January 16, 2015

PUBLIC COMMENT OF Anonymous #11
Re: Pathways to Prevention Draft Report – Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (CFS) Draft Report (P2P Draft ME/CFS Report)

Dear Panel:

I work in the environmental and energy public policy arena and come into research in this are following years of investigating illness patterns relating to environmental toxic exposure. I am also the author of the first peer-reviewed journal study analyzing application of the Americans With Disabilities Act.

The P2P Draft ME/CFS Report makes many important points and I strongly applaud most of the recommendations. I also endorse the Comments of the CFSAC.

In the interest of brevity, I will focus narrowly on four points I believe should be clarified or strengthened to broadly serve the interests of public health and resource efficiency.

(1) ADVOCATE IDENTIFICATION OF BELIEVED TRIGGERS

Most critically, from a public health standpoint, the believed trigger of the illness in acute onset cases should *always* be identified. This is an imperative for flagging emerging epidemic outbreaks caused by specific pathogens. Prospective studies would also be enabled by trigger tracking. (The current outbreak of enterovirus-D68 among hundreds of children throughout the U.S. is one example of a potential pediatric research case cohort.)

The P2P Draft report recommends creation of a registry. I would argue that public health considerations *mandate* creation of a registry that – at a minimum – identifies the geographic residence and occupational exposure history of the patient. This is crucial for identification of toxic environmental exposures.

While etiological investigations have focused predominantly on viral and other pathogenic infections, toxins have also been identified as triggers. (Toxic insult is notably implicated in Gulf War Illness, a condition strikingly similar to – and arguably a variant of – ME.) Pathophysiology likely varies because of (a) the nature of the initial triggering agent, (b) population heterogeneity, and (c) the number, dynamics and ambit of the cascade of dysfunctional neurological, immune, endocrine, autonomic, cardiovascular, and gastrointestinal cycles involved.

Substantial evidence supports the view that this condition can be conceptualized as a multisystem spectrum disorder that results from a dysfunctional reaction to immune assault. In

other words, it is not a specific agent that causes the disease, but a maladaptive host *response* which initiates a series of cascading and interacting cycles. Whether or not this is the case, identification of triggers – especially when added to a more precise elucidation of pathophysiology – would contribute valuable data to the field.

(2) ADVOCATE CHANGE OF NAME TO ME

One can only surmise what the state of the science on Parkinson's would look like had the illness been termed "Chronic Lassitude Disorder."

Nomenclature unduly focusing on the single symptom of fatigue is a prime misdirection.

Consider the following two theoretical patients:

One is a long sedentary 60 year old who reports gradually developing chronic problems with concentration, tension headaches, tender lymph nodes, and joint pain; with all of the symptoms being fairly moderate and consistent.

The other is a highly active athletic 24 year old graduate student in robust health who is suddenly stricken – following a flu-like virus – with over a dozen never before experienced debilitating symptoms, including: a prolonged sense of energy loss following physical and/or cognitive exertion (PEM); severe sleep disturbance; rapid muscular fatigability and muscle pain while exercising; a drastic reduction in the ability to multi-task; difficulty with word retrieval; dyslexia; photophobia; IBS; hypersensitivity to chemicals; loss of adaptability to changes in ambient temperature; orthostatic intolerance; heart palpitations; and Reynaud's Syndrome. The symptoms are wildly fluctuant. Some are severe. Every time the symptoms abate, he eagerly returns to his prior busy schedule. Yet virtually every time he pushes himself beyond his subjective sense of capability, the young man becomes utterly depleted. The experience is something he can only describe using the term "crashing." The student's level of activity and productivity is reduced dramatically to about 30% of his pre-illness onset level.

As things now stand, both of these patients are lumped together in the same purportedly "well defined" research cohort so long as they both have concurrent fatigue.

From a research guidance perspective, this is absurd. Yet it is the outdated CDC case definition (combined with grossly inadequate funding) which has perpetuated the errant narrow focus upon fatigue.

The name change to ME is a long needed improvement. However a name change without a corresponding delineation of the full spectrum and pattern of this complex multisymptom disorder will be of limited value.

(3) THE CARRUTHERS CRITERIA SHOULD BE INCORPORATED AND PROMULGATED

Excellent preliminary guidance for mapping out a full and detailed picture of the disorder is set forth in the International Consensus Criteria (Carruthers, 2011) and the Canadian Consensus Working Case Definition (Carruthers, 2003).

Many experts and patient groups have heralded the Carruthers paradigms as well describing the experience of ME. Publicizing and utilizing the Carruthers criteria can greatly facilitate elucidation of the syndrome and help clarify whether ME should be viewed as a subset of a spectrum disorder or as a distinct condition.

The Carruthers paradigms further provide an organizational framework precise enough to describe a distinct illness, yet having a perspective broad enough to view the different variants.

Notably, many of the symptoms identified by Carruthers and repeatedly identified in the literature remain very poorly delineated. These broadly include autonomic, cardiovascular, endocrine, neurological and cognitive irregularities.

A more specific list would include: post-exertional exhaustion; severe sleep dysfunction; fluctuant working memory and visuo-spatial deficits; word retrieval aphasia; dyslexia; handwriting problems; pronounced clumsiness; slowed information processing; inability to multitask or maintain task focus when subjected to external stimuli; chronic pharyngitis; susceptibility to infection; chemical hypersensitivity; sensory dysfunction (including vision problems); sensory overload susceptibility; muscle and joint pain; muscle weakness and susceptibility to injury; heart palpitation episodes; cerebral hypoperfusion; Raynaud's syndrome; migraines or tension headaches; psychomotor problems; orthostatic abnormalities; drastically reduced ability to tolerate heat …. the list could go on.

(4) BETTER EDUCATION OF THE PUBLIC AND MEDICAL COMMUNITY IS AN IMPERATIVE - AND IT MAY ENABLE ARREST OF THE DISEASE AT AN EARLY STAGE

The strongest weapon in the arsenal of the NIH is education.

The NIH must use its available powers to provide quality information about ME to health care professionals. There is no question that many health care providers remain uninformed about the underlying condition. Advancement in diagnosis and treatment will continue to be impeded as long as front line physicians, the public and the media remain in the dark.

Better recognition of the illness in its complex form will also drastically reduce the cost and suffering burden of patients who are now kicked from specialist to specialist, overtested and improperly medicated for other conditions. For individuals who experience sudden onset following a flu-like infection and then demonstrate the extensive highly-eccentric symptom

clusters well described by Carruthers, diagnosis could be readily made by any knowledgeable physician.

From a public health point of view, this raises the possibility of arresting – and even reversing – the disease process at the prodromal stage, when fewer symptoms may be present. Again, this mandates substantially improved recognition on the part of medical professionals of the precipitating factors and red flag symptoms at the very early stage of the disorder, before the full cascade of dysfunction cycles has erupted. Aggressive early intervention is a low hanging fruit, and may involve something as simple as pharmaceutical support to alleviate sleep disruption and strong guidance on pacing.

The idea of children, adolescents and young adults being effectively sentenced to a lifelong illness that might be avoided simply by more informed pediatricians and internists who provide good counsel seems particularly compelling.

CONCLUSION

ME is a fascinating illness. NIH emphasis on the multisystemic and dysfunctional cascade aspects of the disease should encourage the much needed interdisciplinary approach. It should also attract researchers in emerging disciplines such as symptoms biology (complex interactions and network theory); symptomatology (identifying symptom links and aggregates); epigenetics (investigating gene expression caused by mechanisms rather than DNA); psychoneuroimmunology (focusing on mechanisms underlying brain-to-immune crosstalk); and other emerging fields.

Thank you for your most kind and patient attention.

These comments represent my personal opinion, and do not represent any position held by any organization with which I am affiliated.

Sincerely,

(New York)