

Public Comment
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This is a very hopeful time in the history of Myalgic Encephalomyelitis and the mis-named Chronic Fatigue Syndrome. I will call this disease ME/CFS, for lack of a better term. Despite many obstacles, we have come a long way in the past few years, and the way forward is beginning to become clearer. **We now have most of what we need to make significant and rapid progress.** We have a workable definition. Thanks to researchers at the Pacific Fatigue Laboratory and the University of Utah, we have two measures of the most characteristic and disabling symptom, post-exertional malaise and exhaustion. We have information about several treatments that are not only effective in at least some patients, but also help to clarify the etiology or etiologies of the disease. Rituximab and antivirals as well as less well-studied but effective treatments have changed the game. We can begin to imagine a future very different from our past, a future where patients will be quickly diagnosed and presented with a choice of therapies based on solid evidence of efficacy.

What is holding us back from this brighter future? **What we are lacking is support from the scientific and medical communities and from our government.** We need to change our current reality. In order to do this we must step back from gazing at our bright future and re-enter the darkness of our past. We need to examine the scientific and medical arms of our government and challenge them to make necessary changes based on the information that is now available.

What is our current reality and what could be our future? It is best to examine our current obstacles agency by agency, acknowledge the past reality and look for a way forward.

CDC

The CDC has created two definitions for this disease which effectively make it impossible to study. The empiric (2005) definition has been shown to be so flawed that even the CDC appears to have abandoned it, although they are still spending scarce research dollars to try to justify it. Briefly, that definition is overly broad; it includes many people who do not have ME/CFS, so any research is unlikely to come up with significant conclusions about people who do have ME/CFS. The more commonly used Fukuda (1994) definition also has at least two significant flaws: it does not make the cardinal symptom, post-exertional malaise, mandatory for the diagnosis, and it requires patients to be sick for at least six months before diagnosis. This is like an insurance company sending an adjustor to the scene of an accident six months after the accident occurred. There will be no evidence that the accident occurred, so it will be easy to deny coverage for an accident that never occurred. Because of the Fukuda definition it is unlikely that a single pathogen, if it exists, will ever be found. It is also unlikely that a toxic cause for an immune deficiency could ever be found, because a toxin will likely disburse in six months. The Canadian Consensus definition and the International Consensus definition are both acceptable definitions. **The empiric and Fukuda definitions are not acceptable definitions.**

The CDC has recently arranged a series of phone conversations with advocates. One of the stated goals of these conversations was to increase a sense of trust between the CDC and the

patient community. There are many reasons that patients do not trust the CDC, not the least of which is their failure to adequately investigate past outbreaks. If the CDC continues to use the empiric or the Fukuda definitions it is highly unlikely that any outbreaks will be reported or investigated. There is evidence that outbreaks are continuing to occur, at least in families but probably also in communities. However, because of inaccurate definitions, people are not getting diagnosed with ME/CFS for at least six months, if at all. By the time they are diagnosed any chance of finding the original pathogen or toxic exposure (the most likely causes of geographic outbreaks) is gone. **If the CDC wishes to regain the trust of the patient community they must abandon the Fukuda and empiric definitions.** We cannot “agree to disagree” on this issue, as Dr. Unger has suggested. The CDC is still spending our tax dollars on studies to justify these definitions.

Another way for the CDC to regain the trust and respect of the patient community is to adopt the Canadian Consensus definition of ME/CFS (or the similar International Consensus definition) and to use it to begin doing the epidemiological, longitudinal and laboratory research that is necessary to address the massive personal and financial cost of this disease to the American economy.

The CDC is also spending very scarce research dollars on studies that have no possibility of helping patients or protecting communities from this disease. Rather than working to discover what is helping patients to recover or where the sickest patients are, the CDC is spending money to document that people who feel very sick are not particularly interested in card games. This would be laughable, if we could ignore the people with ME/CFS who are unable to leave their homes and are receiving no medical care at all and no help from CDC research. **The CDC should be spending its money (our taxpayer money) on epidemiological and longitudinal studies that can lead to diagnostic tests and therapies and that can protect our communities against this disease.** That is their mission.

What can the CFSAC do to facilitate more effective research at the CDC? It can ask for semiannual reports of what projects are ongoing at the CDC and what are the budgets for each. In 2009 one of its recommendations stated that “the CFSAC rejects the empirical case definition”. It is vitally important that it **repeat this recommendation and emphasize to the Secretary that the Canadian and Consensus definitions are far better definitions than either the empiric or Fukuda definitions.** There is no time to waste continuing to use faulty definitions. These definitions are damaging to patients. Finally, it can ask to have input into a new 5 year plan for the CDC which includes epidemiological and longitudinal studies.

In addition, the CDC website continues to disseminate false and misleading information to physicians and the general public. **CFSAC should ask that the Toolkit be removed from the website immediately.**

NIH

The NIH funding level for this disease is 5 percent of the funding level for multiple sclerosis, a disease which affects half as many people as ME/CFS. **There should be a Request for Proposals with a dollar amount attached that is at least equivalent to the amount spent**

on MS. There are several obvious studies that need to be done right away. The Lights have received funding to continue their study of gene expression changes associated with post-exertional malaise. Other laboratories should be funded to attempt to reproduce their findings, with the goal to develop and validate a diagnostic test. In addition, money should be available to the Pacific Fatigue Laboratory to validate a second diagnostic test, and there should be an additional study to see if these two modalities correlate. Dr. Lipkin is funded to look for a single pathogen, but funding should be made available to examine the possibility that more than one pathogen may act synergistically to initiate this disease. We also need studies to see how orthostasis is associated with post-exertional malaise. Can the Lights gene expression changes be seen after prolonged standing rather than exercise? Following the success of rituximab therapy in some patients, it is also obvious to look again at the immune system and try to figure out why rituximab works. In addition, cognitive dysfunction is one of the most disabling aspects of ME/CFS. Can cognitive dysfunction be correlated with orthostasis, post-exertional malaise &/or viral infection? These possibilities are only the beginning. There are numerous other questions that must be studied, remembering that **results will only be interpretable if the patient population is appropriately defined.**

The grant review process for ME/CFS at the NIH needs to be improved. It is hard for anyone outside the scientific community to fully appreciate the problems in this area. However, it is clear from comments made at CFSAC meetings by multiple researchers, many very experienced, that the process is not functioning well. An inquiry by the leaders of the NIH into why this is happening and how to make improvements is necessary.

ME/CFS does not belong in OWRH. It is not a “woman’s disease”. It should be housed in one of the Institutes, probably NIAID or NIND. Again, direction and involvement are needed from Dr. Collins and the leaders of the Institutes to find the best place for ME/CFS research to be centered. There are certainly other multi-system diseases studied at the NIH that can serve as examples.

Accountability for funding of ME/CFS projects at the NIH needs to be improved. Pat Fero and Charlotte von Salis have found evidence that some money allocated for ME/CFS is actually being used to study other diseases. Of course, this is not acceptable, especially given the relatively small amount allocated to ME/CFS research.

What can CFSAC do to promote a more effective program for ME/CFS at the NIH? Ask for reports at every meeting on the number of grants, the amount of money allocated and the topics studied. Convene a panel of people who have experience with the NIH grant process to make recommendations about the ME/CFS grant process and make sure that the recommendations are implemented. Make sure that the NIH has a process in place to ensure that funding for ME/CFS is actually being used for ME/CFS projects. **Ask for a specific, appropriate allocation of funds.** Insist that responsibility for ME/CFS be housed in one of the Institutes, and that the highest officials at NIH be involved in and committed to the decision about which Institute is appropriate. Finally, the NIH must insist that all funded studies use the Canadian Consensus or International Consensus definition.

FDA

There is apparently only one drug currently under consideration for the treatment of ME/CFS at the FDA, and it has been under consideration for several years. Part of the problem has been the definition of the disease, which has made it difficult to demonstrate positive benefits from drugs. It is important that **the FDA insists that the Canadian or International Consensus definitions be used in drug trials**. It is also important that the FDA expedite approval for diagnostic tests as they are developed with NIH funding.

One of the obvious problems at the FDA is that ME/CFS has been placed in six different divisions over the past several years. This has meant that no division has developed the expertise to properly evaluate therapies, diagnostic tests or devices for ME/CFS. Like at the NIH, involvement at the highest levels of FDA is needed to find an appropriate, permanent place for issues related to ME/CFS.

FDA action is dependent on the activity of researchers funded by the NIH, CDC and other groups who find possible therapeutic agents and diagnostic tests relevant to this disease. FDA needs to be prepared to handle requests for evaluate them. **CFSAC can encourage preparation by insisting that the FDA use an appropriate definition in its evaluations and have a process to expedite evaluations**. ME/CFS patients have been waiting for a very long time.

Other Issues

It is very important that the CFSAC provide input about the new DSM-5 criteria. I am no expert on this matter and cannot speak about it in any informed way. I refer you to Mary Dimmock and Suzy Chapman, who understand this issue . I urge CFSAC to **formulate an appropriate comment about the DSM-5 as one of your recommendations at this June, 2012 meeting**. This is very important to patients.

It is important to note that CFSAC itself has significant problems at this time. According to the website **there are four vacant seats on the Committee, including the post of Chairman**. This is a huge problem. Without a Chairman who is communicating with the Secretary and with Dr. Koh? How can there be any continuity or institutional memory of all that patients and other experts have taken the trouble to communicate to the Committee if seats are unfulfilled? There could be four additional experts providing input to the Committee? Who is responsible for ensuring that there are a full complement of members. At this point, it is hard to believe that there is any commitment on the part of our Government to provide or listen to advice about ME/CFS.

In addition, it is important to note that the process involved in attending meetings and submitting testimony is getting more opaque and difficult for patients. It is inherently difficult for patients to attend meetings, and it behooves the staff to make it as easy as possible. The meeting this time is one month later than usual, and there was very late notification of how and when to submit testimony. There was inconsistency and confusion about the date for testimony submission. The agenda was not posted by the promised date of June 4, 2012, making it difficult for patients to make plans. When I notified the staff that I intend to attend the meeting I received

no acknowledgement, despite information that seating would be limited. I also received the following instruction about the meeting: *Any object carried by the visitor that is deemed inappropriate will be confiscated and disposed of by the security staff* (italics mine). I asked for advice about what objects would be considered “inappropriate” and have received no reply. This appears to violate my constitutional right to protection from unreasonable search and seizure. This is hardly a friendly atmosphere for an exchange of ideas between a government and its citizens about a serious disease.

I started this testimony with the idea that this is a time for hope. However, it is not surprising that patients and their families feel quite discouraged at this point. It seems as though we are still dealing with many persistent problems: despite the State of the Knowledge meeting, which occurred more than a year ago, total NIH funding for ME/CFS continues to be much lower than diseases with a similar impact on quality of life. The number of studies funded is also low. There is no plan for progress, no consensus on what are the most promising avenues for study. While patients with the means to get to a doctor who offers effective therapies are quite likely to improve now, many patients still struggle to even get a diagnosis and cannot find a knowledgeable doctor or cannot get to one or cannot pay for one.

Why is this? **We don't have the information we need to develop an approach to ME/CFS that can be taught to large number of doctors.** There is no support for clinical research. The doctors who are beginning to know how to treat this disease have no funding for data collection. They are inundated with patients. They have waiting lists that are years long. They have no time to publish their findings, and no financial support to do so. Where is our government? Where are our scientific and medical leaders?

Progress in the diagnosis and treatment of ME/CFS is within our grasp. We have the tools, foremost among them diagnostic criteria, diagnostic tests and effective therapeutic agents. It is time to move forward. Thank you for your dedication to the effort to improve the lives of people with ME/CFS.