

ME RESEARCH

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MEDICAL RESEARCH: Seeking objectivity in ME studies

As Dr. P. Levine of the U.S. National Institute of Health writes:

“There is general agreement that ME is a severe debilitating illness that deserves the utmost attention of the clinical and scientific communities.”

Refuting misconceptions

Despite the volume of attention that ME is getting in the research field, there are a host of misconceptions and biases when it comes to understanding Myalgic Encephalomyelitis (ME) which muddy the results and lead to inappropriate clinical interventions. Without definitive tests as yet, diagnosis relies on self-reported symptoms which fit the American CDC, British or Australian criteria for ME/CFIDS.

As a result, many believe these subjective reports are highly suspect, exaggerated and belie an emotional or malingering condition. Often seen as psychosomatic, many patients are told, “It’s all in your head.” But sound research does not back up this all too common medical bias.

There are an overwhelming number of studies regarding ME and Fibromyalgia. Dr. Michael McGoodwin, MD, has compiled a list of over 2600+ references which can be downloaded from www.vgard.net/pages/medrefs.html (or click on www.vgard.net/downloads/cfsfmna.txt for an instant download of abstracts). A selection of over 100 medical research abstracts covering a range of medical specialties are also available at www.aacfs.org/html/selbibl.htm . (For other lists, conference abstracts and critiques, check out our web links for physicians under [Resources](#).) A sample of research indicating physiological abnormalities distinct to ME is summarized below.

We hope this summary will point doctors, legislators and insurance companies to the research which clearly demonstrates ME is *not* an imaginary illness which desperate people use to cover underlying emotional problems or a desire to avoid social responsibility! To repeat the U.S. Assistant Secretary for Health Dr. P. R. Lee:

“Although we have not yet been able to fully describe the basis for ME, nor do we fully understand the mechanisms of ME, it is very real and it is not the figment of anyone’s imagination. ME is devastating to many who have it.”

Confusing ME with hypochondriasis, malingering and depression

In some ways it is easy to understand why medical professionals and researchers confuse ME with hypochondriasis, malingering and depression. The bizarre range of fluctuating, unpredictable symptoms seems to be beyond explanation. It’s easy to assume, therefore, that people with ME are making these symptoms up. Also many of the symptoms, such as sleep disruption, lethargy and slowed cognitive functioning *look* like depression. Thus, many professionals equate ME with depression, without further investigation.

But if--and this is a big IF--if there is a physiological basis for the circulatory problems evident in many people with ME, for example, and blood (and the oxygen it delivers) isn't flowing properly to the brain and muscles, then a lot of the ME symptoms are explained right there and indicate that people aren't imagining this disease for some perverse emotional benefit to gain attention or to avoid responsibility.

If someone is experiencing perplexing, inexplicable symptoms which fluctuate with no apparent pattern or cause, one is bound to focus a lot on one's illness and seem preoccupied with it. If there is an organic basis for these symptoms, then having an extreme concern about one's condition does not mean that person is a hypochondriac who imagines symptoms in order to gain others' sympathy.

As for malingering and depression, many people with ME try everything in their power to recover and more often than not push themselves beyond their levels of endurance. Most desire to be working and contributing to society. If they experience depression in their ME state, it is not because they are too depressed to care to do anything, it's because they are upset that their bodies won't cooperate with all they long to be able to do. When their energy levels improve enough so they can engage in life again to some degree, their reactive depression will lift.

Lessons from MS, GWS, RED and PPV Research

People with ME still face the bias that their condition is psychosomatic which also was prevalent several decades ago regarding people with MS--until damage to the myelin sheathing was discovered and MRI's confirmed abnormal brain activity. Gulf War veterans who have suffered an array of disturbing and perplexing symptoms have also been treated similarly. Recent evidence of abnormal brain activity in Gulf War Syndrome (GWS) has challenged the biases of the governments and doctors unwilling to recognize the legitimacy of this disease.

One reason people with GWS have been dismissed as psychosomatic hypochondriacs was because their groupings of symptoms varied from person to person. However, recent research has shown significant correlations between the differing arrays of symptoms and the specific area or areas in the basal ganglia and/or brain stem which are affected. (Drs. Robert Haley & James Fleckenstein, http://www.swmed.edu/home_pages/epidemi/gws)

One of the problems with much research is that it looks for a single causal factor in a disease. With the wide variety of symptoms showing up in people with ME, there are likely multiple and/or differing causes for the syndrome of symptoms.

People with post-polio virus (PPV), e.g., used to be classified under CFS until the reason for their similar symptoms to ME was discovered. Another subset of people diagnosed with ME have shown to possess an abnormal RNase L protein and it has been suggested their disease be called RNase-L Enzyme Dysfunction (RED) instead of CFS or ME.

Recent research has also shown that there could be four different causes for MS. This finding may explain why a treatment for MS which relieves one person's symptoms may actually make

another person with MS worse. (Reuters: Washington, June 8, 2000; see archives, www.co-cure.org)

As with MS and GWS, people's subjective ME symptoms are beginning to be explained by numerous research studies. But before going to those studies, it is important to be aware of problems within ME research which promote the bias that this is not a "real" disease.

Problems with Definitions

Chronic Fatigue

A key problem with research and diagnosis is that the parameters of an illness can be poorly defined, thus flawing the research methods used. Part of the difficulty with ME research and diagnosis is in the use of the term "chronic fatigue."

Some believe ME to be a constant state of extreme fatigue which doesn't allow patients to ever get out of bed. This unfounded belief doesn't take into account the fluctuating levels of fatigue and other symptoms which make up ME.

In the general public, many people with their "rat race" existence feel tired all the time or feel "chronically fatigued". They do not, however, have the array of *other* ME symptoms and they are able to still function efficiently enough to carry on basic tasks of daily living.

There are also medical causes for *other* chronically fatiguing conditions which are *not* ME. Depression is one of these conditions, and people with ME are often mistakenly given the primary diagnosis of clinical depression.

Defining 'Recovery' and Following up

A key difficulty in studies which examine the outcomes of treatment is that the term 'recovery' needs to be carefully defined and used consistently across all research studies. As with AA, where the question asked is, 'Does one ever *recover* or is one in a *constant state of recovery*?', researchers need to follow through long enough to see if people who have 'recovered' from ME actually become worse again at some future point, possibly by overexerting themselves.

Some people with ME may label themselves as 'recovered' if they achieve 75% functioning, e.g., of their pre-illness condition for 6 months. (They may then try for 100% and subsequently 'crash' again.) Others who achieve similar levels, e.g. 75%, may still label themselves as disabled because they have not reached pre-illness functioning levels. Researchers need to clearly define what is meant, therefore, by 'partial' and 'full' recovery; 'partial' and 'significant' improvement.

Differentiating ME from Depression is crucial

ME is often equated with depression, and as a result, it is often dismissed as such. There are several important consequences of such an equation on medical treatment and research. The

distinction between ME and depression is crucial for conducting accurate research and formulating appropriate treatments.

Research may find a co-existing depression in *some* people with ME, but it needs to be determined if the depression is the result of the various losses and struggles people with a debilitating physiological illness have. What normal person wouldn't struggle with depression when they have an array of unexplainable, vacillating symptoms along with fatigue levels beyond belief and who, as a result of their inability to function as they once did, lose their jobs, savings, homes, friends and even spouses? Just because some people with ME become depressed as a result of their ME does not mean that ME *is* depression.

Confusion of ME with depression in research and medical practice may also result from finding people who were *already* depressed when ME struck them. Again, this does not mean ME is the same thing as depression. It does not stand to reason that depression causes ME or that ME symptoms are part of a depressive episode, since there are many people who became disabled with ME at a point in their lives when they were extremely active, healthy, content and socially engaged.

By mislabeling ME as depression, appropriate treatments for ME (as they become known) will be not be properly considered by physicians and mental health workers. Such mislabeling diverts attention to the real issues ME people face.

On the other hand, it is equally important to determine the co-existence, if any, of depression in people with ME. *If* the reactive depression described above does become a major depressive episode or a recurring clinical depression, *then* treatment interventions for depression would be appropriate. For people who were depressed *when* they became disabled with ME, it is important that they be treated for the depression so that the depression doesn't complicate their chances of recovery from ME.

Even if ME proved to be a variant of depression (which current research does not bear out), it cannot be "blown off" as something not important. Depression can be a life threatening illness and needs to be taken seriously. Yet people with ME are often not taken seriously because doctors diagnose them as being "simply depressed" as if sheer will power and changed attitudes will do "the trick".

Both conditions, ME and depression, are serious and need to be treated as such. Where they happen to overlap in an individual, both conditions need to be treated. Where either exists in an individual, unrelated to the other condition, it needs to be treated appropriately, either as ME *or* depression in order for the treatment to have any possible therapeutic effects.

Problems with Research Methods

Exercise study

It is well known that exercise can help alleviate symptoms of depression. One group of researchers conducted studies which show people complaining of chronic fatigue can also be

helped through exercise. Based on this finding, insurance companies often demand claimants with ME either go to aerobics classes or be cut off their disability coverage.

The flaw in this study on exercise, however, is that the researchers did not test anyone with chronic fatigue who experienced insomnia. Since most people with legitimate ME have disordered circadian cycles, and there is research which shows that exercise can make ME symptoms worse, eliminating this group of chronically fatigued people and then applying the findings to them is a serious and suspect misapplication of research! (see Dr. P. Corning, www.freenet.carleton.ca/ip/social.services/cfseir/naneir/news/035-Apr99.html)

Another research caution is in order with regard to exercise studies: although exercise has been shown to be helpful as a component in the treatment of insomnia in a variety of conditions, it still needs to be incorporated at an *appropriate phase* in the overall treatment. Research needs to determine whether *other factors* involved in the insomnia of people ME need to be treated first before exercise would prove beneficial.

Depression / ME study

Psychologist Dr. E. Goudsmit notes some conflicting statements by the researchers of a study on blood flow to the brain in people with ME compared with people who have major depression. Although the research found similarities as well as differences, the reviewer notes that while the abstract states that the CFS patients “were not depressed” *according to psychological testing the researchers conducted*, the abstract later refers to them (for no apparent reason) as having “high levels of depression.”

This confusion may reflect a bias on the part of the researchers that they ignored their own test findings to support a *belief* that CFS is depression. There were also conflicting statements in the abstract about whether the SPET scans were taken while subjects performed cognitive tests or when they were at rest. (*British Journal of Psychiatry*, 2000, 176, 550-556 cf. Abstract reviewer: Dr. E. Goudsmit, <http://freespace.virgin.net/david.axford/letter07.htm>)

These problems in methodology and in applying research findings can make an enormous difference in how people with ME are viewed and treated. Care needs to be taken when statements about ME are made based on supposedly unbiased “objective” research. The unwitting biases of researchers and their funders agendas can influence their “results”!

Research supports biological evidence of ME uniqueness

Despite the possible biases in the conclusions by these British researchers, they did note differences on psychological testing and on SPET scans between those who have ME and those who suffer a major depression.

Numerous studies conducted by different researchers and reported in a variety of medical journals and on medical research web sites confirm biological distinctions in people with ME as compared to healthy people, people suffering from depression and those with other illnesses. These differences are summarized below.

RESEARCH: ME vs. Clinical Depression

(For the sake of simplicity, references cited include only the journal name, date, volume and page numbers, or the web site. Article titles and research authors names can be obtained by checking web sites and the journals themselves. In Vancouver, people can find medical journals at the Woodward Medical Library at UBC.)

(The following studies cited are but a small sample of the research. For more information, go to [Resources](#) to click on Web Links to web sites with more research information.)

(The studies cited indicate neuropsychological conditions in a representative number of people with ME, and not necessarily in all subjects with ME who were studied.)

Compared to people with major / clinical / primary depression, people with ME showed:

- CFS and MS groups show significantly lower percentage of self-reproach symptoms on the Beck Depression Inventory than Clinical Depression groups. Depression groups show lower percentage of somatic symptoms than CFS and MS groups.

J Affect Disord 1996 Jun 20:39(1);21-30

- While CFS and Depression subjects were similar in cognitive performance and differed from MS and healthy controls, the most significant impairment noted was in the information processing speed of the CFS group.

J Neurol Neurosurg Psychiatry 1995 Jan: 58(1);38-43

- SPECT scans showed the average number of regional brain defects (mostly in the frontal and temporal lobes) were 1.66 for healthy controls, 9.15 for subjects with AIDS dementia, 6.53 for those with CFS and 6.43 for those with Major Depression, but the mid-cerebral uptake indexes were significantly lower in the CFS and AIDS groups than in the Depression and Healthy groups. The researchers note that CFS “may be due to chronic viral encephalitis; clinical similarities between [ME] and depression may be due to a similar distribution and number of defects in the two disorders.”

AJR Am J Roentgenol 1994 Apr:162(4);943-951

- “Patients with CFS had marked impairment [in functional health status], in comparison with general population and disease comparison groups [of MS, diabetes, heart disease and depression]. Moreover, the degree and pattern of impairment was different from that seen in patients with depression.”

Am J Med 1996 Sep; 101(3):281-290

- CFS groups were distinguished from MS and depression groups by the following: myalgias, post-exertional malaise, headaches, and a group of infectious-type symptoms (i.e., chronic fever and chills, sore throat, swollen glands in the neck or underarm areas).

Am J Med 1996 Jan;100(1):56-64

- Test results suggest upregulation of hypothalamic 5-hydroxytryptamine receptors in patients with postviral fatigue syndrome, but not in people with primary depression.

British Medical Journal 1992 Apr 18;304(6833):1010-1012

- SPET results show both CFS and depression patients had increased blood flow in the right thalamus. But CFS patients also showed increased perfusion in the left thalamus not seen in the depressed group, while they showed no reduction in prefrontal perfusion as seen in the depressed group.

British Journal of Psychiatry, 2000, 176, 550-556

- CFS patients generally performed worse on cognitive tests than healthy controls, but better than patients with severe depressive illness. Both CFS and depressed groups had markedly impaired motor function compared with healthy controls. Depressed subjects showed a significantly greater diurnal improvement in maximal voluntary contraction than healthy controls, and these diurnal changes may differentiate depression from CFS.

Psychological Medicine, 2000 Mar;30(2):433-442

- Compared with healthy controls, and patients with major depression, lupus, and MS, those with CFS have significantly elevated bioactive transforming growth factor-beta (TGF-beta).

J Clin Immunol 1997 Mar;17(2);160-166

- There is increased serotonin activity and significantly higher concentrations of prolactin in the blood of men with CFS than in other men, whereas depressed individuals have unchanged or reduced prolactin responses to D-fenfluramine “making it unlikely that [ME] and depression share a common pathophysiology...”

British Medical Journal 1997;315:164-165

- Contrasting neuroendocrine responses have been observed between depression and CFS.

Baseline-circulating cortisol levels were:

highest in depressed groups; lowest in CFS groups and intermediate in healthy controls;

whereas prolactin responses to selective 5-HT-releasing agent d-fenfluramine were:

lowest in depressed groups; highest in CFS groups and intermediate in healthy controls.

Thus,

Depression is associated with *hypercortisolaemia* and *reduced* central 5-HT neurotransmission;

CFS may be associated with *hypocortisolaemia* and *increased* central 5-HT function.

“These findings attest to biological distinctions between these two disorders.”

Journal of Affective Disorders 1995 Aug 18;34(4);283-289

similarly: J Psychiatr Res 1997 Jan-Feb;31(1);69-82 for a review of neuroendocrine correlates.

RESEARCH: ME biology vs. healthy states

(For the sake of simplicity, references cited include only the journal name, date, volume and page numbers, or the web site. Article titles and research authors names can be obtained by checking web sites and the journals themselves. In Vancouver, people can find medical journals at the Woodward Medical Library at UBC.)

(The following studies cited are but a small sample of the research. For more information, go to [Resources](#) to click on Web Links to web sites with more research information. The studies cited indicate biological and neurocognitive conditions in a representative number of people with ME, and not necessarily in all subjects with ME.)

Immunology

Compared with healthy people, people with ME generally showed:

- T helper-1 and/or T helper-2 imbalance and immune dysregulation; decreased NK cell activity, lymphocyte mitogenic assay, changes in the ratio of T-helper to T-suppressor cells, and changes in CD11b/CD8, HLADR/CD8 and CD38/CD8 have been continuously observed in CFIDS patients
www.immuno-sci-lab.com/fatigue.html
- higher levels of bioactive TGF-beta (transforming growth factor-beta) than in healthy controls, major depression, lupus or MS (both relapse/remitting and chronic progressive)
J Clin Immunol 1997 Mar;17(2):160-166
see also: Cytokine 1991 Jul;3(4):292-298
- lower numbers of natural killer NKH1+ T3 lymphocytes
J Immunol 1987 Nov 15;139(10):3306-3313
- low natural killer (NK) cell cytotoxicity; elevated NKH.1 (CD56), but the killing of K562 tumor cells per CD56 was significantly diminished; an increase in the percentage of suppressor-cytotoxic T lymphocytes + CD8; elevated numbers of CD2 cells; and a significant decrease in suppressor-inducer subset of CD4+ CD45RA+ cells
J Clin Microbiol 1990 Jun;28(6):1403-1410
- reduced CD8 suppressor cell population; increased activation markers on CD8 cells
Lancet 1991 Sep 21;338(8769):707-712
- a higher mean of CD4 / CD8 T-cell ratio
Ann Intern Med 1992 Jan 15;116(2):103-113
- significant increase in proportions of CD4+ ICAM-1+ T cells;

increased density of ICAM-1 (intercellular adhesion molecule 1);
increase in lymphocyte function associated antigens (LFA-1)
Scand J Immunol 1991 Mar;33(3):319-327

- significantly increased TNF- α & IL-6 production and decreased IL-10 production
J. Psychiat Res 1997;Vol 31(1);149-156

- abnormally high level of antibodies to their own cellular proteins were found in about half of those diagnosed with CFS.
Journal of Clinical Investigation 1996;98:1888-1896

Virology

Compared with healthy people, people with ME generally showed:

- clinical and serological associations with various human herpes viruses, particularly EBV (Epstein-Barr), HHV-6, Spuma virus, human T-lymphotropic virus (HTLV) types 1 and 2, human B-lymphotropic virus (HBLV), and possibly mycoplasma incognitus.

www.immuno-sci-lab.com/fatigue.html

- a higher percentage with active replication of human herpesvirus 6 (HHV-6)

- a higher percentage with HHV-6A

- a higher percentage were positive for HHV-6 EA IgG &/or IgM (77% CFS v. 12% healthy)

Ann Intern Med 1992 Jan 15;116(2):103-113

J Clin Microbiol 1995 Jun;33(6):1660-1661

J of Infect Dis 1995 Nov;172(5):1364-1367 (respectively)

similarly, see also:

Scand J Immunol 1991 Mar;33(3):319-327

Microbiol-Immunol 1994;38(7):587-590

J Chronic Fatigue Syndrome 1996;Vol2(1):3-12 (Italian data)

- microplasmal infections in CFS/FM and GWS subjects whereas healthy controls showed no reactivity in blood leucocytes by polymerase chain reaction/hybridisation.

www.anzmes.org/sydney98-day1.htm ; Institute of Molecular Medicine, California

- enterovirus-specific RNA in serum, buffy coat and stool samples (though not in Sweden)

J Med Virol 1995 Feb;45(2):156-161

similarly, see also: Lancet 1988 Jan 23;1(8578):146-150

v. Scand J Infect Dis 1996;28(3):305-307 (Sweden)

- significantly lower mean base levels of latent 2-5A synthetase;
higher levels of bioactive 2-5A and higher levels of RNase L activity

Clin Infect Dis 1994 Jan;18 Suppl 1:S96-S104

- biochemical evidence for a variant low molecular weight (LMW) 2-5A-dependent RNase L protein in a sub-group of CFS patients, suggesting that those with the LMW protein abnormality be identified as having “RNase-L Enzyme Dysfunction Disease” (REDD).

This new enzyme “may explain why CFS patients’ bodies have a hard time maintaining the energy necessary for cellular growth.”

Journal of Interferon and Cytokine Research, 1997; 17:377-385

- the key regulatory enzyme, 2-5A Synthetase, in the interferon induced antiviral defense mechanism is not functioning properly: activated 2-5A synthetase was increased up to 10 fold, intracellular levels of bioactive 2-5A was increased up to 220 fold, and RNase L was elevated up to 45 fold, and the RNase L inhibitor was either in low levels or absent in CFIDS patients.

www.immuno-sci-lab.com/fatigue.html

Neuroendocrinology

Compared with healthy people, people with ME generally showed:

- significantly low baseline arginine-vasopressin (AVP) levels
Acta Neurol Scand 1993 Mar;87(3);234-238
- significant reduction in basal plasma levels of MHPG (3-methoxy-4-hydroxyphenylglycol); significant increase in basal plasma levels of 5-HIAA (5-hydroxyindoleacetic acid)
Biol Psychiatry 1992 Dec 15;32(12);1065-1077
- significantly reduced basal evening glucocorticoid levels;
low 24-h urinary free cortisol excretion,
elevated basal evening ACTH concentrations, and
increased adrenocortical sensitivity to ACTH, but a reduced maximal response
J Clin Endocrinol Metab 1991 Dec;73(6);1224-1234
- increased prolactin and more nausea in response to 5-HT1A receptor agonist buspirone
J Affect Disord 1996 Nov 4;41(1);71-76
- increased serotonin activity and significantly higher concentrations of prolactin in the blood of men with CFS
British Medical Journal 1997;315:164-165

Neurocognitive Studies

Compared with healthy people, people with ME generally showed:

- significant impairment in learning and memory in a subset of CFS patients
Biol Psychiatry 1996 Sep 15;40(6);535-541

- CFS patients generally performed worse than healthy controls on a battery of cognitive tests, including measures of psychomotor speed and memory, and had markedly impaired motor function compared with healthy controls.

Psychological Medicine, 2000 Mar;30(2):433-442

Cardiovascular Findings

Compared with healthy people, people with ME generally showed:

- an abnormal physical response to tests requiring mental effort (Gulf War vets with chronic fatigue didn't have a rise in blood pressure during mental tests whereas vets without CF did).

<http://www.pslgroup.com/dg/1DA4F2.htm>

- 5 different patterns of orthostatic (circulating blood volume) irregularities from a lying down position to standing in CFIDS patients, but absent in healthy subjects:
(1) orthostatic systolic hypotension; (2) orthostatic diastolic hypotension; (3) orthostatic diastolic hypertension; (4) Orthostatic postural tachycardia; and (5) orthostatic narrowing of pulse pressure. These subgroups may account for different responses to various treatments.

Drs. David S. Bell and David Streeten, The Lyndonville [NY] News, reported in chronicfatigue.about.com/health/chronicfatigue/library/weekly/aa072600b.htm

- a great number with neurally mediated hypotension

JAMA 1995 Sep 27;274(12):961-967

- abnormal T-wave inversions and/or flattenings in 24 hour electrocardiogram monitor readings and stationary or declining ejection fraction in the left ventricle.

Infectious Diseases in Clinical Practice, 1997; 6:239-243

see also Chest, 1993; 104:1417-1421

- statistically significantly lower levels of a blood enzyme responsible for oxygen delivery called 2,3 diphosphoglycerate (2,3-DPG)

The Toronto Star, Fri 22 May 1998 "Teenager finds marker that eludes experts"
cited in ME & You, Vol. 14.

- the rate of blood flow during muscle activity is decreased in people with ME rather than increased as in healthy people.

NZ Med J 1989;102(864):126-127 (cited in The CFIDS Chronicle, Summer 1995)

- a higher percentage of irregularly shaped red blood cells which persist in ME subjects from around the world, including subjects from NZ, Australia, South Africa, USA, and BC.
(While irregular shaped RBC increase by the completion of a marathon by healthy people, the normal, higher percentage of regularly shaped RBC returns quickly in their blood.)
cited in The CFIDS Chronicle, Summer 1995; correspondence from Dr. Simpson to MEBC

Sleep, Exercise and Fluctuating Symptoms

Compared with healthy people, people with ME generally showed:

- spend more time in bed, but sleep less efficiently and spend more time awake after initially going to sleep

British Medical Journal 1993 May 1;306(6886):1161-1164

- altered patterns of cortisol, prolactin, and NK cells which accompany the alpha EEG sleep disorder, sleepiness, pain and daytime fatigue

www.immunesupport.com/library/showarticle.cfm?ID=87

- exercised muscles generate clearly abnormal responses in people with CFS, significantly more than in sedentary controls; people with ME release twice as much lactic acid into their bloodstream during exercise as healthy people and sedentary control subjects, so they fatigue much earlier and have significantly lower endurance level.

www.networx.com.au/mall/cfs/meeting (cited in www.cfs-news.org; ME & You, Vol. 14)

- the rate of blood flow during muscle activity is decreased in people with ME rather than increased as in healthy people.

NZ Med J 1989;102(864):126-127 (cited in The CFIDS Chronicle, Summer 1995)

- delayed recovery after exercise involving muscle contractions and also at 24 hours later

European Journal of Neurology 1999 Jan;6(1):63-69 (cited in ME & You, Vol. 15)

- abnormal cardiac thallium-201 SPECT scans suggest abnormal ion channel function in ME and may explain the fluctuating fatigue and other ME symptoms

Med Hypotheses 2000 Jan;54(1):59-63

RESEARCH: Prevalence, Prognosis, and Treatment of ME

Prevalence Studies

“In the U.S., over 500,000 Americans are afflicted with CFS, a fact [sic] reported in a Centers for Disease Control publication dated in 1995. A Harvard University study performed that same year estimated the number to be much higher, with nearly 2.5 million suffering from CFS.” (cited in ME & You, Vol. 14). The differences between these two estimates are staggering. Yet either way, it’s still a lot of people suffering from CFIDS/ME. Still, one has to wonder why two respected U.S. institutions could determine such vastly different estimates.

There is no doubt that it is difficult to determine accurately what percentage of the population has ME. Surveys during the 1990s have led to varying estimates as the studies cited above indicate.

One reason for the differences is that differing criteria for CFS are used. Estimates depend on whether American, British or Australian criteria are used. E.g., in a survey of 1000 urban patients in primary care practice 0.3%, 0.4% and 1.0% had CFS using American CDC, British and Australian case definitions respectively (Arch Intern Med 1993 Dec 27;153(24):2759-2765).

How an ME diagnosis is determined or verified in the studies also is a factor in the results. Some studies take samples from clinical files; others do random-sample telephone and mail-in surveys.

Difficulties with clinical-based studies

In cases using patient files, it may not be clear how those case were selected, especially where insurance companies are sponsoring the research. In one study reported to the 1998 AACFS Conference, the doctor presenting on the “overdiagnosis” of CFS, could not explain how the cases given to him for study by an insurance company were selected. Thus, it’s impossible to determine what biases may be contained in their data.

Another problem with relying on doctors’ files in medical-care based studies is that some doctors who are skeptical about ME as a real disease may underdiagnose the disease. Doctors may also overdiagnose ME where people have chronic fatigue alone and misdiagnose it where people’s chronic fatigue symptoms may be for other reasons: lupus, Lyme’s Disease, MS, undetected cancer, depression, etc.

Relying on clinical files as the source for gathering statistics has another inherent problem, especially in the U.S. Some Americans with ME may not have the economic resources to access medical care and therefore would not be included in the sample. Then there are others who have given up on doctors believing them, so they, too, wouldn’t show up in surveys relying on clinical records.

Difficulties with community-based studies

There are also problems with community-based surveys by phone or mail. Are they relying solely on the self-reports of people questioned, or do they follow those claiming to have CFS up with medical examinations to exclude other illnesses and to determine a true ME condition? Do they distinguish between those who are chronically fatigued and those with CFIDS? People dropping out of studies relying on follow-up sessions and questionnaires also make it difficult to know whether they have ME or not and whether their initial answers are reliable.

Considering all these factors, and relying on studies which try to avoid these methodological pitfalls, we can still get a rough idea of rates of ME, at least in the U.S. How accurately these can be applied to Canadian populations still needs to be verified through Canadian studies.

Figuring out the best statistical estimates

In studies regarding specific groups presented at the 1996 San Francisco and 1998 Cambridge AACFS Conferences, it was found that roughly 1% of nurses had CFS, 2.1% of children between ages 5 and 17 met criteria for CFS-like illness (with almost equal distribution between girls and boys), and that 5.1% of Gulf War vets and 1.2% of Gulf era vet controls met criteria for CFS. In terms of the general population, two studies reported in 1995 indicate varying results. One survey based on the Seattle health care system estimated the prevalence of CFS to be 75 to 267 cases per 100,000 persons (or 0.075 to 0.267%). (Ann Intern Med 1995 Jul 15;123(2);81-88) The other study found that a random community sample of 1,031 persons yielded higher results than previous medical-care based studies, and they found CFS rates of 0.2%. (Am J Community Psychol 1995 Aug;23(4);557-568).

Estimates from two random community samples were presented at the 1998 Cambridge AACFS Conference. In both studies people were classified as having either chronic fatigue or prolonged fatigue. Those fitting into the chronic fatigue category were further classified into subcategories: those with CFS-like disorders and those whose chronic fatigue did not meet CFS criteria and those whose chronic fatigue was explained by other illnesses.

In the 1997 San Francisco study of 14,627 adults, no medical evaluations were done to determine exclusionary (non-ME) medical or psychiatric conditions. In the Chicago study of 28,000 adults across race/ethnicity, socio-economic status and gender lines, medical evaluations were done to exclude other illnesses. In the San Francisco study, 0.2% were classified as having CFS-like disorders. In the Chicago study, lower to upper estimates for CFS-like disorders ranged from 1.5% to 2.1%.

(AACFS Conference, Cambridge, MA, Oct., 1998; www.cfids-me.org/aacfs/session1.html) Another community-based survey of 18,000 people in Chicago yielded estimates that 0.42% of the population had CFS. (CFS Research Review, 2000 (winter):1(1);4-5, cited by Dr. Bruce Carruthers, Vancouver lecture, Nov. 4, 2000)

With these community-based studies ranging from 0.075% to 2.1% of the general population, and a medical-care based study ranging from 0.3% to 1% prior to the 1994 CDC case definition

of ME, it is hard to know exactly how many people have ME/CFIDS. But with many of the studies hovering around 0.2% and the more recent study at 0.42%, the numbers likely fall within this range.

Prognosis

Possible factors in prognosis

In a review of 26 studies examining the prognosis of CFS and chronic fatigue, four studies on children found that 54-94% of children recovered over periods of follow-up. Five studies on CFS in adults found that less than 10% return to levels of functioning equal to what they were able to do prior to illness. In the remaining studies, the more stringently the researchers defined CFS, the poorer the prognosis became. Consistent risk factors for poor prognosis were: older age, more chronic illness, having a psychiatric disorder and holding a belief that the illness is due to physical causes. (QJM 1997; Mar 90(3):223-233) (Editorial note: It could be that those who didn't get better did in fact experience debilitating levels of fatigue because of a physically caused illness!)

Another study found that people who have epidemic-associated CFS (where it appears in clusters of the population) had a better prognosis than sporadic cases. (Arch Intern Med 1997 Apr 14;157(7):750-754)

In a review of research examining possible factors affecting prognosis, studies indicate that those with ME who initially had fewer symptoms and fewer abnormal laboratory findings were more likely to have partial or full recovery. Studies also found that rates of recovery were higher for individuals who suffered ME for less than 5 years. Those whose onset of ME was gradual were less likely to recover than those who had a sudden onset. Those who had mild depression (dysthymia) at the first assessment were associated with a poor prognosis. (Summarized in www.co-cure.org/schopflocher/AISH2B.htm)

Prognosis statistics

The following studies examine the percentages involved in no, partial, and full recovery rates. Discrepancies in the percentages may depend of whether people with chronic fatigue, but not necessarily ME, are included in the study, the number of subjects, and the follow-up intervals. In a paper on "The fluctuation and outcome of CFS over time" presented at the 1998 AACFS Conference, researchers found that over the course of two years with 23 people diagnosed with CFS, symptom severity fluctuated, but at the end of about three and one-half years, 13 remained severely ill (57%), 3 slightly improved and 6 greatly improved (39% total), and only 1 recovered (4%). The presence of a depressive or anxiety disorder at the onset of the CFS in some of these people did not predict illness outcomes. (www.cfids-me.org/aacfs/session1.html).

In a paper for the ME/CFS Society of Edmonton, psychologist Dr. D. Schopflocher summarizes six other follow-up studies where the number of subjects range from 29 to 291 and the follow-up interval ranges from 12 months to 48 months. The percentage of sufferers who partially recovered range from 17 to 57%, although what is meant by partial recovery "is neither clear nor

consistent across these studies.” “The percentage of sufferers who have shown no recovery ranges from 37% to 80% with a total proportion of 57.4%....Almost as alarming is the very small percentage of individuals who have shown complete recovery, a total proportion of only 8.7%.” Dr. Schopflocher notes that in an additional 1995 study of 250 CFS sufferers, 63.6% showed no improvement on follow-up, while only 8.4% showed full recovery. He cites a 1997 study which suggests that a subset of people with ME become more disabled over time. (Summarized in www.co-cure.org/schopflocher/AISH2B.htm)

Adding the 1998 AACFS Conference paper results (Hill et al) to an initial Summary Table compiled by Dr. Schopflocher we can see the following results of the studies mentioned above in order of Follow-Up Intervals (decimal % points have been rounded off):

Study / Date / Researchers	Number subjects	Follow-up Intervals	% no recovery	% partial recovery	% full recovery
'93: Hinds et al	291	n/a	46	35	19
'95: Komaroff et al	250	?	64	28	8
'94: Peterson et al	62	12 mo.	60	40	0
'96: Vercoulen et al	246	18 mo.	80	17	3
'95: Clark et al	79	30 mo.	59	39	2
'94: Wilson et al	103	38.4 mo. (av)	37	57	6
'98: Hill et al	23	c. 42 mo.	57	39	4
'93: Bonner et al,	29	480mo.	45	55	0

References: www.co-cure.org/schopflocher/AISH2B.htm; www.cfids-me.org/aacfs/session1.html

ME Treatment

Survey Results

In a patient survey evaluating the effectiveness of various treatments and charted in The CFIDS Chronicle, 1999 July-August, pages 6-9, ME patients reported that the Top Ten most effective treatments (in the order of effectiveness) were:

1. Pacing one's activities
2. Changing one's outlook
3. Avoiding chemicals
4. Sleep
5. Massage and bodywork therapies
6. Pain relief
7. Avoiding certain foods
8. Yoga, Tai Chi and Chi Gong
9. Cognitive Behavioural Therapy
10. Herbal remedies.

Among the least effective reported by the survey group were: aggressive rest; increased salt (for low blood pressure); antidepressants; magnets, Vitamin B-12; and mercury amalgam removal. In roughly 20-30% of cases, people reported some treatments to actually be harmful, including: beta blockers, colonics, Florinef, Chlorazapan, antidepressants, too much bed rest, and graduated exercise programs.

As Dr. Carruthers explained in a lecture in Vancouver on November 4, 2000, with any treatment used for ME, about 20% of patients find it to be effective to varying extents. (MEBC editorial comment: These differences in treatment effectiveness may point to different causes and illness pathways in people with ME and suggest that researchers study sub-groups of people with ME based on symptom groupings and severity as well as treatment modality effectiveness.)

Recommendations for Physicians

In a National Institute of Allergy and Infectious Diseases (NIAID) publication, it is recommended that doctors follow these treatment principles for patients with CFS:

- Establish a therapeutic alliance with patient
- Dispel misinformation about the disease
- Use a medical team approach
- Prescribe symptomatic treatments
- Urge stress reduction
- Introduce slowly graduated exercise
- Suggest rehabilitation therapy to develop energy conservation techniques
- Schedule regular follow-up visits
- Give emotional support.

(NIAID, Chronic Fatigue Syndrome: Information for Physicians, 1996, National Institutes of Health.)

Healing Journey: Hope for Recovery

Based on a qualitative study of extensive interviews with 11 people with ME, Delcie Hill, a nursing instructor in B.C., has developed a model for recovery for people with ME. *

Defining Recovery

One issue that was important in her group of subjects was defining what constitutes recovery. For some it meant being “cured” so that they would be able to function 100%, the way they did in their pre-illness state. For others, significant improvements and increased functioning was interpreted as “recovery,” whereas for others such levels which still fell short of 100% healing were not viewed as “recovered,” although they may be seen as “recovering.”

But regaining a sense of control in their lives, being able to make choices, and not having or letting the ME “beast” dominate them, was seen as part of their recovery or recovery process.

Finding ways to move ME from the forefront of their lives to the background was crucial to their sense of healing. This might mean taking several days of rest to prepare for a strenuous project at work, or choosing to forego social activities in favour of being able to work part-time. Recovery by these definitions and parameters would fit the research definitions of partial recovery or significant improvement versus full recovery or cure. It also points out the importance of subjective interpretation when using the word.

A Model for Recovery

In listening carefully to their stories, Hill discerned several patterns or stages that assisted in the recovery process. Hill has formulated a model to this end.

Experimenting & Making Choices

Each person's journey was unique and involved a "struggle through a maze of trial and error healing approaches in an attempt to find recovery." Learning which approaches for each individual worked and allowed them to move on and which were dead ends was an important element to making good choices.

Legitimizing

The first step to recovery involves legitimizing the ME. This means being believed and properly diagnosed. It is important that the person with ME internally understands and accepts the disease and its imposition on their life. If others (external sources) accept the condition, the person with ME feels more supported. If this acceptance happens early on in the condition, people have a greater chance of recovery. But legitimization from others does not guarantee the person with ME will accept and work with their disease: they may still resist the diagnosis to their detriment.

Putting the Illness in Its Place

Once the ME has been accepted, patients are able to start putting the illness in its place, as they learn what works for them and what doesn't both in terms of physical healing and the healing of their spiritual/emotional/social beings. Learning to negotiate the "critical balance" is important as people with ME begin to listen to their body, learn what their personal limits are, and respect their bodies' "advice" and live according to their limitations.

Redefining Healthy Self

Finally, having learned to do that, people with ME can redefine what healthy now means for them. It likely is not the same as their pre-illness condition. Instead, they learn to accommodate their limitations and find ways to still enjoy life accordingly. As they do so, the ME no longer dominates their lives, they have taken control, made choices and find the ME to be a background feature of their lives.

This process is rather like having an unruly dog or beast enter one's life, tearing up everything, making messes, demanding total attention to the neglect of other things. Living with ME is rather like learning to tame the beast so that you can live together in some form of harmony.

Hill's model of The Three Relational Processes is summarized in this outline:

Legitimizing

Being Believed and Being Diagnosed
Understanding and Accepting

Putting the Illness in Its Place

Healing of the Body, Mind, & Spirit
Physical Healing
Soul Healing
Negotiating the Critical Balance
Listening to My Body
Learning Limits

Redefining Healthy Self

Accepting a New Lifestyle
Accepting CFS as a Background Habitant
Recovery, according to this model, brings a sense of hope to those who suffer ME and can serve as an important guide to family, friends, colleagues, doctors and counsellors who want to help people with ME to recover.

* Hill, Delcie. Successful Healing Pathways toward Recovery from Chronic Fatigue Syndrome. 1996. Master in the Science of Nursing Thesis, University of British Columbia.