

## ICD-11 proposal submitted by Dr Tarun Dua

Submitted November 06, 2017    Processed November 19, 2018

NB: On November 06, 2017, a proposal for significant changes to the ICD-11 concept term, *Postviral fatigue syndrome*, was submitted to the Beta Proposal Mechanism by Dr Tarun Dua.

Dr Dua is a medical officer working on the *Program for Neurological Diseases and Neuroscience, Management of Mental and Brain Disorders, Department of Mental Health and Substance Abuse, World Health Organization*.

Dr Dua was not a member of the ICD-11 *Joint Task Force* but served as lead WHO Secretariat for ICD-11's *Topic Advisory Group (TAG) for Neurology*.

As *TAG Neurology* had ceased operations in October 2016, it was initially unclear whose proposal this represented. Dr Dua later clarified that this proposal had been submitted “*on behalf of Topic Advisory Group (TAG) on Diseases of the Nervous System, and reiterates the TAG’s earlier conclusions.*”

Proposal Mechanism, ICD-11 Beta draft (now Maintenance Platform):

<https://icd.who.int/dev11/proposals/l-m/en#/http://id.who.int/icd/entity/569175314?readOnly=true&action=DeleteEntityProposal&stableProposalGroupId=303c7493-554a-44c8-8e00-bd0c6c4cc6ef>

### Proposal for Deletion of the Entity

#### Postviral fatigue syndrome

##### Rationale

##### Chronic Fatigue Syndrome Proposal

This proposal recommends to remove Myalgic encephalitis/Chronic Fatigue Syndrome (ME/CFS) from the nervous system diseases chapter. The rationale for the proposal is lack of evidence regarding any neurological etiopathogenesis of chronic fatigue syndrome. We suggest that ME/CFS be classified in the Signs and Symptoms Block of the ICD-11 as a child of Symptoms, signs or clinical findings of the musculoskeletal system. The classification in this position according to symptom patterns and severity would be consistent with existing evidence: the syndrome consists of a multitude of symptoms, has an ill-defined pathophysiological etiology, and is a diagnosis of exclusion requiring medical evaluation [1]. When there is sufficient evidence and understanding of the pathophysiological mechanisms, diagnostic biomarkers, and specific treatments, the syndrome can be appropriately classified within the proper block.

##### ME/CFS is a Syndrome of a Constellation of Symptoms and Signs

The predominant symptom of those with ME/CFS present is severe fatigue, a manifestation of skeletal muscle dysfunction. In addition, these patients may report pain, cognitive symptoms, myalgia, impaired memory or concentration, gastrointestinal problems, headaches, and arthralgia. Less commonly, individuals report dizziness, nausea, anorexia, and night sweats. Signs include tender lymph nodes and a sore throat [2].

Epidemiological and Pathophysiological evidence is limited, conflicting, and does not support ME/CFS as a disease of the nervous system or with a principally neurobiological underpinning

The underlying pathophysiological basis of ME/CFS remains unclear. This is in part due to methodological limitations in epidemiological studies given variability in case definitions [1, 3-5].

Prevalence and incidence of ME/CFS varies greatly across age, gender, ethnicity, socioeconomic strata and country, without clear explanation of the differences [6-12].

Much of the study to date on biological mechanisms has been focused on the central nervous system and immune systems with conflicting results [2]. Very limited evidence points to the nervous system as the site of pathology[13], with no clear patterns of CNS involvement [14-17].

Though serotonergic and cortisol responses have been abnormal, no consistent alterations in the function of the hypothalamo-pituitary-adrenal axis, stress hormone pathways, or immune system have been identified among those with ME/CFS [18-20]. Further, research examining metabolic, sleep or psychological models of the disease is also inconclusive. The etiology and pathogenesis of CFS are hypothesized to be multi-systemic, multifactorial and require predisposing (genetic, lifestyle), precipitating (infection, psychological stress) and perpetuating factors (psychosocial processes)[2]. For example, it has been demonstrated that a stereotyped syndrome of disabling fatigue, musculoskeletal pain, neurocognitive symptoms, and mood disturbance occurred after viral infection by infection with Epstein-Barr virus (glandular fever), *Coxiella burnetii* (Q fever) and Ross River virus (epidemic polyarthritis)[21].

Given the persistent lack of an understanding of etiology of ME/CFS, a European database has been established to examine biomarker research for clinical use; the ME/CFS EUROMENE database has confirmed the presence of heterogeneous evidence regarding neurological, immune and metabolic markers that vary by gender, and hypothesize a multifactorial syndrome with environmental and immunological factors as the biological basis of ME/CFS [22].

The definitions and classification of ME/CFS emphasize the need for a systems-based approach.

There are at least 20 case definitions of ME/CFS, and no systematic evidence was present that any definition “specifically identified patients with a neuroimmunological condition” [1]. Definitions including CDC 1994-Fukuda [23], ME-International Consensus Criteria (ME-ICC)[24], and the 2015 Institute of Medicine report on ME/CFS proposing the new name of systemic exertion intolerance disease (SEID) [3-5], further highlight that there is a changing understanding of the nature and cause of the illness. These changing definitions and classifications further reflect the need for a systemic characterization of the illness while recognizing the impact on multiple organ systems, and that varying types of exertion (emotional, cognitive, or physical), are characteristics of the syndrome. There are thirteen synonyms in the Foundation layer; only reinforce the opinion that this is a very imprecise disorder. It is interesting to note that Akureyri (mentioned twice) is a city in Iceland and again to mention Iceland disease and Icelandic disease! All this has to be cleaned and taken out in the new position of CFS. The body site is NOT entire brain and a virus does NOT cause it.

The treatment of ME/CFS centers around graduated exercise and psychologically based treatments.

It is also important to recognize that diagnosis and appropriate referral for treatment are established and accessible in a variety of settings (such as primary care, emergency departments, mental and behavioral health clinics, medical subspecialties (infectious diseases, cardiology, and rheumatology as well as pediatrics) [25, 26]. The most robust evidence of symptomatic treatment with observed functional benefits is limited to Cognitive behavioral therapy and graded exercise [27-31].

ME/CFS is thus not a disease of the nervous system. It should be categorized in the Signs and Symptoms chapter given the lack of clear evidence pointing to the etiology and pathophysiology of this syndrome until evidence to organ placement is clarified in years to come.

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