stanford study – white matter abnormalities and reduced regional gray and white matter volume – as associated with the neurological disease ME. ME is a well-described disease entity based on the documented, clinical observation by highly qualified medical doctors

of thousands of actual patients with the disease. CFS, as it is currently case defined, is based on a political negotiation made between US Department of Health and Human Services (HHS) bureaucrats and medically unqualified UK psychiatrists in 1994. CFS corresponds to no single clinical entity ever observed in actual patients. In addition to chronic fatigue, the 1988 Holmes definition of CFS required 8 of 11 listed symptoms. The 1991 Oxford definition of CFS required no symptoms other than chronic fatigue. The CDC-assembled 1994 CFS definitional committee diplomatically split the difference and arbitrarily required any 4 of 8 listed self-reported and sketchily described symptoms for a case of CFS.

The Fukuda case definition of CFS is a research concept that is an abstraction. No extensive clinical observation of actual patients was considered. The definition was allegedly only intended as a theoretical framework to assemble research subjects who MIGHT have an identifiable disease. Inexplicably, this abstract research concept was turned verbatim into CFS diagnostic criteria that can still be found in the CDC's "CFS Toolkit" of diagnostic and treatment guidelines today, 20 years later. In other words, **doctors are presently diagnosing and treating a research abstraction called CFS, rather than any actual disease – or even any related group of diseases – found in nature.**

The "encephalomyelitis" part of the term ME means inflammation of the brain and spinal chord. Brain inflammation was recently confirmed in ME patients selected using the International Consensus Criteria for ME. (Nakatomi, 2014; Carruthers, 2011) The name ME and its classic descriptions are consistent with the Stanford brain study findings. Dr. E. Donald Acheson in 1959 reviewing 14 outbreaks of infectious disease, by then named myalgic encephalomyelitis, involving thousands of patients stated:

"All the outbreaks shared the following characteristics: (1) headache; (2) myalgia; (3) paresis [muscle weakness, partial paralysis]; (4) symptoms or signs other than paresis suggestive of ***damage to the brain, spinal cord or peripheral nerves****; (5) mental symptoms; (6) low or absent fever in most cases; (7) no mortality."* [Emphasis added] (Acheson, 1959)

The common symptom of fatigue is not even mentioned in classic descriptions of ME – not because ME patients did not experience and report fatigue, but because fatigue is such a commonly reported symptom that it is not useful for making differential medical diagnoses. The ME International Consensus Criteria and IC Primer do not even list self-reported chronic fatigue, or any type of fatigue, as a symptom of ME. **Responses to standard fatigue questionnaires are, therefore, of no use for diagnosing ME, or for measuring its severity or improvement.** Nevertheless, the concepts of CFS, ME/CFS, and CFS/ME are all based on self-reported fatigue which is only "measurable" by questionnaires – the "instruments" of social science.

Many patients and media reports viewed the Stanford brain study as vindication that CFS is "real." However, by the currently used Fukuda definition and CDC logic, CFS can never be "real." The fatigue must be "unexplained" and "self-reported." The findings of the Stanford brain study are likely to be found as "exclusionary" for CFS by the dogmatic US Centers for Disease Control (CDC) – as they have found all similar physical findings in CFS-labelled research subjects for the past 26 years.

How could brain-scan abnormalities ever be a "biomarker" for the diverse group of patients assembled under the umbrella term CFS? None of the poorly described symptoms that might indicate some neurological involvement – "impaired memory or concentration," "headache of a new type or severity" and "unrefreshing sleep" – in the current "CFS Toolkit" is required for a CFS diagnosis. Abnormal brain scans could never be a biomarker for CFS because an unknown portion of CFS-diagnosed patients is likely to have no physical brain abnormalities, whatsoever. **If the Stanford subjects had been evaluated for ME using the ICC, which require at least one symptom indicating neurological impairment, the results could be applied to a specific patient group – the group with the neurological disease ME**. Instead, biomedical research using nonspecific CFS-labelled subjects will keep going around in circles as it always has done and always will do.

The fatigue experienced by ME patients is no more "unexplained" than the fatigue experienced by cancer and MS patients. Because the fatigue experienced by ME patients is a bioalarm indicating an underlying disease process and not "unexplained," no patient with ME, strictly speaking, can meet the Fukuda case definition of CFS. The impossibility of a single patient simultaneously meeting both the ICC-ME and Fukuda-CFS case definitions makes the CFS-hybrid terms "ME/CFS" and "CFS/ME" ambiguous and nonsensical.

The CDC has consistently denied any neurological involvement in their conception of CFS. After a quarter century of CFS research, there is still no symptom suggesting any neurological disease or, indeed, the presence of any specific disease, required for a CFS diagnosis or for use as a CFS research subject. **The problem is bad faith at the CDC and the rest of the Department of Health and Human Services – not the lack of scientific evidence.**

If the CDC, NIH, psychologists, and psychiatrists wish to continue their research of the subjective symptom of chronic fatigue or their search for a distinct chronic fatigue syndrome and its elusive subgroups, they should not do so at the expense of patients with the distinct neurological disease myalgic encephalomyelitis. It is unethical and hypocritical of the CDC and the rest of HHS to keep ME hidden within a hypothetical chronic fatigue syndrome. **There is an urgent need for ME, as defined by the ICC, to be officially listed as exclusionary for a CFS diagnosis or for use as a CFS research subject.** Just as the presence of CFS subjects without ME confounds ME research, the presence of ME subjects without CFS confounds CFS research. If the CDC is sincere in wishing to research CFS, they should immediately announce that subjects with ME – just as subjects with other fatiguing diseases such as cancer and MS – should be excluded from use as CFS-labelled research subjects.

Copies of the ME IC Primer must be distributed to doctors so they can recognize and rule out ME before making a CFS diagnosis. Doctors must also be educated that in the new US ICD-10-CM, official October 2015, ME is coded for billing and reporting purposes as G93.3 as a neurological disease. **CFS and unspecified chronic fatigue are coded *together* as R53.82 as general symptoms.**

HHS could actually make itself useful by distributing the ME IC Primer to doctors and medical personnel and informing them how to use the new ICD-10-CM codes. Instead, HHS has chosen to engage in expensive boondoggles such as the unneeded, million-dollar HHS/IOM redefinition

of "ME/CFS" or the useless, farcical NIH P2P "ME/CFS" Workshop. Both of these HHS initiatives are set up and stage managed so that they can only cause more confusion, more harm to patient care, and more confounding of research.

References:

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