

DATE: January 12, 2015

TO: Sylvia Burwell; Francis Collins; Tom Frieden; Susan Maier; David Murray; Wanda Jones; CFSAC; P2P committee.

FROM: Lisa Petrison, Ph.D.

RE: NIH P2P Report on "ME/CFS"

Following is a list of some of the most important problems that I see in the recent draft report from the NIH P2P committee charged with looking at "ME/CFS."

First, the opening sentence is misleading, inconsistent with the comments in the rest of the report, and factually inaccurate.

"Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a chronic, complex, multi-faceted condition characterized by extreme fatigue and other symptoms that are not improved by rest."

This makes it seem like the most important thing that people should know about ME is that it consists of "fatigue" (plus other symptoms that aren't important enough to mention specifically).

Especially considering the historical characterization of the disease as "chronic fatigue syndrome," this introductory statement will encourage physicians, researchers, government officials and others to continue to overlook the much more critical health problems that patients with ME face.

I request that the first sentence be rewritten to include specific mention of some of the more debilitating issues of ME, including cognitive dysfunction, orthostatic intolerance, pain, inability to tolerate a wide variety of environmental stimuli, and post-exertional relapse.

Second, the word "fatigue" used in the first sentence and then throughout the document is not an appropriate characterization of any of the health issues that people with ME endure.

Ever since the Lake Tahoe epidemic in the mid 1980's, severely ill patients have repeatedly tried to make medical professionals understand that describing their profound lack of ability to participate in normal activity as "fatigue" is as inappropriate as saying that the limitations that ALS patients experience are due to "fatigue."

The activity-limiting state experienced in this disease is nothing like what healthy people ever experience when they are tired or fatigued. It is much more like paralysis or like the feelings of inflammation that people experience when they are fighting the flu.

Research literature now demonstrates that ME patients indeed have abnormal physiological markers (including gene and heat shock protein expression, low cerebral oxygenation, inflammation, oxidative stress and C4a complement levels) subsequent to activity. (1)

Healthy people do not display these same markers no matter how much exercise they've done, how hard they've been working, or how little sleep they've been getting.

People with ME are ill, just as people with a bad case of the flu or with ALS are ill. This is not the same thing as being fatigued.

In addition to being an inaccurate description of ME patients' health problems, the word "fatigue" (by any definition) is not specific enough to be used as a primary descriptive symptom for this disease or for any other disease.

People with cancer, AIDS, Parkinson's, ALS, MS and many other conditions also experience an enormous decline in their ability to be active, for instance.

It would be wholly inappropriate for the government to point to "fatigue" as the defining symptom of any of those diseases. And it is wholly inappropriate for the government to continue to focus on "fatigue" as the defining symptom for ME.

I request that it be noted in the report that the problems that force ME patients to limit their activity appear to be nothing like the fatigue that healthy people experience.

I also request that the report suggest that the use of the term "fatigue" to characterize this disease may be inappropriate in general.

I further request that the focus on "fatigue" be decreased throughout the report. For instance, it could replace the mention of "fatigue" in the first paragraph with a comment about patients having "an abnormally limited ability to participate in physical or mental activity."

Third, positive governmental action toward this disease seems more likely if specific funding recommendations are provided in the report.

The primary stumbling block in terms of advancement for ME now is that there has been very limited governmental research funding in the past - and that virtually all of the available funds have been wasted on poor-quality projects.

I request that the report elaborate on the extent to which this disease has historically been underfunded.

Further, I request that the report suggest a specific NIH dollar figure that would provide a chance for scientific progress and that would be similar to the amount being spent on similarly devastating diseases (such as MS, autism, lupus, Parkinson's or Alzheimer's).

I also request that the report recommend that funding needs to go toward high-quality biomedical research projects, with primary emphasis on severely ill subjects.

Fourth, discussion in the report needs to be directed toward the relationship between ME and CFS, and should not be referring to the artificial construct of "ME/CFS" as if it actually exists.

"ME" has been an established disease since the 1950's, with many articles on illness outbreaks published in prestigious journals. It has had a quite consistent definition since that time.

Existing definitions of "ME" point to a specific group of patients who are very ill and who have a recognizable pattern of specific symptoms.

"CFS" was created by a CDC committee during the late 1980's. It has been characterized since that time by a variety of non-specific definitions, none of which look much like the descriptions of ME from the literature.

Existing definitions of "CFS" point to a very broad group of individuals, including many people who are only very mildly sick and experience only non-specific symptoms rather than the ones repeatedly reported to be characteristic of ME.

In 2012, the CDC website suggested that ME and CFS were different conditions, stating: "The name myalgic encephalomyelitis (ME) was coined in the 1950's to clarify well-documented outbreaks of the disease; however, ME is accompanied by neurologic and muscular signs and has a case definition distinct from that of CFS." (2)

"ME/CFS" is a term that first began being used by the government a little more than a year ago. It is of particular concern to many in the ME community because of the possibility that it may be interpreted as stating that ME is just another name for the government's badly named and badly defined "CFS" concept.

I wrote about this topic in a brief comment to the CFS Advisory Committee to the DHHS last month. (3)

I request that the report bring up the idea that establishing an official disease of "ME" using an appropriate definition for those who have ME (rather than forcing those people to be diagnosed as having the non-specific non-disease of "ME/CFS") might help to clear up some of the current confusion about the definition and move scientific progress forward.

Fifth, the continuing discussion of papers using only the Oxford definition as if the findings of those papers have any relevance whatsoever to ME patients needs to be put to a halt.

The report acknowledges that the Oxford definition is flawed. Every “ME/CFS” specialist and every ME patient I know wholeheartedly agrees with that.

I thus request that the report state that any published work done using only the Oxford definition should not be assumed to be applicable to people with ME, unless and until that research is replicated with a subject population selected using a less flawed definition.

The Chronic Fatigue Advisory Committee (CFSAC) has submitted a list of recommendations regarding this P2P report. (4) Although these recommendations unfortunately do not discuss the relationship between “ME” and “CFS” or suggest that ME be recognized as its own diagnosis, in general I feel that the adoption of their recommendations would significantly improve the report.

Thank you for your attention to these issues.

Cordially,

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REFERENCES:

(1) Background information on medical abnormalities in ME or CFS.

<http://paradigmchange.me/me-medical-abnormalities/>

(2) CDC 2012 website page discusses the difference between “ME” and “CFS.”

<http://paradigmchange.me/wp-content/uploads/2015/01/CDC-ME-vs.-CFS.jpg>

(3) Statement on “The Problem with “ME/CFS” (text follows).

<http://paradigmchange.me/wp/mecfs/>

(4) CFSAC recommendations for the P2P report.

<https://dl.dropboxusercontent.com/u/57025850/P2P%20Library/P2P%20CFSAC%20unofficial.pdf>

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The Problem with “ME/CFS”

By Lisa Petrison, Ph.D.

The term “Myalgic Encephalomyelitis” was first used in 1956, to refer to a series of illness outbreaks that had been reported around the world since the 1930’s.

By the mid 1980’s, there had been more than 100 papers published in the medical literature about M.E., with very detailed descriptions of illness presentation and typical illness course.

In 1985, several hundred individuals in the Lake Tahoe area came down with severe and classic M.E. Other U.S. clusters of M.E. also were reported.

The members of the Holmes Committee responding to those outbreaks were aware of the medical literature about the established disease of M.E.

Nonetheless, the committee decided not to acknowledge that the affected individuals were suffering from M.E.

Instead, in 1988, the committee created a totally new illness category, which it called “Chronic Fatigue Syndrome.”

Considering that fatigue was the least of these patients’ concerns, the Holmes Committee’s decision to use that name was as problematic then as it is today.

An even bigger problem was that the definition written by the committee was so broad that it allowed many individuals who did not have M.E. to be diagnosed as having “CFS.”

Over the subsequent 26 years, the government definition of CFS became even broader.

During the past year or so, the government has begun to refer to the condition that it recognizes as follows: “Chronic fatigue syndrome (ME/CFS).”

This makes me concerned that the government is now suggesting that M.E. is just another name for “CFS” – and therefore that everything that it says about CFS should apply to M.E. as well.

If this indeed is what the government is suggesting, it is highly inappropriate.

M.E. is a disease with a history going back more than 60 years. It has an established specific definition that is very different than the definitions that the government continues to use for “CFS.”

Those in this community have asked numerous times that the definition of CFS be changed to an established definition of M.E., through the adoption of the International Consensus Criteria or the Canadian Consensus Criteria.

Even better would be for the government to officially recognize M.E. as its own illness category, using an existing M.E. definition.

On the other hand, it would be unscientific for the government to imply that just because their creation of CFS in 1988 was in response to an M.E. outbreak, their definition for CFS should hold sway over M.E.

M.E. already has a definition. It is an international definition that has been consistent since 1956. It is a definition wholly unlike any definition that the government ever has used for CFS.

It is not within the purview of the government of the United States to change the definition of M.E. to their definition of CFS.

Thank you.

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References

1) A 1956 article describing the established disease of M.E.

Lindan R. Benign Myalgic Encephalomyelitis. Can Med Assoc J. 1956 Oct 1;75(7):596-7. PMID: 20325349

“The onset resembles that of poliomyelitis with headaches, lassitude, neck stiffness and sore throat accompanied by pains in the limbs and back, and possibly paraesthesiae and palsies. In contrast to poliomyelitis, however, the fever is never very high; the temperature rarely exceeds 100 degrees F and may persist for long periods. The clinical picture is dominated by the severe muscular pains, accompanied at first by spasms and exaggerated tendon reflexes. These pains are not transient; they often persist long after any local signs have subsided and may be accompanied by an exquisite tenderness, but at no time does any muscular wasting develop. A further distinguishing feature of the disease is the onset of behavioural changes, such as emotional lability, irritability and depression....Disturbances of the cranial nerves such as diplopia and nystagmus, facial weakness, deafness or, in some cases hyperacusis, are common. A high proportion of cases show evidence of involvement of the reticuloendothelial system with enlargement of the cervical lymph nodes, particularly those in the posterior triangle, and, in some patients, hepatitis and splenomegaly.”

2) A list of some Myalgic Encephalomyelitis outbreaks.

1934 Los Angeles County Hospital – Atypical Poliomyelitis

1936 Fond Du Lac, Wisconsin – St. Agnes Convent – Encephalitis

1937 Erstfeld, Switzerland – Abortive Poliomyelitis

1937 St. Gallen, Switzerland – Frohburg Hospital – Abortive Poliomyelitis

1939 Middlesex, England – Harefield Sanatorium – persistent Myalgia following sore throat

1939 Degersheim, Switzerland – Abortive Poliomyelitis

1945 Hospital of the University of Pennsylvania – epidemic Pleurodynia with prominent neurological symptoms

1946 Iceland – disease resembling Poliomyelitis with the character of Akureyri disease

1948 Iceland, North Coast towns – epidemic simulating Poliomyelitis

1949 Adelaide, South Australia – a disease resembling Poliomyelitis

1950 Louisville, Kentucky — St. Joseph’s Infirmary – outbreak in nurses’ training school described as “epidemic Neuromyasthenia”

1950 Upper State New York — outbreak resembling the Iceland disease, simulating acute Anterior Poliomyelitis

1952 London, England – Middlesex Hospital Nurses’ Home – Encephalomyelitis associated with Poliomyelitis virus

1952 Copenhagen, Denmark – epidemic Myositis

1952 Lakeland, Florida – epidemic Neuromyasthenia

1953 Coventry and District, England – an illness resembling Poliomyelitis observed in nurses

1953 Rockville, Maryland – Chestnut Lodge Hospital – Poliomyelitis-like epidemic Neuromyasthenia

1953 Jutland, Denmark – epidemic Encephalitis with vertigo

1954 Seward, Alaska – benign Myalgic Encephalomyelitis (Iceland Disease)

1954 Berlin, Germany – British army – further outbreak of a disease resembling Poliomyelitis

1954 Liverpool, England – outbreak among medical and nursing staff in a local hospital

1955 Dalston, Cumbria, England – epidemic and sporadic outbreak of an unusual disease

1955 London, England – Royal Free Hospital – outbreak in staff and patients of Benign Myalgic Encephalomyelitis

1955 Perth, Australia – virus epidemic in waves

1955 Gilfac Goch, Wales – outbreak of benign Myalgic Encephalomyelitis

1955 Durban City, South Africa – Addington Hospital – outbreak among nurses of “Durban Mystery Disease”

1955 Segbwema, Sierra Leone – outbreak of Encephalomyelitis

1955 Patreksfjorour and Porshofn, Iceland – unusual response to polio vaccine

1955 Northwest London, England – nurses’ residential home – acute Infective Encephalomyelitis simulating poliomyelitis

1956 Ridgefield, Connecticut – epidemic Neuromyasthenia

1956 Punta Gorda Florida – outbreak of epidemic Neuromyasthenia

1956 Newton-le-Willows, Lancashire, England – Lymphocytic Meningoencephalitis with myalgia

1956 Pittsfield and Williamstown, Massachusetts – benign Myalgic Encephalomyelitis

1956 Coventry, England – epidemic malaise, benign Myalgic Encephalomyelitis

1957 Brighton, South Australia – Cocksakie Echo virus Meningitis, epidemic Myalgic Encephalomyelitis

1958 Athens, Greece – nurses’ school – outbreak of benign Myalgic Encephalomyelitis with periostitis and arthropathy noted.

1958 Southwest London, England – reports of sporadic cases of Myalgic Encephalomyelitis

1959 Newcastle Upon Tyne, England – outbreak of benign Myalgic Encephalomyelitis

1961 Basel, Switzerland – sporadic cases of benign Myalgic Encephalomyelitis

1961 New York State – outbreak of epidemic Neuromyasthenia in a convent

1964 Northwest London, England – epidemic malaise, epidemic Neuromyasthenia

1964 Franklin, Kentucky – outbreak of Neuromyasthenia in a factory

1967 Edinburgh, Scotland – sporadic cases resembling benign Myalgic Encephalomyelitis

1968 Fraidek, Lebanon – benign Myalgic Encephalomyelitis

1969 Brooklyn, New York – State University of New York Downstate Medical Center – epidemic Neuromyasthenia, unidentified symptom complex

1970 Lackland Air Force Base, Texas – epidemic Neuromyasthenia

1970 London, England – Great Ormond Street Hospital for Children – outbreak of Neuromyasthenia among nurses

1975 Sacramento, California – Mercy San Juan Hospital – Infectious Venulitis, epidemic Phelobodynia

1976 Southwest Ireland – epidemic Neuromyasthenia, benign Myalgic Encephalomyelitis

1977 Dallas – Fort Worth, Texas – epidemic Neuromyasthenia

1979 Southampton, England – Myalgic Encephalomyelitis

1980 West Kilbridge, Ayrshire, Scotland – epidemic Myalgic Encephalomyelitis

1980 San Francisco, California – epidemic persistent flu-like illness

1981 Stirlingshire, Scotland – sporadic Myalgic Encephalomyelitis

1982 West Otago, Dunedin and Hamilton, New Zealand – Myalgic Encephalomyelitis

1983 Los Angeles, California – an unknown, chronic symptom complex involving profound “fatigue”

1984 Lake Tahoe Area of California/Nevada – Eventually characterized as Chronic Fatigue Syndrome

3) A paper about the Tahoe epidemic (still not included in the P2P literature review).

Buchwald D, Cheney PR, Peterson DL, Henry B, Wormsley SB, Geiger A, Ablashi DV, Salahuddin SZ, Saxinger C, Biddle R, et al. A chronic illness characterized by fatigue, neurologic and immunologic disorders, and active human herpesvirus type 6 infection. *Ann Intern Med.* 1992 Jan 15;116(2):103-13. PMID: 1309285

4) Peer-reviewed articles about Myalgic Encephalomyelitis published by 1988.

Blattner RJ. Benign myalgic encephalomyelitis (Akureyri disease, Iceland disease). *J Pediatr.* 1956 Oct;49(4):504-6. PMID: 13358047

Lindan R. Benign Myalgic Encephalomyelitis. *Can Med Assoc J.* 1956 Oct 1;75(7):596-7. PMID: 20325349

Galpine JF, Brady C. Benign myalgic encephalomyelitis. *Lancet.* 1957 Apr 13;272(6972):757-8. PMID: 13417586

Acheson ED. Benign myalgic encephalomyelitis. *Lancet.* 1957 Apr 20;272(6973):834-5. PMID: 13417614

—. EPIDEMIC myalgic encephalomyelitis. *Br Med J.* 1957 Oct 19;2(5050):927-8. PMID: 13472011

—. [Benign epidemic myalgic encephalomyelitis]. *Recenti Prog Med.* 1957 Nov;23(5):525-31. Italian. PMID: 13518620

Deisher JB. Benign myalgic encephalomyelitis (Iceland disease) in Alaska. *Northwest Med.* 1957 Dec;56(12):1451-6. PMID: 13484090

Galpin JF. Benign myalgic encephalomyelitis. *Br J Clin Pract.* 1958 Mar;12(3):186-8 passim. PMID: 13510534

Greene IM. Benign myalgic encephalomyelitis; syndrome mimicking anterior poliomyelitis. *J Fla Med Assoc.* 1958 Apr;44(10):1105-6. PMID: 13525606

Gsell O. Encephalitis myalgica epidemica, a poliomyelitis-like disease; epidemic neuromyasthenia, benign myalgic encephalomyelitis. *Schweiz Med Wochenschr.* 1958 May 17;88(20):488-91. German. PMID: 13568694

Bhatia BB, Chandra S, Bhushan C. Benign myalgic encephalomyelitis. *J Indiana State Med Assoc.* 1958 Oct;31(8):327-8. PMID: 13611265

Acheson ED. The clinical syndrome variously called benign myalgic encephalomyelitis, Iceland disease and epidemic neuromyasthenia. *Am J Med.* 1959 Apr;26(4):569-95. PMID: 13637100

Daikos GK, Garzonis S, Paleologue A, Bousvaros GA, Papadoyannakis N. Benign myalgic encephalomyelitis: an outbreak in a nurses' school in Athens. *Lancet.* 1959 Apr 4;1(7075):693-6. PMID: 13642848

Bornstein B, Bechar M, Lass H. Benign myalgic encephalomyelitis. (Report of five cases). *Psychiatr Neurol (Basel).* 1960 Mar;139:132-40. PMID: 13802904

Klajman A, Pinkhas B, Rannon L. [An outbreak of an epidemic of benign myalgic encephalomyelitis]. *Harefuah.* 1960 May 15;58:314-5. Hebrew. PMID: 14409571

Pool JH, Walton JN, Brewis EG, Uldall PR, Wright AE, Gardner PS. Benign myalgic encephalomyelitis in Newcastle upon Tyne. *Lancet.* 1961 Apr 8;1(7180):733-7. PMID: 13737057

Price JL. Myalgic encephalomyelitis. *Lancet.* 1961 Apr 8;1(7180):737-8. PMID: 13737972

Gsell O. [Benign myalgic encephalomyelitis, epidemic pseudoneurasthenia]. *Schweiz Med Wochenschr.* 1963 Feb 2;93:197-200. German. PMID: 13950994

Kendell RE. The psychiatric sequelae of benign myalgic encephalomyelitis. *Br J Psychiatry.* 1967 Aug;113(501):833-40. PMID: 6048369

Mourad S, Chidiac J. Benign myalgic encephalomyelitis in Lebanon. *J Med Liban.* 1969;22(6):735-40. PMID: 5370523

McEvedy CP, Beard AW. Concept of benign myalgic encephalomyelitis. *Br Med J.* 1970 Jan 3;1(5687):11-5. PMID: 5411596

Innes SG. Encephalomyelitis resembling benign myalgic encephalomyelitis. *Lancet*. 1970 May 9;1(7654):969-71. PMID: 4191935

Lyle WH. Encephalomyelitis resembling benign myalgic encephalomyelitis. *Lancet*. 1970 May 23;1(7656):1118-9. PMID: 4191997

—. Benign myalgic encephalomyelitis. *Med J Aust*. 1970 Jul 4;2(1):3. PMID: 5447847

Walther H. [Epidemic myalgic encephalomyelitis]. *Schweiz Rundsch Med Prax*. 1972 Apr 11;61(15):469-80. German. PMID: 5022278

Ramsay AM. Benign myalgic encephalomyelitis. *Br J Psychiatry*. 1973 May;122(570):618-9. PMID: 4717041

Parish JG. Benign myalgic encephalomyelitis. *Br J Psychiatry*. 1973 Jun;122(571):735. PMID: 4716076

Ramsay AM, Dowsett EG, Dadswell JV, Lyle WH, Parish JG. Icelandic disease (benign myalgic encephalomyelitis or Royal Free disease) *Br Med J*. 1977 May 21;1(6072):1350. PMID: 861618

—. Epidemic myalgic encephalomyelitis. *Br Med J*. 1978 Jun 3;1(6125):1436-7. PMID: 647324

Wookey C. Epidemic myalgic encephalomyelitis. *Br Med J*. 1978 Jul 15;2(6131):202. PMID: 678851

Behan PO. Post-infectious encephalomyelitis: some aetiological mechanisms. *Postgrad Med J*. 1978 Nov;54(637):755-9. PMID: 34143

Thomas M. Epidemiological approaches to 'epidemic neuromyasthenia': syndromes of unknown aetiology (epidemic myalgic encephalopathies). *Postgrad Med J*. 1978 Nov;54(637):768-70. PMID: 746024

Pampiglione G, Harris R, Kennedy J. Electro-encephalographic investigations in myalgic encephalomyelitis. *Postgrad Med J*. 1978 Nov;54(637):752-4. PMID: 746023

Ramsay AM, Rundle A. Clinical and biochemical findings in ten patients with benign myalgic encephalomyelitis. *Postgrad Med J*. 1979 Dec;55(654):856-7. PMID: 548947

Church AJ. Myalgic encephalomyelitis “an obscene cosmic joke”? *Med J Aust.* 1980 Apr 5;1(7):307-8. PMID: 7393056

Bishop J. Epidemic myalgic encephalomyelitis. *Med J Aust.* 1980 Jun 14;1(12):585-6, 609. PMID: 7402153

Behan PO. Epidemic myalgic encephalomyelitis. *Practitioner.* 1980 Aug;224(1346):805-7. PMID: 7433399

Church AJ. Myalgic encephalomyelitis. *Med J Aust.* 1980 Aug 23;2(4):224. PMID: 7432298

May PG, Donnan SP, Ashton JR, Ogilvie MM, Rolles CJ. Personality and medical perception in benign myalgic encephalomyelitis. *Lancet.* 1980 Nov 22;2(8204):1122-4. PMID: 6107734

Goodwin CS. Was it benign myalgic encephalomyelitis? *Lancet.* 1981 Jan 3;1(8210):37-8. PMID: 6109065

— —. Know your organizations: the Myalgic Encephalomyelitis Association. *Health Visit.* 1982 Jul;55(7):350. PMID: 6921182

Parish G. Myalgic encephalomyelitis: faulty fibres? *Nurs Mirror.* 1981 Oct 7;153(15):41-2. PMID: 6913031

Ramsay M. Myalgic encephalomyelitis: a baffling syndrome. *Nurs Mirror.* 1981 Oct 7;153(15):40-1. PMID: 6913030

Parish JG. Myalgic encephalomyelitis. *Lancet.* 1981 Apr 25;1(8226):950-1. PMID: 6112360

Layzer RB. Myoglobinaemia in benign myalgic encephalomyelitis. *Lancet.* 1981 Mar 21;1(8221):670. PMID: 6110899

Fegan KG, Behan PO, Bell EJ. Myalgic encephalomyelitis—report of an epidemic. *J R Coll Gen Pract.* 1983 Jun;33(251):335-7. PMID: 6310104

Keighley BD, Bell EJ. Sporadic myalgic encephalomyelitis in a rural practice. *J R Coll Gen Pract.* 1983 Jun;33(251):339-41. PMID: 6310105

Calder BD, Warnock PJ. Coxsackie B infection in a Scottish general practice. *J R Coll Gen Pract.* 1984 Jan;34(258):15-9. PMID: 6319691

Gow PJ. Myalgic encephalomyelitis. *N Z Med J.* 1984 Sep 12;97(763):620. PMID: 6591048

Bell EJ, McCartney RA. A study of Coxsackie B virus infections, 1972-1983. *J Hyg (Lond).* 1984 Oct;93(2):197-203. PMID: 6094660

—. Myalgic encephalomyelitis. *N Z Med J.* 1984 Oct 10;97(765):698-9. PMID: 6592485

—. Myalgic encephalomyelitis. *N Z Med J.* 1984 Nov 14;97(767):782. PMID: 6593632

Gow PJ. Myalgic encephalomyelitis. *N Z Med J.* 1984 Dec 12;97(769):868. PMID: 6595571

—. Myalgic encephalomyelitis. *N Z Med J.* 1985 Jan 23;98(771):20-1. PMID: 3855509

Maurizi CP. Raphe nucleus encephalopathy (myalgic encephalomyelitis, epidemic neuromyasthenia). *Med Hypotheses.* 1985 Apr;16(4):351-4. PMID: 4010573

Byrne E, Trounce I, Dennett X. Chronic relapsing myalgia (Post viral): clinical, histological, and biochemical studies. *Aust N Z J Med.* 1985 Jun;15(3):305-8. PMID: 3864422

Staines D. Myalgic encephalomyelitis hypothesis. *Med J Aust.* 1985 Jul 22;143(2):91. PMID: 4021881

Rowlandson PH, Stephens JA. Cutaneous reflex responses recorded in children with various neurological disorders. *Dev Med Child Neurol.* 1985 Aug;27(4):434-47. PMID: 2993087

Simpson LO, Shand BI, Olds RJ. Blood rheology and myalgic encephalomyelitis: a pilot study. *Pathology.* 1986 Apr;18(2):190-2. PMID: 3093959

McCartney RA, Banatvala JE, Bell EJ. Routine use of mu-antibody-capture ELISA for the serological diagnosis of Coxsackie B virus infections. *J Med Virol.* 1986 Jul;19(3):205-12. PMID: 3016163

Blackmore RJ. Myalgic encephalomyelitis and Immunovir. *N Z Med J.* 1986 Jul 9;99(805):513. PMID: 3461389

Matthew C. Myalgic encephalomyelitis. *N Z Med J*. 1986 Sep 10;99(809):678. PMID: 3463904

Taerk GS, Toner BB, Salit IE, Garfinkel PE, Ozersky S. Depression in patients with neuromyasthenia (benign myalgic encephalomyelitis). *Int J Psychiatry Med*. 1987;17(1):49-56. PMID: 3583562

Archer MI. The post-viral syndrome: a review. *J R Coll Gen Pract*. 1987 May;37(298):212-4. Review. PMID: 3320358

Mukherjee TM, Smith K, Maros K. Abnormal red-blood-cell morphology in myalgic encephalomyelitis. *Lancet*. 1987 Aug 8;2(8554):328-9. PMID: 2886780

Matthew C. Myalgic encephalomyelitis and the doctor. *N Z Med J*. 1987 Sep 9;100(831):569. PMID: 3451147

Behan PO, Behan WM. Postviral fatigue syndrome. *Crit Rev Neurobiol*. 1988;4(2):157-78. Review. PMID: 3063394

Ho-Yen DO, Carrington D, Armstrong AA. Myalgic encephalomyelitis and alpha-interferon. *Lancet*. 1988 Jan 16;1(8577):125. PMID: 2891971

Byrne E. Idiopathic chronic fatigue and myalgia syndrome (myalgic encephalomyelitis): some thoughts on nomenclature and aetiology. *Med J Aust*. 1988 Jan 18;148(2):80-2. PMID: 3336341

Lloyd A, Hanna DA, Wakefield D. Interferon and myalgic encephalomyelitis. *Lancet*. 1988 Feb 27;1(8583):471. PMID: 2893889

Maros K. Myalgic encephalomyelitis? *Med J Aust*. 1988 Apr 18;148(8):424. PMID: 3357477

Wakefield D, Lloyd A, Dwyer J, Salahuddin SZ, Ablashi DV. Human herpesvirus 6 and myalgic encephalomyelitis. *Lancet*. 1988 May 7;1(8593):1059. PMID: 2896906

Jennekens FG, van Gijn J. [Postviral fatigue syndrome or myalgic encephalomyelitis]. *Ned Tijdschr Geneesk*. 1988 May 28;132(22):999-1001. Dutch. PMID: 3380192

Bell EJ, McCartney RA, Riding MH. Cocksackie B viruses and myalgic encephalomyelitis. *J R Soc Med*. 1988 Jun;81(6):329-31. PMID: 2841461

Archard LC, Bowles NE, Behan PO, Bell EJ, Doyle D. Postviral fatigue syndrome: persistence of enterovirus RNA in muscle and elevated creatine kinase. *J R Soc Med*. 1988 Jun;81(6):326-9. PMID: 3404526

Lloyd AR, Wakefield D, Boughton C, Dwyer J. What is myalgic encephalomyelitis? *Lancet*. 1988 Jun 4;1(8597):1286-7. PMID: 2897549

Holborow PL. Pathophysiology of myalgic encephalomyelitis. *Med J Aust*. 1988 Jun 6;148(11):598, 600. PMID: 3374430

—-. Myalgic encephalomyelitis, or what? *Lancet*. 1988 Jul 9;2(8602):100-1. PMID: 2898668

Murdoch JC. Cell-mediated immunity in patients with myalgic encephalomyelitis syndrome. *N Z Med J*. 1988 Aug 10;101(851):511-2. PMID: 3261407

Gordon N. Myalgic encephalomyelitis. *Dev Med Child Neurol*. 1988 Oct;30(5):677-82. Review. PMID: 3068084

—-. Myalgic encephalomyelitis. *N Z Med J*. 1988 Oct 26;101(856 Pt 1):672. PMID: 3186016

Willoughby EW. Myalgic encephalomyelitis. *N Z Med J*. 1988 Nov 9;101(857):773. PMID: 3186037

Hyde B, Bergmann S. Akureyri disease (myalgic encephalomyelitis), forty years later. *Lancet*. 1988 Nov 19;2(8621):1191-2. PMID: 2903396

—-. Myalgic encephalomyelitis. *N Z Med J*. 1988 Nov 23;101(858):800-1. PMID: 3194079

Murdoch JC. The myalgic encephalomyelitis syndrome. *Fam Pract*. 1988 Dec;5(4):302-6. Review. PMID: 2852613

5) Peer-reviewed articles mentioning predecessor conditions to M.E. published by 1988.

Sigurdsson B., Sigurdjonsson J, Sigurdsson JH, Thorkelsson J, Gudmundsson KR. A disease epidemic in Iceland simulating poliomyelitis. *Am J Hyg*. 1950 Sep;52(2):222-38. PMID: 14771044

Sigurjonsson J, Sigurdsson B, Sigurdsson JH, Thorkelsson J, Gudmundson KR. Epidemic disease in Iceland simulating poliomyelitis. *Acta Psychiatr Neurol Scand*. 1951;26(1):70-90. PMID: 14856807

White DN, Burtch RB. Iceland disease: a new infection simulating acute anterior poliomyelitis. *Neurology*. 1954 Jul;4(7):506-16. PMID: 13176669

Hardtke EF. Iceland disease in Indiana: a case report. *J Indiana State Med Assoc*. 1955 Mar;48(3):245-50. PMID: 14354224

Sigurdsson B. Clinical findings six years after outbreak of Akureyri disease. *Lancet*. 1956 May 26;270(6926):766-7. PMID: 13320872

Poskanzer DC, Henderson DA, Kunkle EC, Kalter SS. Epidemic protracted debility at Punta Gorda, Florida: an illness resembling Iceland disease. *Trans Am Neurol Assoc*. 1957-1958;82nd Meeting:121-3; discussion 123-5. PMID: 13530059.

Shelokov A, Habel K, Verder E, Welsh W. Epidemic neuromyasthenia; an outbreak of poliomyelitislike illness in student nurses. *N Engl J Med*. 1957 Aug 22;257(8):345-55. PMID: 13464938

Hook O. Iceland disease. *Nord Med*. 1957 Mar 7;57(10):373-5. PMID: 13430983.

Poskanzer DC, Henderson DA, Kunkle C, Kalter SS, Clement WB, Bond JO. Epidemic neuromyasthenia; an outbreak in Punta Gorda, Florida. *N Engl J Med*. 1957 Aug 22;257(8):356-64. PMID: 13464939

Clement WB, Gorda P, Henderson DA, Lawrence JW, Bond JO. Epidemic neuromyasthenia, an outbreak in Punta Gorda, Florida; an illness resembling Iceland disease. *J Fla Med Assoc*. 1958 Oct;45(4):422-6. PMID: 13587882.

Fraumeni JF Jr. Epidemic neuromyasthenia. *South Med J*. 1959 Oct;52:1192-7. PMID: 13824661

Henderson DA, Shelokov A. Epidemic neuromyasthenia; clinical syndrome. *N Engl J Med*. 1959 Apr 16;260(16):814-8 concl. PMID: 13644592

Sigurdjonsson J. Poliomyelitis & Akureyri disease; differentiation of poliomyelitis from poliomyelitis-like disease with characteristics of Akuteyri disease. *Nord Med*. 1959 Jan 29;61(5):174-7. PMID: 13623058

Fraumeni JF Jr. Epidemic neuromyasthenia. *South Med J*. 1959 Oct;52:1192-7. PMID: 13824661

Albrecht RM, Oliver VL, Poskanzer DC. Epidemic Neuromyasthenia: Outbreak in a convent in New York State. *JAMA*. 1964 Mar 21;187:904-7. PMID: 14100144

Holt GW. Epidemic Neuromyasthenia: The Sporadic Form. *Am J Med Sci*. 1965 Jan;249:98-112. PMID: 14254837 Miller G, Chamberlin R, McCormack WM. An outbreak of neuromyasthenia in a Kentucky factory—the possible role of a brief exposure to organic mercury. *Am J Epidemiol*. 1967 Nov;86(3):756-64. PMID: 6081389

Adamson JR. Epidemic neuromyasthenia. *N Engl J Med*. 1969 Oct 2;281(14):798. PMID: 5807934

Hart RH. Epidemic neuromyasthenia. *N Engl J Med*. 1969 Oct 2;281(14):797-8. PMID: 5807933

Steigman AJ. Epidemic neuromyasthenia. *N Engl J Med*. 1969 Oct 2;281(14):797. PMID: 5807932

Trimble GX. Epidemic neuromyasthenia. *N Engl J Med*. 1969 Jul 10;281(2):105-6. PMID: 5784765

Graybill JR, Silva J Jr, O'Brien MS, Reinartz JA. Epidemic neuromyasthenia. A syndrome or disease? *JAMA*. 1972 Mar 13;219(11):1440-3. PMID: 5066895

Dillon MJ, Marshall WC, Dudgeon JA, Steigman AJ. Epidemic neuromyasthenia: outbreak among nurses at a children's hospital. *Br Med J*. 1974 Feb 23;1(5903):301-5. PMID: 4819151

—. Editorial: Epidemic neuromyasthenia. *Harefuah*. 1975 Jan 1;88(1):32-4. Hebrew. PMID: 1112545

Sutton RN. Ill defined neurological diseases of possible viral origin. *Postgrad Med J*. 1978 Nov;54(637):747-51. PMID: 746022

Ball AP. Disease due to echovirus type 19 in Birmingham, England, 1975: relationship to 'epidemicneuromyasthenia'. *Postgrad Med J.* 1978 Nov;54(637):737-40. PMID: 746021

Corridan JP. 'Epidemic neuromyasthenia' in Southwest Ireland. *Postgrad Med J.* 1978 Nov;54(637):731-6. PMID: 746020

Wookey C. Royal free disease: the tip of the Iceland disease iceberg. *Nurs Times.* 1978 Apr 27;74(17):702-3. PMID: 652544

Dillon MJ. 'Epidemic neuromyasthenia' at the Hospital for Sick Children, Great Ormond Street, London. *Postgrad Med J.* 1978 Nov;54(637):725-30. PMID: 746019

Ramsay AM. 'Epidemic neuromyasthenia' 1955-1978. *Postgrad Med J.* 1978 Nov;54(637):718-21. PMID: 746017

—. 'Epidemic neuromyasthenia' 1934-1977: current approaches. Proceedings of a symposium held by the Council of the Royal Society of Medicine at 1 Wimpole Street, London, W.1, on 7 April 1978. *Postgrad Med J.* 1978 Nov;54(637):705-74. PMID: 746016

Behan PO. Post-infectious encephalomyelitis: some aetiological mechanisms. *Postgrad Med J.* 1978 Nov;54(637):755-9. PMID: 34143

Parish JG. Early outbreaks of 'epidemic neuromyasthenia'. *Postgrad Med J.* 1978 Nov;54(637):711-7. PMID: 370810

Knave B, Mindus P, Struwe G. Neurasthenic symptoms in workers occupationally exposed to jet fuel. *Acta Psychiatr Scand.* 1979 Jul;60(1):39-49. PMID: 474176

Ballow M, Seeley J, Purtilo DT, St Onge S, Sakamoto K, Rickles FR. Familial chronic mononucleosis. *Ann Intern Med.* 1982 Dec;97(6):821-5. PMID: 7149489

Gear JH. Nonpolio causes of polio-like paralytic syndromes. *Rev Infect Dis.* 1984 May-Jun;6 Suppl 2:S379-84. PMID: 6740077

Salit IE. Sporadic postinfectious neuromyasthenia. *CMAJ.* 1985 Oct 1;133(7):659-63. PMID: 4042036

McHugh SM. Sporadic postinfectious neuromyasthenia. CMAJ. 1986 Jan 15;134(2):106. PMID: 3942909

Salit IE. Post-infectious fatigue. Can Fam Physician. 1987 May;33:1217-9. PMID: 21263931

6) Dr. Gary Holmes and Dr. Jonathan Kaplan of the Holmes Committee discussed Myalgic Encephalomyelitis in a paper focused on the Tahoe cohort in 1987:

Holmes GF, Kaplan JE, Stewart JA, Hunt B, Pinsky PF, Schonberger LB. A cluster of patients with a chronic mononucleosis-like syndrome: Is Epstein-Barr virus the cause? JAMA. 1987 May 1; 257 (17).

“Since the 1930’s, several reports have described syndromes of chronic debilitating fatigue associated with low-grade fever, myalgias, arthralgias, sore throat, headaches, neurological complaints, and a variety of other symptoms. Although these syndromes are remarkably similar, they have been described by several names, including Akureyri disease, Iceland disease, atypical poliomyelitis, benign myalgic encephalomyelitis, epidemic neuromyasthenia, encephalomyelitis and postviral syndrome. Despite intensive searches for the etiologic agents of these syndromes, all have remained idiopathic. Some reports, however, have described syndromes that were thought to represent recurrent acute infectious mononucleosis.

“In the past 15 years, Epstein-Barr virus (EBV) has been established as the cause of most cases of infectious mononucleosis, and EBV serological data has become commercially available. The suggestion that the fatigue syndrome might represent recurrent infectious mononucleosis has prompted recent attempts to link the syndrome with EBV. Several studies have described a syndrome of chronic fatigue that is similar to those described earlier and that is associated with persistently elevated serum titres of antibody against the early antigen (EA), viral capsid antigen (VC), and nuclear antigen (EBNA) of EBV). This syndrome has become known as chronic mononucleosis or, more specifically, chronic EBV disease (CEBV).

“In September 1985, we investigated a cluster of mononucleosis-like illnesses, thought to represent CEBV, in Nevada. The results suggest that EBV serology is inadequate for diagnosing these illnesses and that the illnesses may not be caused by EBV. However, they also suggest

that some patients with these illnesses have an abnormality of infectious and/or immunologic origin.”

7) The paper published in 1988 by the Holmes Committee creating an illness called “Chronic Fatigue Syndrome.”

Holmes GP, Kaplan JE, Gantz NM, Komaroff AL, Schonberger LB, Straus SE, Jones JF, Dubois RE, Cunningham-Rundles C, Pahwa S, et al. Chronic fatigue syndrome: a working case definition. *Ann Intern Med.* 1988 Mar;108(3):387-9. PMID: 2829679

8) The Fukuda definition of CFS.

Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. *Ann Intern Med.* 1994 Dec 15;121(12):953-9.

9) The Reeves definition of CFS.

Reeves WC, Wagner D, Nisenbaum R, Jones JF, Gurbaxani B, Solomon L, Papanicolaou DA, Unger ER, Vernon SD, Heim C. Chronic fatigue syndrome—a clinically empirical approach to its definition and study. *BMC Med.* 2005 Dec 15;3:19. PMID: 16356178

10) The International Consensus Criteria:

Carruthers BM, van de Sande MI, De Meirleir KL, Klimas NG, Broderick G, Mitchell T, Staines D, Powles AP, Speight N, Vallings R, Bateman L, Baumgarten-Austrheim B, Bell DS, Carlo-Stella N, Chia J, Darragh A, Jo D, Lewis D, Light AR, Marshall-Gradisbik S, Mena I, Mikovits JA, Miwa K, Murovska M, Pall ML, Stevens S. Myalgic Encephalomyelitis: International Consensus Criteria. *J Intern Med.* 2011 Jul 20. PMID: 21777306

11) The Canadian Consensus Criteria:

Carruthers BM, Jain, AK, De Meirleir KL, Peterson DL, Klimas NG, Lerner AM, Bested AC, Henry PF, Joshi P, Powles ACP, Sherkey JA, van de Sande M. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Clinical Working Case Definition, Diagnostic and Treatment Protocols. *Journal of Chronic Fatigue Syndrome*, Vol. 11(1), 2003.