



Paradigm Change

M.E. Treatments

No treatments for Myalgic Encephalomyelitis (M.E.) or for the broader category of Chronic Fatigue Syndrome (CFS) have been officially approved thus far in the U.S.

Here is a summary of treatment modalities that have been reported anecdotally or in the medical literature to have positive effects on the illness.

Pathogens:

M.E. patients appear to have a problem with a wide variety of pathogens that normal people's bodies naturally keep in check. Many of these are usually controlled by the Natural Killer Cells, which (along with other components of the immune system) have been found to be dysfunctional in this disease.

Commonly, M.E. patients show abnormal levels of some or all of the following pathogens: herpes family viruses (e.g. EBV, CMV, HHV-6, HHV-7); enteroviruses; various insect-borne bacteria (e.g. borrelia, bartonella, ehrlichia); systemic parasites (e.g. babesia, toxoplasma gondii); other bacteria (chlamydia pneumoniae, streptococcus, staphylococci, rickettsiae); mycoplasma; coxiella burnetii (Q fever); parvovirus B19; intestinal parasites (e.g. blastocystis, giardia, other amoebas, worms); and fungi (e.g. aspergillus, candida).

These infections are mostly reactivated intracellular ones, meaning that they show up as IgG rather than IgA or IgM on lab tests. Infections can be systemic or settle into specific organs in the body.

While it seems like killing these infections would be a good idea, many M.E. patients (especially those who are severely ill) have a very hard time with this. Like AIDS patients, they often get what is known as an IRIS (Immune Reconstitution Inflammatory Syndrome) response. Because inflammation is particularly problematic in M.E., this sort of "die-off" or "Herxheimer" response can make patients significantly sicker, sometimes permanently so.

Even when pathogen killers are tolerated, they usually work slowly in M.E. patients. Often months are needed before improvements are noted, and patients who discontinue the treatments often relapse.

Ampligen is an experimental intravenous drug that has been used in M.E. on a compassionate care basis off and on since the mid-1990s. It appears to work as an



Paradigm Change

“immunomodulator,” changing the cytokine balance so that the sufferer’s system can better address infections while simultaneously experiencing less damage from runaway inflammation. Many extremely ill patients report experiencing substantial improvements while on the drug and a few studies have been published demonstrating its effectiveness, but the effects have not been consistent across patients and the drug has yet to be approved. The drug is currently offered on a “cost-recovery” basis to patients (as much as \$50,000 a year, only some of which is ever covered by insurance), and only a handful of M.E. specialists offer it. Thus, few M.E. patients have access to it.

A number of doctors specializing in M.E. have experimented with drugs targeting herpes family viruses, since these viruses can cause serious damage when they are not kept in check by the immune system. For instance, CMV attacks the heart; EBV causes non-Hodgkins lymphoma; and HHV-6A (an uncommon virus often found in severely ill ME/CFS sufferers) causes severe neurological damage. “Heavy duty” drugs that have been studied include valgancyclovir, cidafovir, foscarnet and ribavirin; other drugs commonly used for herpes simplex (such as valacyclovir, famcyclovir and acyclovir) also are used.

Many patients do not tolerate antiviral drugs (more because of “die-off” responses than side effects); some do not benefit; and a few report significant improvements. Studies done on valgancyclovir by Dr. Jose Montoya of Stanford University suggest that patients who have been sick for less time may be more likely to show a positive response to the drug.

“Lyme Literate Medical Doctors” (LLMD’s) attempt to treat bacteria, mycoplasma and parasites. Because of the nature of the infections, certain drugs (such as doxycycline, minocycline, azithromycin, clarithromycin, rifaximin and metronidazole) tend to be most commonly prescribed. As with the herpes family viruses, these treatments prompt a range of results: many patients cannot tolerate the drugs, some experience no benefit, and a few get significantly better.

Nystatin is a drug used to target overgrowths of candida in the intestinal tract. Other antifungals such as fluconazole target fungal infections throughout the body. Fungal infections tend to become resistant to these drugs fairly easily, meaning that they can be a recurring problem.

Some doctors use transfer factors, herbs or other supplements to attempt to address pathogens, in addition to or instead of prescription drugs. These also can provoke “die-off” responses.

Research from 2009 reporting an association between M.E. and the retrovirus XMRV led to a few patients experimenting with the antiretroviral drugs raltegravir, zidovudine and



Paradigm Change

tenofovir, found in laboratories to be effective at controlling the virus. Again, some patients found that an IRIS response kept them from being able to tolerate the drugs (problems with side effects seemed less common); some patients showed no change; and a few patients reported improvements (though without getting close to full recoveries). XMRV has since been generally accepted as not being associated with the disease.

GcMAF, a substance that activates macrophages to kill pathogens, has been tried in M.E. as well as in AIDS and cancer. M.E. patients report the usual mixed results seen with the other pathogen killers.

Toxins:

M.E. patients tend to have problems with toxins in general, but especially with inflammatory toxins. Toxins that are particularly inflammatory include ones made by environmental molds and other microorganisms (such as those present in water-damaged buildings and fields treated with the pesticide Roundup); certain metals (such as mercury and aluminum); and naphthalene.

One study reported finding mycotoxins (made by toxic molds) in the urine of 93% of M.E. patients, and many patients trace their start of M.E. to a toxic mold exposure. A leading researcher and physician in the field, Ritchie Shoemaker, reports that most M.E. patients have HLA DR genotypes that he believes are associated with difficulties detoxifying mold and/or Lyme toxin, resulting in innate immune system regulation problems.

Shoemaker's recommendations include evacuation from moldy buildings, the drug cholestyramine to remove toxins through the intestines, and treatments aimed at restoring neuropeptide regulation of immune function and poor capillary circulation. However, severely affected M.E. patients frequently report not tolerating the cholestyramine and not experiencing much noticeable improvement from moving or the other treatments. It is possible that removal of patients from a moldy environment (or the proper remediation of mold present) may prevent further declines or allow slow long-term improvements, however.

Some patients state that just as some people have a hyper-reactivity to gluten, they have a hyper-reactivity to even tiny amounts of mold toxin. They say that by staying out of moldy buildings and certain outdoor environments (or showering after visiting), and by discarding contaminated belongings, they have experienced dramatic health improvements and become more able to tolerate treatments such as pathogen killers.

The mercury in vaccines, amalgam fillings and seafood is thought by some to possibly be problematic for M.E. sufferers. Many patients report first getting sick, or permanently



Paradigm Change

getting much worse, after getting a vaccine, but whether this is due to the inflammation from the immune activation, the mercury, the adjuvants, or a contamination with some kind of pathogen is unclear.

Some patients report that their condition became worse after improper removal of amalgam fillings (the protocol recommended for this population is to use a dental dam and other techniques to prevent the inhalation or ingestion of the loosened-up material). A few patients also report doing better after careful removal of root canals.

Naphthalene is a chemical present in some kinds of mothballs. Some doctors report that patients have experienced severe reactions, such as passing out, as a result of tiny exposures.

Most M.E. patients react negatively to a variety of chemicals, such as bleach, tar, gasoline, air “fresheners,” pesticides and perfume. Some display Multiple Chemical Sensitivity (MCS), with even tiny amounts of any kinds of chemicals causing severe reactions.

Techniques for the removal of toxins from the system include nutritional supplements to support natural processes; binding them for removal through the intestines (with cholestyramine or natural substances); and sweating them out (e.g. with regular or far-infrared saunas or at hot springs). Many M.E. patients get very sick when they attempt to detox, and regardless improvements tend to come slowly.

The Gut:

M.E. sufferers generally have a variety of problems with their intestinal tract, including dysbiosis (fewer “good” microorganisms and more “bad” ones than normal people have); intestinal permeability (“leaky gut”); inflammation; and gut problems (such as “Irritable Bowel Syndrome”). With recent medical thought suggesting that a high percentage of immunity stems from the gut, many M.E. doctors have focused their attention on improving its function.

Ideally, probiotics crowd out candida, problematic bacteria and other pathogens in the gut. Supplementing probiotics (with general or specific strains) is a common treatment, with most M.E. patients finding that they need to introduce massive quantities (such as can be obtained only with homemade kefir or yogurt) to get any noticeable results. Transplants of fecal matter from healthy donors (such as newborn babies) also have been proposed in an attempt to introduce a better balance of microorganisms into the intestines.



Paradigm Change

Avoidance of sugar and other refined carbohydrates is usually counseled, to attempt to keep candida from blossoming. Targeted antibiotics or herbs to address specific pathogenic bacteria or parasites in the intestines are sometimes used.

M.E. sufferers also frequently have high stomach pH and insufficient digestive enzyme production, and thus can benefit from supplements with hydrochloric acid and enzymes.

Leaky gut is a problem in autism as well as M.E., with no particularly effective drugs or supplements yet available to address the problem. A main intervention here is to look at diet, since undigested particles of certain kinds of foods can cause severe inflammation if they penetrate the inner wall of the intestinal tract. Gluten is a main offender, with many people finding that even tiny amounts of wheat are enough to set off a major reaction. Other foods can be problematic as well.

As in autism, the diet that seems most consistently helpful for M.E. patients is the “caveman” one: vegetables, meats, nuts, olive oil and possibly small amounts of certain fruits. Because M.E. sufferers tend to be sensitive to toxins, avoidance of processed and non-organic foods is preferable.

Nutritional Deficiencies:

Proper methylation is needed for the utilization of glutathione. If this does not occur, people have problems with a wide variety of systemic processes, including detoxification, energy production and control of pathogens. A number of researchers have suggested that methylation difficulties are present in autism, and Dr. Rich van Konyenburg and other ME/CFS specialists have speculated that this may be the case in M.E. as well.

At the root of the problem may be a difficulty in converting folic acid to an activated form of folate. Supplementing with folinic acid (present in the drug leucovorin) or tetrahydrofolate (present in the drug Deplin and supplements containing Metafolin) can overcome this problem. Other nutrients (such as SAM-e, phosphatidyl choline, phosphatidyl serine and high doses of B12) also may be helpful or necessary to address methylation difficulties, some doctors say.

Some people find intravenous or nebulized glutathione to be of help as well.

A number of doctors have focused on the role of the mitochondria in the disease. They suggest that supplementing with nutrients such as magnesium, B vitamins, ribose, acetyl-l-carnitine, NADH (nicotinamide adenine dinucleotide, the active form of niacin), and ubiquinone (a form of Coenzyme Q10) can be particularly helpful in giving patients the “fuel” they need to make more energy. Intravenous “Myers’ Cocktails” consisting of



Paradigm Change

magnesium, B vitamins and other nutrients can be especially effective, some patients say.

Some patients find intravenous or high-dose oral Vitamin C to be helpful, apparently by neutralizing some of the oxidative stress characteristic in the disease. Intravenous Vitamin C in high doses will turn into hydrogen peroxide in the space between the cells, making it more difficult for Lyme and other infections to survive and giving many patients a “die-off” reaction.

Alpha Lipoic Acid is thought to have a number of benefits related to M.E., including addressing oxidative stress, support of the liver and detoxification of mercury. It is used in oral and intravenous forms.

Intravenous administration of nutrients had the added value of giving the patient an infusion of saline, helpful since blood volume in the disease tends to be low.

Some doctors believe that many M.E. sufferers are relatively deficient in a variety of nutrients, especially B vitamins (such as B6 and B12) and minerals (such as zinc, lithium, copper, manganese, selenium, chromium, potassium and molybdenum as well as magnesium).

Vitamin D3 levels tend to be low in M.E., although not all doctors agree that it's a good idea to attempt to fix this.

A few small studies report that M.E. patients may do better as a result of supplementing omega-3 oils (such as fish or flax oil). Some patients report that omega-6 oils (such as black currant seed oil, borage oil or evening primrose oil) may be helpful as well.

Many M.E. sufferers find that supplementing vitamins or minerals can cause them to feel immediately much worse. This seems to be a result of the body's processes starting up, with pathogens being killed off or toxins released. Thus, they may need to use caution even with supplements that seem that they should be innocuous.

Hormones:

The endocrine system is thought to be one of the core dysfunctions in M.E., with the hypothalamic-pituitary-adrenal (HPA) axis being particularly problematic. Addressing hormonal issues thus can be of benefit to some patients, though this has to be done carefully.



Paradigm Change

Adrenals tend to be shrunken in M.E. and often produce lower amounts of various hormones than they should. Unfortunately, a default for many doctors is to prescribe prednisone or other high-dose steroids, and this can make M.E. patients much worse. More successful tends to be gentler support with supplements (such as ginseng, licorice or adrenal extract), DHEA and/or or very low doses of natural hydrocortone.

Aldosterone is a steroid hormone that controls blood volume and increases blood pressure. Many M.E. patients tend to be deficient in this and as a result have abnormally low blood pressure. Fludrocortisone (an aldosterone analogue) and additional salt intake can sometimes be helpful.

The thyroid is problematic in M.E., but supplements such as Synthroid or Armour (which contain T4) usually are not helpful. Some doctors say that supplementation of T3 can be appropriate for some patients, but others report very negative results.

Some patients, especially those who are very debilitated, are very low in human growth hormone and improve as a result of injections of it.

Some M.E. patients report feeling much improved as a result of supplementing oxytocin, a “feel good” hormone released at especially high levels during childbirth, breastfeeding and orgasm.

Melatonin is a hormone that regulates circadian rhythm and that serves as an antioxidant. Some M.E. patients have found it helpful for sleep and in general.

Although few M.E. doctors prescribe artificial estrogen to their patients, some believe that bioidentical estrogen can be appropriate in some cases. Testosterone can be helpful for both men and women, some doctors suggest.

Natural progesterone can be of help to many women with M.E., particularly those who experience PMS, some doctors believe.

Vasopressin (also known as ADH, anti-diuretic hormone) can be low in M.E. Desmopressin is sometimes used to treat this.

A few M.E. doctors are experimenting with supplementing with Vasointestinal Peptide (VIP), a hormone that appears to have particular potential in treating Multiple Chemical Sensitivity and in promoting flow through the liver.



Paradigm Change

Immunomodulators:

Inflammation is a major problem for M.E. patients, and is possibly the root of the illness. This seems to stem from environmental toxins, pathogens and dysfunctions in the immune system.

Certain drugs and supplements have the potential of serving to decrease this inflammation. Ampligen (discussed above) seems to be especially effective. Others that can have a bit of an effect include low doses of naltrexone (an opioid antagonist), Immunovir, Nexavir and curcumin.

Intravenous immunoglobulin (IVIG) has antiviral and anti-inflammatory effects, and some M.E. patients report benefiting from it. Unfortunately, it is very expensive.

A few other drugs (such as infliximab) have anti-inflammatory effects, but because they require infusions or injections they are not very commonly used.

Sleep:

Sleep dysfunction is a core problem in M.E. Patients have problems sleeping, and they awake from sleep not feeling refreshed.

Although sleep disorders are not believed to be at the core of the illness, some doctors order sleep studies in the hope that correcting any problems will allow patients' sleep to improve.

One theory about sleep issues in M.E. is that they are at least partly due to problems with glutamate, an excitatory neurotransmitter that also is an issue in autism. Some patients report getting much better sleep when they use benzodiazapine drugs such as Klonopin or Xanax. A downside of the drugs is that they can cause withdrawal problems if patients decide to discontinue using them.

Other sleep medications or muscle relaxants sometimes are used as well.

Drugs:

M.E. patients often react negatively to a variety of chemicals, including prescription drugs. A few drugs do seem to be helpful, at least for some patients.



Paradigm Change

M.E. patients suffer from various sorts of pain, especially fibromyalgia/trigger point pain and migraine headaches. Medications used include anticonvulsants, NSAIDS, migraine drugs and opiates.

Beta blockers, antihypotensives and other drugs that act on the circulatory system can be helpful for stabilizing blood pressure and heart beat rate, thus providing some protection against postural orthostatic tachycardia syndrome (POTS), orthostatic intolerance (OI) and post-exertional malaise (PEM).

M.E. patients often have an excess of fibrin in their blood, causing hypercoagulation. This can be treated with heparin or with supplements such as certain kinds of enzymes.

Anticonvulsants (e.g. lamotrigine, carbamazepine, gabapentin, pregabalin) can be helpful with addressing some of the neurological dysfunction in the illness.

Some studies suggest that antidepressants can be useful in M.E., but severely ill patients often get much worse as a result of using them. Even in those cases when they are helpful, usually only small doses are needed or tolerated.

Stimulants (e.g. methylphenidate, modafanil) were frequently recommended in the early days of the illness, but most gains on them tend to be short-lived.

The excitatory NMDA (N-methyl-D-aspartate) receptor appears to be overactivated in ME/CFS, and some drugs (such as memantine) have the potential of addressing that.

Rituximab, a drug mostly used to treat cancer, is a chimeric monoclonal antibody against the protein CD20, found on the surface of B cells. Two studies found that in alone or in combination with methotrexate, it could be helpful for M.E.

Serotonin antagonists and acetylcholine-esterase inhibitors occasionally are used.

Cognitive problems in M.E. sometimes respond to “smart drugs” like piracetam, some doctors treating the illness believe.

Alternative Treatments:

M.E. patients generally have lower-than-normal levels of oxygen in their bodies, and some patients report that they benefit from hyperbaric oxygen therapy (HBOT) or regular administration of oxygen. As with most M.E. treatments, some patients report negative results -- apparently, in this case, because the administration of oxygen can kill intracellular pathogens and make the recipient more open to oxidative stress.



Paradigm Change

A few dozen M.E. patients have experimented with getting stem cell infusions in Latin American countries, and a few of these have reported positive results.

Neural therapy involves the injection of small amounts of procaine, homeopathics or other substances into trigger points or interference fields in the body. Some patients suggest that that this treatment has been very helpful in allowing toxins to move through the body rather than remaining trapped in tissues such as the brain, and in providing pain relief.

For M.E. patients who are only mildly or moderately ill, yoga or other exercise that helps the lymph move through the body has been reported to be of benefit for detoxification. Cranial sacral therapy and massage also may be helpful for this.

UVB irradiation of a small amount of the blood is thought by some practitioners to be potentially helpful in addressing pathogens and toxins in M.E.

A number of studies suggest that acupuncture or certain herbs used in Traditional Chinese Medicine can be helpful in M.E.

Some M.E. patients state that other “energetic” treatments, such as homeopathy or Laser Energetic Detox (LED), have been particularly helpful for them.

Ozone therapy is a controversial treatment that some people believe can be helpful in M.E. by killing pathogens and dissolving toxins. Ozone cannot be inhaled, but is administered in a variety of other ways.

Also controversial is the use of Rife, a treatment that uses electromagnetic frequencies to attempt to kill pathogens, as an alternative or addition to prescription drugs or herbs.

Colonics and coffee enemas are used by some patients to help to detoxify the intestines, liver and gall bladder.

Dark chocolate was found in one study to have positive benefits in M.E., apparently because the flavonoids helped to synthesize nitric oxide and reduce the stickiness of the blood.

Activity:

A consistent finding across research studies is that M.E. patients do better if they are careful not to push themselves beyond their boundaries to exercise or to be active. This is the case regardless of whether the specific techniques used are called “pacing” or



Paradigm Change

“graded exercise therapy” or “cognitive-behavioral therapy” or “staying within the energy envelope.”

Being modestly active seems a little better than not being active at all at helping patients to avoid becoming deconditioned, provided that they don't do too much and crash as a result.

Patients may benefit from having help available, so that they do not have to push themselves as much to do more than they are comfortably able.

Stress:

Stress is not a good thing in any illness, and it may be even more detrimental for M.E. patients than for people with other diseases. Stress-reduction techniques may be appropriate.

-Keith Berndtson, M.D.; Lisa Petrisson, Ph.D.



Paradigm Change

M.E. TREATMENTS

MEDICAL LITERATURE

Overview

Kreijkamp-Kaspers S, Brenu EW, Marshall S, Staines D, Van Driel ML. Treating chronic fatigue syndrome - a study into the scientific evidence for pharmacological treatments. *Aust Fam Physician*. 2011 Nov;40(11):907-12. PMID: 22059223

While conventional and complementary medicines are widely used by CFS patients, the evidence for effectiveness in CFS is very limited.

*

Alraek T, Lee MS, Choi TY, Cao H, Liu J. Complementary and alternative medicine for patients with chronic fatigue syndrome: a systematic review. *BMC Complement Altern Med*. 2011 Oct 7;11:87. PMID: 21982120

The literature does not support the idea that complementary and alternative medicine therapies are helpful in CFS.

*

Porter NS, Jason LA, Boulton A, Bothne N, Coleman B. Alternative medical interventions used in the treatment and management of myalgic encephalomyelitis/chronic fatigue syndrome and fibromyalgia. *J Altern Complement Med*. 2010 Mar;16(3):235-49. PMID: 20192908

A literature review suggested that of alternative treatments, acupuncture, several types of meditative practice, magnesium, l-carnitine, and S-adenosylmethionine show the most potential for further research. I

*

Van Houdenhove B, Pae CU, Luyten P. Chronic fatigue syndrome: is there a role for non-antidepressant pharmacotherapy? *Expert Opin Pharmacother*. 2010 Feb;11(2):215-23. PMID: 20088743



Paradigm Change

The authors summarize their opinions about the use of drugs in CFS: “Antiviral, immunological and antibiotic therapies, although sometimes associated with symptom amelioration, can be more harmful than beneficial. Stimulants seem to benefit some CFS patients but their long-term effects is uncertain. Although antidepressants are not curative for the illness, they might be useful for some symptomatic aspects and co-morbid anxiety and depression. There is little or no evidence that CFS patients benefit from other pharmacological agents (e.g., steroids) or from dietary supplements and complementary medicine products.”

*

Gur A, Oktayoglu P. Central nervous system abnormalities in fibromyalgia and chronic fatigue syndrome: new concepts in treatment. *Curr Pharm Des.* 2008;14(13):1274-94. PMID: 18537652

The authors review various drugs that they think could be helpful in CFS.

*

Logan AC, Wong C. Chronic fatigue syndrome: oxidative stress and dietary modifications. *Altern Med Rev.* 2001 Oct;6(5):450-9. PMID: 11703165

The authors discuss the dietary supplements glutathione, N-acetylcysteine, alpha-lipoic acid, oligomeric proanthocyanidins, Ginkgo biloba, and Vaccinium myrtillus (bilberry) to address oxidative stress in CFS. Food intolerances and celiac disease are also discussed.

Ampligen

Strayer DR, Carter WA, Stouch BC, Stevens SR, Bateman L, Cimoch PJ, Lapp CW, Peterson DL; Chronic Fatigue Syndrome AMP-516 Study Group, Mitchell WM. A double-blind, placebo-controlled, randomized, clinical trial of the TLR-3 agonist rintatolimod in severe cases of chronic fatigue syndrome. *PLoS One.* 2012;7(3):e31334. PMID: 22431963

Rintatolimod (Ampligen) produced objective improvement in exercise tolerance and a reduction in CFS/ME related concomitant medication usage.

*



Paradigm Change

Suhadolnik RJ, Reichenbach NL, Hitzges P, Adelson ME, Peterson DL, Cheney P, Salvato P, Thompson C, Loveless M, Müller WE, et al. Changes in the 2-5A synthetase/RNase L antiviral pathway in a controlled clinical trial with poly(I)-poly(C12U) in chronic fatigue syndrome. *In Vivo*. 1994 Jul-Aug;8(4):599-604. PMID: 7893988

Poly(I)-poly(C12U) (Ampligen) is a biologically active drug in CFS, with effects on RNase L activity correlated with cognitive improvement.

*

Suhadolnik RJ, Reichenbach NL, Hitzges P, Sobol RW, Peterson DL, Henry B, Ablashi DV, Müller WE, Schröder HC, Carter WA, et al. Upregulation of the 2-5A synthetase/RNase L antiviral pathway associated with chronic fatigue syndrome. *Clin Infect Dis*. 1994 Jan;18 Suppl 1:S96-104. PMID: 8148461

CFS patients differed significantly from controls in having a lower mean basal level of latent 2-5A synthetase, a higher pretreatment level of bioactive 2-5A, and a higher level of pretherapy RNase L activity. Therapy with poly(I).poly(C12U) (Ampligen) resulted in a significant decrease in HHV-6 activity and in downregulation of the 2-5A synthetase/RNase L pathway in temporal association with clinical and neuropsychological improvement.

*

Strayer DR, Carter WA, Brodsky I, Cheney P, Peterson D, Salvato P, Thompson C, Loveless M, Shapiro DE, Elsasser W, et al. A controlled clinical trial with a specifically configured RNA drug, poly(I).poly(C12U), in chronic fatigue syndrome. *Clin Infect Dis*. 1994 Jan;18 Suppl 1:S88-95. PMID: 8148460

CFS patients given poly(I).poly(C12U) (Ampligen) had increased Karnofsky performance scores, exhibited a greater ability to do work during exercise treadmill testing, displayed an enhanced capacity to perform the activities of daily living, had a reduced cognitive deficit, and required less use of other medications.

Rituximab

Fluge O, Bruland O, Risa K, Storstein A, Kristoffersen EK, Sapkota D, Næss H, Dahl O, Nyland H, Mella O. Benefit from B-Lymphocyte Depletion Using the Anti-CD20 Antibody Rituximab in Chronic Fatigue Syndrome. A Double-Blind and Placebo-Controlled Study. *PLoS One*. 2011;6(10):e26358. PMID: 22039471



Paradigm Change

Major CFS symptom relief during cancer chemotherapy in a patient with synchronous CFS and lymphoma spurred a pilot study of B-lymphocyte depletion using the anti-CD20 antibody Rituximab, which demonstrated significant clinical response in three CFS patients. The delayed responses starting from 2-7 months after Rituximab treatment, in spite of rapid B-cell depletion, suggests that CFS is an autoimmune disease and may be consistent with the gradual elimination of autoantibodies preceding clinical responses.

*

Fluge Ø, Mella O. Clinical impact of B-cell depletion with the anti-CD20 antibody rituximab in chronic fatigue syndrome: a preliminary case series. *BMC Neurol.* 2009 Jul 1;9:28. PMID: 19566965

CFS patients experienced improvements when treated with chemotherapy usually used for cancer patients; this suggests that B-cell abnormalities play a role in the disease.

Antivirals

Watt T, Oberfoell S, Balise R, Lunn MR, Kar AK, Merrihew L, Bhangoo MS, Montoya JG. Response to valganciclovir in chronic fatigue syndrome patients with human herpesvirus 6 and Epstein-Barr virus IgG antibody titers. *J Med Virol.* 2012 Dec;84(12):1967-74. PMID: 23080504

This study looks at the drug valganciclovir, which has been reported to improve physical and cognitive symptoms in patients with chronic fatigue syndrome (CFS) with elevated human herpesvirus 6 (HHV-6) and Epstein-Barr virus (EBV) IgG antibody titers. Patients were categorized as responders if they experienced at least 30% improvement in physical and/or cognitive functioning. Thirty-two patients (52%) were categorized as responders. Longer treatment was associated with improved response.

*

Lerner AM, Beqaj SH, Deeter RG, Fitzgerald JT. Valacyclovir treatment in Epstein-Barr virus subset chronic fatigue syndrome: thirty-six months follow-up. *In Vivo.* 2007 Sep-Oct;21(5):707-13. PMID: 18019402

A group of CFS patients improved on the drug valacyclovir.

*



Paradigm Change

Kogelnik AM, Loomis K, Hoegh-Petersen M, Rosso F, Hischier C, Montoya JG. Use of valganciclovir in patients with elevated antibody titers against Human Herpesvirus-6 (HHV-6) and Epstein-Barr Virus (EBV) who were experiencing central nervous system dysfunction including long-standing fatigue. *J Clin Virol.* 2006 Dec;37 Suppl 1:S33-8. PMID: 17276366

The use of the antiviral drug valganciclovir resulted in significant improvements amongst a small group of CFS patients.

*

Lerner AM, Beqaj SH, Deeter RG, Dworkin HJ, Zervos M, Chang CH, Fitzgerald JT, Goldstein J, O'Neill W. A six-month trial of valacyclovir in the Epstein-Barr virus subset of chronic fatigue syndrome: improvement in left ventricular function. *Drugs Today (Barc).* 2002 Aug;38(8):549-61. PMID: 12582420

Valacyclovir may be effective when used to treat persistent Epstein-Barr virus (EBV) in CFS.

*

Drago F, Ranieri E, Pastorino A, Casazza S, Crovato F, Rebora A. Epstein-Barr virus-related primary cutaneous amyloidosis. Successful treatment with acyclovir and interferon-alpha. *Br J Dermatol.* 1996 Jan;134(1):170-4. PMID: 8745909

The researchers present data that support an endogenous reactivation of EBV infection and suggest a causal relationship with primary amyloidosis.

*

See DM, Tilles JG. alpha-Interferon treatment of patients with chronic fatigue syndrome. *Immunol Invest.* 1996 Jan-Mar;25(1-2):153-64. PMID: 8675231

Therapy with alpha interferon had a significant effect on the quality of life in a subgroup of patients with CFS manifesting an isolated decrease in natural killer cell function.

*

Straus SE, Dale JK, Tobi M, Lawley T, Preble O, Blaese RM, Hallahan C, Henle W. Acyclovir treatment of the chronic fatigue syndrome. Lack of efficacy in a placebo-controlled trial. *N Engl J Med.* 1988 Dec 29;319(26):1692-8. PMID: 2849717



Paradigm Change

Acyclovir (a herpes antiviral) was not helpful in a trial.

Antibiotics

Vermeulen RC, Scholte HR. Azithromycin in chronic fatigue syndrome (CFS), an analysis of clinical data. *J Transl Med.* 2006 Aug 15;4:34. PMID: 16911783

The antibiotic azithromycin resulted in a decrease in symptoms in a subset of CFS patients, all of whom had lower levels of plasma acetylcarnitine. The authors speculate that the drug protected the patients from oxidative stress.

Transfer Factor

De Vinci C, Levine PH, Pizza G, Fudenberg HH, Orens P, Pearson G, Viza D. Lessons from a pilot study of transfer factor in chronic fatigue syndrome. *Biotherapy.* 1996;9(1-3):87-90. PMID: 8993764

Of the 20 patients in the placebo-controlled trial of transfer factor, improvement was observed in 12 patients, generally within 3-6 weeks of beginning treatment.

*

Ablashi DV, Levine PH, De Vinci C, Whitman JE Jr, Pizza G, Viza D. Use of anti HHV-6 transfer factor for the treatment of two patients with chronic fatigue syndrome (CFS). Two case reports. *Biotherapy.* 1996;9(1-3):81-6. PMID: 8993763

Specific Human Herpes virus-6 (HHV-6) transfer factor (TF) preparation, administered to two chronic fatigue syndrome patients, inhibited the HHV-6 infection. Prior to treatment, both patients exhibited an activated HHV-6 infection. TF treatment significantly improved the clinical manifestations of CFS in one patient who resumed normal duties within weeks, whereas no clinical improvement was observed in the second patient.

IVIG

Ghio M, Contini P, Setti M, Ubezio G, Mazzei C, Tripodi G. sHLA-I Contamination, a novel mechanism to explain ex vivo/in vitro modulation of IL-10 synthesis and release in CD8(+)



Paradigm Change

T lymphocytes and in neutrophils following intravenous immunoglobulin infusion. *J Clin Immunol.* 2010 May;30(3):384-92. PMID: 20127276

IVIG might modulate IL-10 via the immunomodulatory activities of sHLA-I contaminant molecules inducing transcriptional and post-transcriptional modulation of IL-10 in CD8(+) T lymphocytes and neutrophils.

*

Kerr JR, Cunniffe VS, Kelleher P, Bernstein RM, Bruce IN. Successful intravenous immunoglobulin therapy in 3 cases of parvovirus B19-associated chronic fatigue syndrome. *Clin Infect Dis.* 2003 May 1;36(9):e100-6. PMID: 12715326

A 5-day course of IVIG therapy led to clearance of parvovirus B19 viremia, resolution of symptoms, resolution of cytokine dysregulation and improvement in physical and functional ability in a group of three CFS patients.

*

Rowe KS. Double-blind randomized controlled trial to assess the efficacy of intravenous gammaglobulin for the management of chronic fatigue syndrome in adolescents. *J Psychiatr Res.* 1997 Jan-Feb;31(1):133-47. PMID: 9201655

Researchers did a trial of IVIG on a group of adolescents with CFS.

*

Vollmer-Conna U, Hickie I, Hadzi-Pavlovic D, Tymms K, Wakefield D, Dwyer J, Lloyd A. Intravenous immunoglobulin is ineffective in the treatment of patients with chronic fatigue syndrome. *Am J Med.* 1997 Jul;103(1):38-43. PMID: 9236484

No dose of intravenous immunoglobulin was associated with a specific therapeutic benefit in a group of CFS patients. Adverse reactions, typically constitutional symptoms, were reported by 70% to 80% of patients, with no relationship to immunoglobulin treatment.

*

Peterson PK, Shepard J, Macres M, Schenck C, Crosson J, Rechtman D, Lurie N. A controlled trial of intravenous immunoglobulin G in chronic fatigue syndrome. *Am J Med.* 1990 Nov;89(5):554-60. PMID: 2239975



Paradigm Change

In a trial of 28 CFS patients, no clinical improvements were noted. Major adverse experiences were observed in 20% of both the IV IgG and placebo groups.

*

Lloyd A, Hickie I, Wakefield D, Boughton C, Dwyer J. A double-blind, placebo-controlled trial of intravenous immunoglobulin therapy in patients with chronic fatigue syndrome. *Am J Med.* 1990 Nov;89(5):561-8. PMID: 2146875

Immunomodulatory treatment with immunoglobulin is effective in a significant number of patients with CFS, a finding that supports the concept that an immunologic disturbance may be important in the pathogenesis of this disorder.

Arsenic

Tarello W. Chronic fatigue syndrome (CFS) associated with *Staphylococcus* spp. bacteremia, responsive to potassium arsenite 0.5% in a veterinary surgeon and his coworking wife, handling with CFS animal cases. *Comp Immunol Microbiol Infect Dis.* 2001 Oct;24(4):233-46. PMID: 11561958

The blood of a veterinary surgeon (the author) and his coworking wife, both diagnosed with CFS, proved Staph-positive. Micrococci-like organisms in the blood were repeatedly observed in a 3-year period. Several medicaments, including antibiotics, proved unsuccessful. Following treatment with a low dosage arsenical drug (potassium arsenite 0.5%, im., 1 ml/12 h, for 10 days) both patients experienced complete remission. At the post-treatment control made 1 month later, micrococci had disappeared from the blood, and the CD4/CD8 ratio was raising.

*

Tarello W. Chronic Fatigue Syndrome (CFS) in 15 dogs and cats with specific biochemical and microbiological anomalies. *Comp Immunol Microbiol Infect Dis.* 2001 Jul;24(3):165-85. PMID: 11440190

Seven dogs and eight cats diagnosed with CFS experienced resolution of their symptoms with a low dosage arsenical drug (thiacetarsamide sodium, Caparsolate, i.v., 0.1 ml/kg/day). Previously observed micrococci disappeared from the blood at post-treatment controls made 10-30 days later.

*



Paradigm Change

Tarello W. Chronic fatigue and immune dysfunction syndrome associated with *Staphylococcus* spp. bacteraemia responsive to thiacetarsamide sodium in eight birds of prey. *J Vet Med B Infect Dis Vet Public Health*. 2001 May;48(4):267-81. PMID: 15129582

Eight birds of prey examined between 1992 and 1995 and sharing common symptoms (asthenia, inability to fly, poor appetite and emaciation) underwent laboratory tests revealing immunodeficiency, anaemia, high creatine kinase levels and low serum magnesium levels. In all patients, micrococcus-like organisms found adhering to the outer surface of many red blood cells, had disappeared at post-treatment controls. An arsenic-based medication was successful in relieving the immune and haematological dysfunctions within 2-4 weeks.

Probiotics

Rao AV, Bsted AC, Beaulne TM, Katzman MA, Iorio C, Berardi JM, Logan AC. A randomized, double-blind, placebo-controlled pilot study of a probiotic in emotional symptoms of chronic fatigue syndrome. *Gut Pathog*. 2009 Mar 19;1(1):6.

CFS patients who received 24 billion colony forming units of *Lactobacillus casei* strain Shirota (LcS) daily for two months had a decrease in anxiety symptoms. PMID: 19338686

*

Sullivan A, Nord CE, Evengård B. Effect of supplement with lactic-acid producing bacteria on fatigue and physical activity in patients with chronic fatigue syndrome. *Nutr J*. 2009 Jan 26;8:4.

Severely ill CFS patients were given the probiotics *Lactobacillus paracasei* ssp. *paracasei* F19, *Lactobacillus acidophilus* NCFB 1748 and *Bifidobacterium lactis* Bb12. The study reported neurocognitive functioning improvements, but no changes in fatigue or physical activity. PMID: 19171024

Nutritional Support

Lundell K, Qazi S, Eddy L, Uckun FM. Clinical activity of folinic acid in patients with chronic fatigue syndrome. *Arzneimittelforschung*. 2006;56(6):399-404. PMID: 16889122



Paradigm Change

CFS frequently is a folinic acid responsive clinical entity accompanied by B-cell immunodeficiency and inappropriate antibody responses to EBV.

*

Teitelbaum JE, Johnson C, St Cyr J. The use of D-ribose in chronic fatigue syndrome and fibromyalgia: a pilot study. *J Altern Complement Med.* 2006 Nov;12(9):857-62. PMID: 17109576

D-ribose was effective at improving CFS patients' energy, sleep, mental clarity, pain intensity and overall feelings of well-being.

*

Werbach MR. Nutritional strategies for treating chronic fatigue syndrome. *Altern Med Rev.* 2000 Apr;5(2):93-108. PMID: 10767667

CFS patients have a variety of nutritional deficiencies. Supplementing with B vitamins, vitamin C, magnesium, sodium, zinc, l-tryptophan, l-carnitine, coenzyme Q10 and essential fatty acids may be considered.

*

Heap LC, Peters TJ, Wessely S. Vitamin B status in patients with chronic fatigue syndrome. *J R Soc Med.* 1999 Apr;92(4):183-5. PMID: 10450194

CFS patients showed deficiencies in various B vitamins, especially B6. This did not appear to be due to insufficient intake.

*

Dykman KD, Tone C, Ford C, Dykman RA. The effects of nutritional supplements on the symptoms of fibromyalgia and chronic fatigue syndrome. *Integr Physiol Behav Sci.* 1998 Jan-Mar;33(1):61-71. PMID: 9594356

Nutritional supplements resulted in a reduction in initial symptom severity, with continued improvement in the period between initial assessment and the follow-up, in a group of CFS sufferers.

*



Paradigm Change

See DM, Cimoch P, Chou S, Chang J, Tilles J. The in vitro immunomodulatory effects of glyconutrients on peripheral blood mononuclear cells of patients with chronic fatigue syndrome. *Integr Physiol Behav Sci.* 1998 Jul-Sep;33(3):280-7. PMID: 9829439

Addition of glyconutrient homogenate to PBMC from patients with CFS stimulated with phytohemagglutinin significantly increased the expression of each glycoprotein. The glyconutrient preparation significantly enhanced NK cell activity versus human herpes virus 6 (HHV-6)-infected H9 cells in an 8 h ⁵¹Cr release assay compared to placebo for PBMC from patients with CFS ($p < .01$). Finally, apoptosis was significantly higher in patients with CFS. The percentage of apoptotic cells was significantly decreased in PBMC from patients with CFS that had been incubated for 48 h with glyconutrients.

Carnitine

Famularo G, De Simone C, Trinchieri V, Mosca L. Carnitines and its congeners: a metabolic pathway to the regulation of immune response and inflammation. *Ann N Y Acad Sci.* 2004 Nov;1033:132-8. PMID: 15591010

The possible use of carnitine in CFS and other conditions is discussed.

*

Vermeulen RC, Scholte HR. Exploratory open label, randomized study of acetyl- and propionylcarnitine in chronic fatigue syndrome. *Psychosom Med.* 2004 Mar-Apr;66(2):276-82. PMID: 15039515

The authors compared 2 g/d acetyl-L-carnitine, 2 g/d propionyl-L-carnitine, and its combination in 3 groups of 30 CFS patients during 24 weeks. Acetylcarnitine and propionylcarnitine showed beneficial effect on fatigue and attention concentration. Less improvement was found by the combined treatment. Acetylcarnitine had main effect on mental fatigue and propionylcarnitine on general fatigue.

*

Plioplys AV, Plioplys S. Amantadine and L-carnitine treatment of Chronic Fatigue Syndrome. *Neuropsychobiology.* 1997;35(1):16-23. PMID: 9018019

In a group of 30 CFS patients, l-carnitine demonstrated significant improvements within 4-8 weeks. Amantadine, used to treat fatigue in MS, was poorly tolerated by CFS patients.



Paradigm Change

NADH

Alegre J, Rosés JM, Javierre C, Ruiz-Baqués A, Segundo MJ, de Sevilla TF. Nicotinamide adenine dinucleotide (NADH) in patients with chronic fatigue syndrome. *Rev Clin Esp.* 2010 Jun;210(6):284-8. PMID: 20447621

Administration of oral NADH was associated to a decrease in anxiety and maximum heart rate, after a stress test in patients with CFS.

*

Santaella ML, Font I, Disdier OM. Comparison of oral nicotinamide adenine dinucleotide (NADH) versus conventional therapy for chronic fatigue syndrome. *P R Health Sci J.* 2004 Jun;23(2):89-93. PMID: 15377055

NADH was effective in CFS for three months, but the positive results faded after that.

*

Forsyth LM, Preuss HG, MacDowell AL, Chiazze L Jr, Birkmayer GD, Bellanti JA. Therapeutic effects of oral NADH on the symptoms of patients with chronic fatigue syndrome. *Ann Allergy Asthma Immunol.* 1999 Feb;82(2):185-91. PMID: 10071523

31% of a group of CFS patients responded favorably to NADH, compared to 8% to a placebo.

Magnesium

Gaby AR. Intravenous nutrient therapy: the "Myers' cocktail". *Altern Med Rev.* 2002 Oct;7(5):389-403. PMID: 12410623

The use of the "Myers' cocktail" for CFS and other diseases is discussed.

*

Manuel y Keenoy B, Moorkens G, Vertommen J, Noe M, Nève J, De Leeuw I. Magnesium status and parameters of the oxidant-antioxidant balance in patients with chronic fatigue:



Paradigm Change

effects of supplementation with magnesium. *J Am Coll Nutr.* 2000 Jun;19(3):374-82. PMID: 10872900

In a CFS population, lower antioxidant capacity found in moderate Mg deficiency was not due to a deficit in Mg dietary intakes and was not accompanied by increased lipid susceptibility to in vitro peroxidation. Nevertheless, Mg supplementation was followed by an improvement in Mg body stores, in serum vitamin E and its interrelated stage of lipid peroxidation.

*

Takahashi H, Imai K, Katanuma A, Sugaya T, Hisano K, Motoya S, Aoki S, Sugiyama T, Yachi A. A case of chronic fatigue syndrome who showed a beneficial effect by intravenous administration of magnesium sulphate. *Arerugi.* 1992 Nov;41(11):1605-10. PMID: 1492795

A CFS sufferer was treated successfully with intravenous magnesium.

*

Cox IM, Campbell MJ, Dowson D. Red blood cell magnesium and chronic fatigue syndrome. *Lancet.* 1991 Mar 30;337(8744):757-60. PMID: 1672392

A clinical trial showed that magnesium supplementation may be helpful in CFS.

Essential Fatty Acids

Puri BK, Holmes J, Hamilton G. Eicosapentaenoic acid-rich essential fatty acid supplementation in chronic fatigue syndrome associated with symptom remission and structural brain changes. *Int J Clin Pract.* 2004 Mar;58(3):297-9. PMID: 15117099

Supplementation of an essential fatty acid rich in eicosapentaenoic acid (EPA) was followed by marked improvement in clinical condition after six weeks. Accurate quantification of the lateral ventricular volumes in the baseline and 16-week follow-up registered images of high-resolution magnetic resonance imaging structural scans showed that the treatment was accompanied by a marked reduction in the lateral ventricular volume during this period.

*



Paradigm Change

Puri BK. The use of eicosapentaenoic acid in the treatment of chronic fatigue syndrome. *Prostaglandins Leukot Essent Fatty Acids*. 2004 Apr;70(4):399-401. PMID: 15041033

A series of patients with chronic fatigue syndrome were treated solely with a high-eicosapentaenoic acid-containing essential fatty acid supplement. All showed improvement in their symptomatology within eight to 12 weeks.

*

Warren G, McKendrick M, Peet M. The role of essential fatty acids in chronic fatigue syndrome. A case-controlled study of red-cell membrane essential fatty acids (EFA) and a placebo-controlled treatment study with high dose of EFA. *Acta Neurol Scand*. 1999 Feb;99(2):112-6. PMID: 10071170

Treatment with an essential fatty acid product (Efamol Marine) did not result in benefits compared to a placebo for CFS patients.

*

Behan PO, Behan WM, Horrobin D. Effect of high doses of essential fatty acids on the postviral fatigue syndrome. *Acta Neurol Scand*. 1990 Sep;82(3):209-16. PMID: 2270749

High doses of essential fatty acids containing linolenic, gamma-linolenic, eicosapentaenoic and docosahexaenoic acids were helpful in CFS.

Vitamin C

Kodama M, Kodama T. The clinical course of interstitial pneumonia alias chronic fatigue syndrome under the control of megadose vitamin C infusion system with dehydroepiandrosterone-cortisol annex. *Int J Mol Med*. 2005 Jan;15(1):109-16. PMID: 15583836

A combination of high-dose intravenous Vitamin C and DHEA was effective at treating both CFS and interstitial pneumonia.

*

Kodama M, Kodama T, Murakami M. The value of the dehydroepiandrosterone-annexed vitamin C infusion treatment in the clinical control of chronic fatigue syndrome (CFS). I. A



Paradigm Change

Pilot study of the new vitamin C infusion treatment with a volunteer CFS patient. *In Vivo*. 1996 Nov-Dec;10(6):575-84. PMID: 8986467

A combination of intravenous Vitamin C and DHEA was effective in treating a CFS patient.

*

Kodama M, Kodama T, Murakami M. The value of the dehydroepiandrosterone-annexed vitamin C infusion treatment in the clinical control of chronic fatigue syndrome (CFS). II. Characterization of CFS patients with special reference to their response to a new vitamin C infusion treatment. *In Vivo*. 1996 Nov-Dec;10(6):585-96. PMID: 8986468

The authors found that a combination of intravenous Vitamin C, DHEA and antibiotics (erythromycin and chloramphenicol) was effective in treating CFS manifested as “chronic pneumonia.”

Adrenal Hormones

Ben-Zvi A, Vernon SD, Broderick G. Model-based therapeutic correction of hypothalamic-pituitary-adrenal axis dysfunction. *PLoS Comput Biol*. 2009 Jan;5(1):e1000273. PMID: 19165314

Treatment strategies addressing cortisol problems may be effective in CFS.

*

Wheatland R. Chronic ACTH autoantibodies are a significant pathological factor in the disruption of the hypothalamic-pituitary-adrenal axis in chronic fatigue syndrome, anorexia nervosa and major depression. *Med Hypotheses*. 2005;65(2):287-95. PMID: 15885924

Corticosteroid supplements may be an effective treatment for CFS.

*

Cleare AJ, O'Keane V, Miell JP. Levels of DHEA and DHEAS and responses to CRH stimulation and hydrocortisone treatment in chronic fatigue syndrome. *Psychoneuroendocrinology*. 2004 Jul;29(6):724-32. PMID: 15110921



Paradigm Change

DHEA levels are raised in CFS and correlate with the degree of self-reported disability. Hydrocortisone therapy leads to a reduction in these levels towards normal, and an increased DHEA response to CRH, most marked in those who show a clinical response to this therapy.

*

Kakumanu SS, Mende CN, Lehman EB, Hughes K, Craig TJ. Effect of topical nasal corticosteroids on patients with chronic fatigue syndrome and rhinitis. *J Am Osteopath Assoc.* 2003 Sep;103(9):423-7. PMID: 14527077

Treating the symptoms of rhinitis with topical nasal corticosteroids in patients with CFS does not appear to alleviate daytime fatigue or associated nasal, musculoskeletal, or cognitive complaints.

*

Baschetti R. Fludrocortisone and chronic fatigue syndrome. *N Z Med J.* 2003 Aug 8;116(1179):U549. PMID: 14513090

*

Blockmans D, Persoons P, Van Houdenhove B, Lejeune M, Bobbaers H. Combination therapy with hydrocortisone and fludrocortisone does not improve symptoms in chronic fatigue syndrome: a randomized, placebo-controlled, double-blind, crossover study. *Am J Med.* 2003 Jun 15;114(9):736-41. PMID: 12829200

Low-dose combination therapy of hydrocortisone and fludrocortisone was not effective in patients with CFS.

*

Cleare AJ, Miell J, Heap E, Sookdeo S, Young L, Malhi GS, O'Keane V. Hypothalamo-pituitary-adrenal axis dysfunction in chronic fatigue syndrome, and the effects of low-dose hydrocortisone therapy. *J Clin Endocrinol Metab.* 2001 Aug;86(8):3545-54. PMID: 11502777

The authors treat 32 patients with low-dose hydrocortisone and conclude that the improvement in fatigue seen in some patients with CFS during treatment is accompanied by a reversal of the blunted cortisol responses to human CRH.

*



Paradigm Change

Cleare AJ, O'Keane V, Miell J. Plasma leptin in chronic fatigue syndrome and a placebo-controlled study of the effects of low-dose hydrocortisone on leptin secretion. *Clin Endocrinol (Oxf)*. 2001 Jul;55(1):113-9. PMID: 11453960

Low dose hydrocortisone therapy caused increases in plasma leptin levels, with this biological response being more marked in those CFS subjects who showed a positive therapeutic response to hydrocortisone therapy.

*

Rowe PC, Calkins H, DeBusk K, McKenzie R, Anand R, Sharma G, Cuccherini BA, Soto N, Hohman P, Snader S, Lucas KE, Wolff M, Straus SE. Fludrocortisone acetate to treat neurally mediated hypotension in chronic fatigue syndrome: a randomized controlled trial. *JAMA*. 2001 Jan 3;285(1):52-9. PMID: 11150109

Fludrocortisone as monotherapy for was no more efficacious than placebo for amelioration of symptoms in CFS.

*

Cleare AJ, Heap E, Malhi GS, Wessely S, O'Keane V, Miell J. Low-dose hydrocortisone in chronic fatigue syndrome: a randomised crossover trial. *Lancet*. 1999 Feb 6;353(9151):455-8. PMID: 9989716

In some patients with CFS, low-dose hydrocortisone reduces fatigue levels in the short term.

*

McKenzie R, O'Fallon A, Dale J, Demitrack M, Sharma G, Deloria M, Garcia-Borreguero D, Blackwelder W, Straus SE. Low-dose hydrocortisone for treatment of chronic fatigue syndrome: a randomized controlled trial. *JAMA*. 1998 Sep 23-30;280(12):1061-6. PMID: 9757853

Hydrocortisone treatment was associated with some improvement in symptoms of CFS.

*

Peterson PK, Pheley A, Schroepel J, Schenck C, Marshall P, Kind A, Haugland JM, Lambrecht LJ, Swan S, Goldsmith S. A preliminary placebo-controlled crossover trial of



Paradigm Change

fludrocortisone for chronic fatigue syndrome. Arch Intern Med. 1998 Apr 27;158(8):908-14. PMID: 9570178

Low-dose fludrocortisone did not provide enough benefit to be evident in a preliminary blinded trial of unselected patients with chronic fatigue syndrome.

Growth Hormone

Moorkens G, Wynants H, Abs R. Effect of growth hormone treatment in patients with chronic fatigue syndrome: a preliminary study. Growth Horm IGF Res. 1998 Apr;8 Suppl B:131-3. PMID: 10990148

A group of 20 patients received growth hormone therapy. Although quality of life, as assessed using two different questionnaires, did not improve significantly during GH treatment, four patients were able to resume work after a long period of sick leave.

Melatonin

van Heukelom RO, Prins JB, Smits MG, Bleijenberg G. Influence of melatonin on fatigue severity in patients with chronic fatigue syndrome and late melatonin secretion. Eur J Neurol. 2006 Jan;13(1):55-60. PMID: 16420393

Melatonin was more effective than a placebo at improving CFS patients' scores on a variety of measures.

*

Williams G, Waterhouse J, Mugarza J, Minors D, Hayden K. Therapy of circadian rhythm disorders in chronic fatigue syndrome: no symptomatic improvement with melatonin or phototherapy. Eur J Clin Invest. 2002 Nov;32(11):831-7. PMID: 12423324

Melatonin and bright-light phototherapy appear ineffective in CFS.

*

van de Luit L, van der Meulen J, Cleophas TJ, Zwinderman AH. Amplified amplitudes of circadian rhythms and nighttime hypotension in patients with chronic fatigue syndrome:



Paradigm Change

improvement by inopamil but not by melatonin. *Angiology*. 1998 Nov;49(11):903-8. PMID: 9822046

In a pilot study of four CFS patients, inopamil (200 mg) reduced nighttime hypotension ($p < 0.05$), whereas melatonin (4 mg) increased nighttime hypotension.

Orthostatic Intolerance

Sutcliffe K, Gray J, Tan MP, Pairman J, Wilton K, Parry SW, Newton JL. Home orthostatic training in chronic fatigue syndrome--a randomized, placebo-controlled feasibility study. *Eur J Clin Invest*. 2010 Jan;40(1):18-24. PMID: 19912315

Home orthostatic training is well tolerated and generally complied with. A likely physiological rationale for HOT in CFS is related to reductions in orthostatic intolerance. An adequately powered study including strategies to enhance compliance is warranted.

*

Wyller VB, Thaulow E, Amlie JP. Treatment of chronic fatigue and orthostatic intolerance with propranolol. *J Pediatr*. 2007 Jun;150(6):654-5. PMID: 17517256

The authors describe the effect of propranolol in an adolescent with chronic fatigue syndrome and orthostatic intolerance.

*

Naschitz J, Dreyfuss D, Yeshurun D, Rosner I. Midodrine treatment for chronic fatigue syndrome. *Postgrad Med J*. 2004 Apr;80(942):230-2. PMID: 15082846

Midodrine treatment, directed at the autonomic nervous system, resulted in correction of the dysautonomia followed by improvement of fatigue in one patient.

Pain Management

Meeus M, Ickmans K, Struyf F, Hermans L, Van Noesel K, Oderkerk J, Declerck LS, Moorkens G, Hans G, Grosemans S, Nijs J. Does acetaminophen activate endogenous pain inhibition in chronic fatigue syndrome/fibromyalgia and rheumatoid arthritis? A



Paradigm Change

double-blind randomized controlled cross-over trial. *Pain Physician*. 2013 Mar-Apr;16(2):E61-70. PMID: 23511692

After intake of acetaminophen, pain thresholds increased slightly in CFS/FM patients, and decreased in the RA and the control group. Acetaminophen may have a limited positive effect on central pain inhibition in this disease.

*

Marshall R, Paul L, Wood L. The search for pain relief in people with chronic fatigue syndrome: a descriptive study. *Physiother Theory Pract*. 2011 Jul;27(5):373-83. PMID: 21039301

Physiotherapy and complementary alternative medicine treatments may help people manage painful CFS symptoms.

*

Meeus M, Nijs J, Van Oosterwijck J, Van Alsenoy V, Truijen S. Pain physiology education improves pain beliefs in patients with chronic fatigue syndrome compared with pacing and self-management education: a double-blind randomized controlled trial. *Arch Phys Med Rehabil*. 2010 Aug;91(8):1153-9. PMID: 20684894

A 30-minute educational session on pain physiology in CFS patients imparted a better understanding of pain and brings about less worry about pain.

Stimulants

Young JL. Chronic fatigue syndrome: 3 cases and a discussion of the natural history of attention-deficit/hyperactivity disorder. *Postgrad Med*. 2013 Jan;125(1):162-8. PMID: 23391682

Case studies of three patients whose CFS symptoms improved after treatment with stimulants for their ADHD are presented.

*

Valdizán Usón JR, Idiazábal Alecha MA. Diagnostic and treatment challenges of chronic fatigue syndrome: role of immediate-release methylphenidate. *Expert Rev Neurother*. 2008 Jun;8(6):917-27. PMID: 18505357



Paradigm Change

The use of immediate-release methylphenidate in CFS was shown to be helpful in one small study.

*

Young JL, Redmond JC. Fibromyalgia, chronic fatigue, and adult attention deficit hyperactivity disorder in the adult: a case study. *Psychopharmacol Bull.* 2007;40(1):118-26. PMID: 17285103

ADHD medications can be effective in CFS.

*

Blockmans D, Persoons P, Van Houdenhove B, Bobbaers H. Does methylphenidate reduce the symptoms of chronic fatigue syndrome? *Am J Med.* 2006 Feb;119(2):167.e23-30. PMID: 16443425

The amphetamine derivative methylphenidate was better than a placebo at relieving fatigue and concentration disturbances in a minority of CFS patients.

*

Olson LG, Ambrogetti A, Sutherland DC. A pilot randomized controlled trial of dexamphetamine in patients with chronic fatigue syndrome. *Psychosomatics.* 2003 Jan-Feb;44(1):38-43. PMID: 12515836

A short trial suggests that dexamphetamine may be useful in the management of CFS.

5-HT₃ Receptor Antagonists

The GK, Bleijenberg G, Buitelaar JK, van der Meer JW. The effect of ondansetron, a 5-HT₃ receptor antagonist, in chronic fatigue syndrome: a Source randomized controlled trial. *J Clin Psychiatry.* 2010 May;71(5):528-33. PMID: 20122367

Ondansetron, a 5-HT₃ receptor antagonist, was no better than a placebo at helping fatigue severity and functional impairment in adults with CFS.

*



Paradigm Change

The GK, Prins J, Bleijenberg G, van der Meer JW. The effect of granisetron, a 5-HT₃ receptor antagonist, in the treatment of chronic fatigue syndrome patients--a pilot study. *Neth J Med.* 2003 Sep;61(9):285-9. PMID: 14692441

Treatment with granisetron, a 5-HT₃ antagonist, resulted in significant improvement in fatigue severity and functional impairment in a group of CFS patients. Activity level showed no significant increase.

*

Späth M, Welzel D, Färber L. Treatment of chronic fatigue syndrome with 5-HT₃ receptor antagonists--preliminary results. *Scand J Rheumatol Suppl.* 2000;113:72-7. PMID: 11028837

Patients with CFS improved on both oral tropisetron and oral ondansetron.

Acetylcholine-Esterase Inhibitors

Turan T, Izgi HB, Ozsoy S, Tanriverdi F, Basturk M, Asdemir A, Beşirli A, Esel E, Sofuoglu S. The effects of galantamine hydrobromide treatment on dehydroepiandrosterone sulfate and cortisol levels in patients with chronic fatigue syndrome. *Psychiatry Investig.* 2009 Sep;6(3):204-10. PMID: 20046396

CFS patients had lower cortisol levels and higher DHEAS levels than controls. Galantamine hydrobromide treatment was effective in bringing down the DHEA levels.

*

Blacker CV, Greenwood DT, Wesnes KA, Wilson R, Woodward C, Howe I, Ali T. Effect of galantamine hydrobromide in chronic fatigue syndrome: a randomized controlled trial. *JAMA.* 2004 Sep 8;292(10):1195-204. PMID: 15353532

Galantamine hydrobromide, an acetyl cholesterone inhibitor, did not demonstrate benefits over a placebo in a group of CFS patients.

*

Kawamura Y, Kihara M, Nishimoto K, Taki M. Efficacy of a half dose of oral pyridostigmine in the treatment of chronic fatigue syndrome: three case reports. *Pathophysiology.* 2003 May;9(3):189-194. PMID: 14567934



Paradigm Change

Three patients with CFS responded somewhat positively to small doses of pyridostigmine, an acetylcholine-esterase inhibitor.

Antidepressants

Pae CU, Marks DM, Patkar AA, Masand PS, Luyten P, Serretti A. Pharmacological treatment of chronic fatigue syndrome: focusing on the role of antidepressants. *Expert Opin Pharmacother*. 2009 Jul;10(10):1561-70. PMID:19514866

A literature review suggests that antidepressant use in CFS remains “controversial.”

*

Amsterdam JD, Shults J, Rutherford N. Open-label study of s-citalopram therapy of chronic fatigue syndrome and co-morbid major depressive disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008 Jan 1;32(1):100-6. PMID: 17804135

The use of s-citalopram appears to have potential in addressing a variety of CFS symptoms.

*

Thomas MA, Smith AP. An investigation of the long-term benefits of antidepressant medication in the recovery of patients with chronic fatigue syndrome. *Hum Psychopharmacol*. 2006 Dec;21(8):503-9. PMID: 16981220

Antidepressants can be effective in treating CFS.

*

Hickie IB, Wilson AJ, Wright JM, Bennett BK, Wakefield D, Lloyd AR. A randomized, double-blind placebo-controlled trial of moclobemide in patients with chronic fatigue syndrome. *J Clin Psychiatry*. 2000 Sep;61(9):643-8. PMID: 11030484

In a blinded trial of the antidepressant moclobemide, there were some improvements. This seems to be apart from its effect on mood.

*



Paradigm Change

Hickie I. Nefazodone for patients with chronic fatigue syndrome. Aust N Z J Psychiatry. 1999 Apr;33(2):278-80. PMID: 10336228

In a trial of 10 CFS patients, 80% reported at least some improvement from fatigue from the antidepressant Nefazodone.

*

Natelson BH, Cheu J, Hill N, Bergen M, Korn L, Denny T, Dahl K. Single-blind, placebo phase-in trial of two escalating doses of selegiline in the chronic fatigue syndrome. Neuropsychobiology. 1998;37(3):150-4. PMID: 9597672

Selegiline has a small but significant therapeutic effect in CFS which appears independent of an antidepressant effect.

*

White PD, Cleary KJ. An open study of the efficacy and adverse effects of moclobemide in patients with the chronic fatigue syndrome. Int Clin Psychopharmacol. 1997 Jan;12(1):47-52. PMID: 9179634

The antidepressant moclobemide was not successful in helping a group of CFS patients.

*

Natelson BH, Cheu J, Pareja J, Ellis SP, Policastro T, Findley TW. Randomized, double blind, controlled placebo-phase in trial of low dose phenelzine in the chronic fatigue syndrome. Psychopharmacology (Berl). 1996 Apr;124(3):226-30. PMID: 8740043

A group of CFS patients responded positively to phenelzine, an monoamine oxidase inhibitor.

*

Goodnick PJ, Sandoval R, Brickman A, Klimas NG. Bupropion treatment of fluoxetine-resistant chronic fatigue syndrome. Biol Psychiatry. 1992 Nov 1;32(9):834-8. PMID: 1450297

Nine CFS patients who either could not tolerate or did not respond to fluoxetine showed significant response when administered 300 mg/day of bupropion for an 8-week period. Measures of T1 microsomal antibodies also decreased over treatment time; increases in



Paradigm Change

natural killer cell numbers correlated inversely with change in plasma levels of free methylhydroxyphenolglycol ($r = -0.88$, $p < 0.05$).

Fezam (Piracetam and Cinnarizine)

Boiko AN, Batysheva TT, Matvievskaia OV, Manevich TM, Gusev EI. Characteristics of the formation of chronic fatigue syndrome and approaches to its treatment in young patients with focal brain damage. *Neurosci Behav Physiol*. 2007 Mar;37(3):221-8. PMID: 17294097

Fezam (which contains piracetam and cinnarizine) was helpful in treating symptoms of CFS patients with focal brain lesions.

*

Boiko AN, Batysheva TT, Matvievskaia OV, Manevich TM, Gusev EI. The peculiarities of formation and approaches to the treatment of chronic fatigue syndrome in young patients with focal brain damage. *Zh Nevrol Psikhiatr Im S S Korsakova*. 2006;Spec No 3:122-9. PMID: 17172247

The drug fezam (piracetam plus cinnarizine) led to a decrease in fatigue severity in a group of CFS patients.

Other Drugs/Supplements

Young JL. Use of lisdexamfetamine dimesylate in treatment of executive functioning deficits and chronic fatigue syndrome: A double blind, placebo-controlled study. *Psychiatry Res*. 2013 May 15;207(1-2):127-33. PMID: 23062791

This study suggests that the dopaminergic medication lisdexamfetamine dimesylate could be a safe and efficacious treatment for the executive functioning deficits often associated with CFS.

*

Fagermoen E, Sulheim D, Winger A, Andersen AM, Vethe NT, Saul JP, Thaulow E, Wyller VB. Clonidine in the treatment of adolescent chronic fatigue syndrome: a pilot study for the NorCAPITAL trial. *BMC Res Notes*. 2012 Aug 7;5:418. PMID: 22871021



Paradigm Change

This pilot study assessed the feasibility and safety of clonidine in adolescent chronic fatigue syndrome (CFS).

*

Spitzer AR, Broadman M. Treatment of the narcoleptiform sleep disorder in chronic fatigue syndrome and fibromyalgia with sodium oxybate. *Pain Pract.* 2010 Jan-Feb;10(1):54-9. PMID: 20629967

Of CFS patients treated for sleep disorders with sodium oxybate, 75% experienced significant fatigue relief, and 60% experienced significant relief of pain.

*

Staines DR, Brenu EW, Marshall-Gradisnik S. Postulated vasoactive neuropeptide immunopathology affecting the blood-brain/blood-spinal barrier in certain neuropsychiatric fatigue-related conditions: A role for phosphodiesterase inhibitors in treatment? *Neuropsychiatr Dis Treat.* 2009;5:81-9. PMID: 19557103

Vasoactive neuropeptides (VNs) such as PACAP and VIP have critical roles as neurotransmitters, vasodilators including perfusion and hypoxia regulators, and immune and nociception modulators, and have the potential of being of help in CFS and other conditions.

*

The GK, Bleijenberg G, van der Meer JW. The effect of acclidine in chronic fatigue syndrome: a randomized controlled trial. *PLoS Clin Trials.* 2007 May 18;2(5):e19. PMID:17525791

Treatment with Acclidine in CFS did not result in significant differences compared with the placebo group.

*

McDermott C, Richards SC, Thomas PW, Montgomery J, Lewith G. A placebo-controlled, double-blind, randomized controlled trial of a natural killer cell stimulant (BioBran MGN-3) in chronic fatigue syndrome. *QJM.* 2006 Jul;99(7):461-8. PMID: 16809351

The NK cell stimulant, BioBran MGN-3, was not successful in reducing fatigue in CFS patients.



Paradigm Change

*

----. Soil-based organisms improve immune function: shift cytokine profile from TH2 to TH1. *Posit Health News*. 1998 Spring;(No 16):16-8. PMID: 11365013

SRL 172, a protein derived from a soil-based organism, appears to shift the cytokine profile in persons with Gulf War Syndrome and CFS from TH2 back to the more effective TH1 profile.

Herbal Medicines

Zhang ZX, Wu LL, Chen M. Effect of lixu jieyu recipe in treating 75 patients with chronic fatigue syndrome. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2009 Jun;29(6):501-5.

The Chinese herbals combination Lixu Jieyu was effective at reducing fatigue, increasing Th and T cells, and decreasing the CD4/CD8 ratio in a group of CFS patients.

*

Shin HY, An NH, Cha YJ, Shin EJ, Shin TY, Baek SH, Kim CH, Lyu YS, Lee EJ, Kim HM. Effect of Kuibitang on lipopolysaccharide-induced cytokine production in peripheral blood mononuclear cells of chronic fatigue syndrome patients. *J Ethnopharmacol*. 2004 Feb;90(2-3):253-9. PMID: 15013189

Kuibitang (KBT) is clinically used to treat patients suffering from chronic fatigue syndrome (CFS) in South Korea. These results provide evidence of a novel activity of the KBT that regulate cytokines production related with CFS.

*

Hartz AJ, Bentler S, Noyes R, Hoehns J, Logemann C, Sinift S, Butani Y, Wang W, Brake K, Ernst M, Kautzman H. Randomized controlled trial of Siberian ginseng for chronic fatigue. *Psychol Med*. 2004 Jan;34(1):51-61. PMID: 14971626

Overall efficacy for Siberian ginseng in CFS was not demonstrated. However, the findings of possible efficacy for patients with moderate fatigue suggests that further research may be of value.

*



Paradigm Change

Shin HY, Shin CH, Shin TY, Lee EJ, Kim HM. Effect of bojungikki-tang on lipopolysaccharide-induced cytokine production from peripheral blood mononuclear cells of chronic fatigue syndrome patients. *Immunopharmacol Immunotoxicol*. 2003 Nov;25(4):491-501. PMID: 14686792

Bojungikki-tang (BIT), a Chinese herb, significantly inhibited in peripheral blood mononuclear cells LPS-induced tumor necrosis factor (TNF)-alpha, interleukin (IL)-6, IL-10, transforming growth factor (TGF)-beta1 production. It may be useful in CFS.

*

Redman DA. *Ruscus aculeatus* (butcher's broom) as a potential treatment for orthostatic hypotension, with a case report. *J Altern Complement Med*. 2000 Dec;6(6):539-49. PMID: 11152059

The herb *Ruscus aculeatus* may have potential in treating orthostatic hypotension in CFS.

*

See DM, Broumand N, Sahl L, Tilles JG. In vitro effects of echinacea and ginseng on natural killer and antibody-dependent cell cytotoxicity in healthy subjects and chronic fatigue syndrome or acquired immunodeficiency syndrome patients. *Immunopharmacology*. 1997 Jan;35(3):229-35. PMID: 9043936

Both echinacea and ginseng significantly enhanced NK-function of CFS and AIDS patients. Similarly, the addition of either herb significantly increased antibody-dependent cellular cytotoxicity of peripheral blood mononuclear cells from all subject groups.

Sauna

Beever R. Far-infrared saunas for treatment of cardiovascular risk factors: summary of published evidence. *Can Fam Physician*. 2009 Jul;55(7):691-6. PMID: 19602651

A review of the literature finds one study providing weak evidence that far infrared saunas can be of help in CFS.

*



Paradigm Change

Pall ML. Do sauna therapy and exercise act by raising the availability of tetrahydrobiopterin? *Med Hypotheses*. 2009 Oct;73(4):610-3. PMID: 19581054

Sauna therapy may act to increase BH4 availability via two distinct pathways.

*

Masuda A, Munemoto T, Tei C. A new treatment: thermal therapy for chronic fatigue syndrome. *Nihon Rinsho*. 2007 Jun;65(6):1093-8.

Far-infrared ray (FIR) dry sauna therapy helped a few patients to experience decreased fatigue and pain. PMID: 17561703

Miscellaneous Treatments

Akarsu S, Tekin L, Ay H, Carli AB, Tok F, Simşek K, Kiralp MZ. The efficacy of hyperbaric oxygen therapy in the management of chronic fatigue syndrome. *Undersea Hyperb Med*. 2013 Mar-Apr;40(2):197-200. PMID: 23682549

CFS patients receiving 15 treatments of hyperbaric therapy demonstrated improved test outcomes on a visual analog fatigue scale, a fatigue severity scale and a fatigue quality of life scale.

*

Ho RT, Chan JS, Wang CW, Lau BW, So KF, Yuen LP, Sham JS, Chan CL. A randomized controlled trial of qigong exercise on fatigue symptoms, functioning, and telomerase activity in persons with chronic fatigue or chronic fatigue syndrome. *Ann Behav Med*. 2012 Oct;44(2):160-70. PMID: 22736201

In a group of patients with chronic fatigue or CFS, fatigue symptoms, mental functioning and telomerase activity were significantly improved in a group practicing qigong exercises compared to controls.

*

Shin SR, Han AL. Improved chronic fatigue symptoms after removal of mercury in patient with increased mercury concentration in hair toxic mineral assay: a case. *Korean J Fam Med*. 2012 Sep;33(5):320-5. PMID: 23115707



Paradigm Change

A Korean patient's toxic chronic fatigue symptoms improved after he was given mercury removal therapy.

*

Matsui T, li K, Hojo S, Sano K. Cervical neuro-muscular syndrome: discovery of a new disease group caused by abnormalities in the cervical muscles. *Neurol Med Chir (Tokyo)*. 2012;52(2):75-80. PMID: 22362287

The researchers' previous study of whiplash injury found that abnormalities in the cervical muscles cause autonomic dystonia. More than 84% of CFS patients treated for this reported good outcomes.

*

Liu KP, Fang M, Dai DC, Jiang SY, Zuo YZ. A study of median frequencies of skeletal muscle undergoing Tuina intervention in patients with chronic fatigue syndrome. *Zhong Xi Yi Jie He Xue Bao*. 2011 Oct;9(10):1083-7. PMID: 22015189

The Chinese treatment of tuina can improve the symptom of patients with CFS.

*

Sathyapalan T, Beckett S, Rigby AS, Mellor DD, Atkin SL. High cocoa polyphenol rich chocolate may reduce the burden of the symptoms in chronic fatigue syndrome. *Nutr J*. 2010 Nov 22;9:55. PMID: 21092175

A study of 10 CFS patients suggests that high cocoa liquor/polyphenol rich chocolate may improve symptoms.

*

Nijs J, Adriaens J, Schuermans D, Buyl R, Vincken W. Breathing retraining in patients with chronic fatigue syndrome: a pilot study. *Physiother Theory Pract*. 2008 Mar-Apr;24(2):83-94. PMID: 18432511

Many CFS patients have diminished lung function, and breathing retraining can help to address that.

*



Paradigm Change

Yaqob A, Danersund A, Stejskal VD, Lindvall A, Hudecek R, Lindh U. Metal-specific lymphocyte reactivity is downregulated after dental metal replacement. *Neuro Endocrinol Lett.* 2006 Feb-Apr;27(1-2):189-97. PMID: 16648791

Replacement of incompatible dental materials resulted in down-regulation of metal-induced lymphocyte sensitivity in vitro, as well as in the improvement of health status of majority of patients with unspecific CFS-like symptoms.

*

Bentler SE, Hartz AJ, Kuhn EM. Prospective observational study of treatments for unexplained chronic fatigue. *J Clin Psychiatry.* 2005 May;66(5):625-32. PMID: 15889950

Of a group of CFS sufferers, the percentage of users who found a treatment helpful was greatest for coenzyme Q10 (69% of 13 subjects), dehydroepiandrosterone (DHEA) (65% of 17 subjects), and ginseng (56% of 18 subjects). The use of yoga predicted subsequent fatigue improvement and yoga ($p = .002$). Magnesium ($p = .002$) was strongly associated with fatigue worsening from 6 months to 2 years. Yoga appeared to be most effective for subjects who did not have unclear thinking associated with the fatigue.

*

Weatherley-Jones E, Nicholl JP, Thomas KJ, Parry GJ, McKendrick MW, Green ST, Stanley PJ, Lynch SP. A randomised, controlled, triple-blind trial of the efficacy of homeopathic treatment for chronic fatigue syndrome. *J Psychosom Res.* 2004 Feb;56(2):189-97. PMID: 15016577

There is weak but equivocal evidence that the effects of homeopathic medicine are superior to placebo in CFS.

Staphylococcus Toxoid

Zachrisson O, Colque-Navarro P, Gottfries CG, Regland B, Möllby R. Immune modulation with a staphylococcal preparation in fibromyalgia/chronic fatigue syndrome: relation between antibody levels and clinical improvement. *Eur J Clin Microbiol Infect Dis.* 2004 Feb;23(2):98-105. PMID: 14735403

This explorative study suggests that repeated administration of the Staphypan Berna vaccine in patients with fibromyalgia/CFS causes a serological response to several



Paradigm Change

staphylococcal antigens, particularly to certain extracellular toxins and enzymes. This response is related to the clinical outcome of treatment.

*

Zachrisson O, Regland B, Jahreskog M, Jonsson M, Kron M, Gottfries CG. Treatment with staphylococcus toxoid in fibromyalgia/chronic fatigue syndrome--a randomised controlled trial. *Eur J Pain*. 2002;6(6):455-66. PMID:12413434

Treatment with staphylococcus toxoid injections over 6 months led to significant improvement in patients with FM and CFS. Maintenance treatment is required to prevent relapse.

*

Andersson M, Bagby JR, Dyrehag L, Gottfries C. Effects of staphylococcus toxoid vaccine on pain and fatigue in patients with fibromyalgia/chronic fatigue syndrome. *Eur J Pain*. 1998;2(2):133-142. PMID: 10700309

The effect of vaccination with a staphylococcus toxoid was compared with the effect of injections of sterile water. Results suggest that treatment with staphylococcus toxoid may be a fruitful strategy in patients with fibromyalgia and CFS.

Acupuncture

Liu CZ, Lei B. Effect of acupuncture on serum malonaldehyde content, superoxide dismutase and glutathione peroxidase activity in chronic fatigue syndrome rats. *Zhen Ci Yan Jiu*. 2012 Feb;37(1):38-40, 58. PMID: 22574567

Acupuncture can adjust metabolism of serum oxygen free radicals in rats that have been subjected to a forced-swim condition meant to simulate CFS.

*

Xu W, Zhou RH, Li L, Jiang MW. Observation on therapeutic effect of chronic fatigue syndrome treated with coiling dragon needling and moving cupping on back. *Zhongguo Zhen Jiu*. 2012 Mar;32(3):205-8. PMID: 22471128



Paradigm Change

The therapeutic effect of chronic fatigue syndrome treated through acupuncture with coiling dragon needling and moving cupping on back is superior to treatment with prednisone.

*

Zhang W, Liu ZS, Xu HR, Liu YS. Observation on therapeutic effect of acupuncture of Back-shu acupoints for chronic fatigue syndrome patients. *Zhen Ci Yan Jiu*. 2011 Dec;36(6):437-41, 448. PMID: 22379791

Acupuncture at Back-shu point has a good therapeutic effect (including immediate and midterm effect) in the treatment of chronic fatigue syndrome patients.

*

Chen XH, Li LQ, Zhang W, Yang J, Dai YS, Xu DH, Tang CZ. Randomized controlled study on acupuncture treatment for chronic fatigue syndrome. *Zhongguo Zhen Jiu*. 2010 Jul;30(7):533-6. PMID: 20862932

Acupuncture was more helpful than sham treatment at improving brain, physical and overall treatment in CFS patients.

*

Wang JH, Chai TQ, Lin GH, Luo L. Effects of the intelligent-turtle massage on the physical symptoms and immune functions in patients with chronic fatigue syndrome. *J Tradit Chin Med*. 2009 Mar;29(1):24-8. PMID: 19514184

Compared to conventional massage, the “intelligent turtle” massage used in CFS demonstrates more improvements on IgA, IgM and IgG levels as well as improvement of symptoms.

*

Wang JJ, Song YJ, Wu ZC, Chu XO, Wang XH, Wang XJ, Wei LN, Wang QM. A meta analysis on randomized controlled trials of acupuncture treatment of chronic fatigue syndrome. *Zhen Ci Yan Jiu*. 2009 Dec;34(6):421-8.

A literature review suggests that while acupuncture may be helpful for CFS, more studies are needed.



Paradigm Change

*

Wang JJ, Song YJ, Wu ZC, Chu XO, Wang QM, Wei LN, Wang XJ, Meng H. Randomized controlled study on influence of acupuncture for life quality of patients with chronic fatigue syndrome. *Zhongguo Zhen Jiu*. 2009 Oct;29(10):780-4.

Acupuncture was helpful in improving the quality of life in CFS patients, especially in physiological field and individual perception to well being.

*

Wang JJ, Song YJ, Wu ZC, Chu XO, Wang QM, Wang XJ, Wei LN, Meng H, Wang XH. Randomized controlled clinical trials of acupuncture treatment of chronic fatigue syndrome. *Zhen Ci Yan Jiu*. 2009 Apr;34(2):120-4.

Acupuncture was better than sham acupuncture at relieving CFS patients' mental fatigue.

*

Huang Y, Liao XM, Li XX, Song YB. Clinical observation on the effects of Bo's abdominal acupuncture in 40 cases of chronic fatigue syndrome. *J Tradit Chin Med*. 2008 Dec;28(4):264-6. PMID: 19226895

Acupuncture helped CFS patients to feel less fatigued and better in general.

*

Chen GL, Xiao GM, Zheng XL. Observation on therapeutic effect of multiple cupping at back-shu points on chronic fatigue syndrome. *Zhongguo Zhen Jiu*. 2008 Jun;28(6):405-7. PMID: 18630535

The use of cups in Chinese acupuncture was effective at relieving fatigue in CFS, compared to the use of acupuncture alone.

*

Wang T, Zhang Q, Xue X, Yeung A. A systematic review of acupuncture and moxibustion treatment for chronic fatigue syndrome in China. *Am J Chin Med*. 2008;36(1):1-24. PMID: 18306446

Studies in China suggest that acupuncture can be helpful for CFS, but the poor quality means that more scientifically rigorous studies need to be done.



Paradigm Change

*

Yao F, Ji Q, Zhao Y, Feng JL. Observation on therapeutic effect of point pressure combined with massage on chronic fatigue syndrome. *Zhongguo Zhen Jiu*. 2007 Nov;27(11):819-20. PMID: 18085145

Acupressure has the potential of being effective in CFS.

*

Yiu YM, Ng SM, Tsui YL, Chan YL. A clinical trial of acupuncture for treating chronic fatigue syndrome in Hong Kong. *Zhong Xi Yi Jie He Xue Bao*. 2007 Nov;5(6):630-3. PMID: 17997936

Acupuncture is effective for CFS.

*

Yuemei L, Hongping L, Shulan F, Dongfang G. The therapeutic effects of electrical acupuncture and auricular-plaster in 32 cases of chronic fatigue syndrome. *J Tradit Chin Med*. 2006 Sep;26(3):163-4. PMID:17078435

Electrical acupuncture was more effective in CFS than oral hydrocortisone.

Combination Therapies

Myhill S, Booth NE, McLaren-Howard J. Targeting mitochondrial dysfunction in the treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) - a clinical audit. *Int J Clin Exp Med*. 2013;6(1):1-15. PMID: 23236553

An audit of 138 ME/CFS patients revealed that all had measureable mitochondrial dysfunction. A basic treatment regime (including stone-age diet, good sleep, nutritional supplements and getting the right balance between work and rest) improved mitochondrial function in a sample of these.

*



Paradigm Change

Mutter J, Naumann J, Guethlin C. Elimination of xenobiotics in a female patient with fibromyalgia, chronic fatigue, and trunk obesity. *Forsch Komplementmed.* 2007 Feb;14(1):39-44. PMID: 17341886

Following therapy consisting of dietary advise, chelating agents, supplements and acupuncture, a CFS patient became symptom free.

*

Guo J. Chronic fatigue syndrome treated by acupuncture and moxibustion in combination with psychological approaches in 310 cases. *J Tradit Chin Med.* 2007 Jun;27(2):92-5. PMID: 17710799

Acupuncture plus moxibustion combined with a psychological approach appears to be an effective therapy for CFS.

*

Uchida A. Therapy of chronic fatigue syndrome. *Nihon Rinsho.* 1992 Nov;50(11):2679-83. PMID: 1287242

A group of Japanese researchers reported that Intravenous immunoglobulin therapy, magnesium and sizofirann (a biological response modifier targeting natural killer cells) were successful in improving the health of their CFS patients.

Oxidative Stress -- Animal Models of CFS

Surapaneni DK, Adapa SR, Preeti K, Teja GR, Veeraragavan M, Krishnamurthy S. Shilajit attenuates behavioral symptoms of chronic fatigue syndrome by modulating the hypothalamic-pituitary-adrenal axis and mitochondrial bioenergetics in rats. *J Ethnopharmacol.* 2012 Aug 30;143(1):91-9. PMID: 22771318

Shilajit, a traditional Indian remedy, was helpful in reversing the fatigue experienced by rats in a forced-swim trial.

*

Singh PK, Chopra K, Kuhad A, Kaur IP. Role of *Lactobacillus acidophilus* loaded floating beads in chronic fatigue syndrome: behavioral and biochemical evidences. *Neurogastroenterol Motil.* 2012 Apr;24(4):366-e170. PMID: 22296294



Paradigm Change

Based on the findings of a forced-swim rat study, the researchers suggest a therapeutic role of lactobacillus acidophilus especially when incorporated into alginate beads for the treatment of CFS.

*

Sachdeva AK, Kuhad A, Chopra K. Epigallocatechin gallate ameliorates behavioral and biochemical deficits in rat model of load-induced chronic fatigue syndrome. *Brain Res Bull.* 2011 Jul 28. PMID: 21821105

In a rat model of CFS, treatment with EGCG was helpful in reducing oxido-nitrosative stress and serum TNF-alpha levels and at reversing behavioral changes.

*

Sheng R, Xu X, Tang Q, Bian D, Li Y, Qian C, He X, Gao X, Pan R, Wang C, Luo Y, Xia Y, Dai Y. Polysaccharide of Radix Pseudostellariae Improves Chronic Fatigue Syndrome Induced by Poly I:C in Mice. *Evid Based Complement Alternat Med.*, 2011. PMID: 20008077

In a mouse model of CFS, the Chinese herb Radix Pseudostellariae was effective.

*

Gupta A, Vij G, Chopra K. Possible role of oxidative stress and immunological activation in mouse model of chronic fatigue syndrome and its attenuation by olive extract. *J Neuroimmunol.* 2010 Sep 14;226(1-2):3-7. PMID: 20537729

In a mouse model of CFS, olive extract was helpful in relieving oxidative stress.

*

Sachdeva AK, Kuhad A, Tiwari V, Arora V, Chopra K. Protective effect of epigallocatechin gallate in murine water-immersion stress model of chronic fatigue syndrome. *Basic Clin Pharmacol Toxicol.* 2010 Jun;106(6):490-6. PMID:20088847

In a mouse model of CFS, epigallocatechin gallate was found to be effective at addressing oxidative-nitrosative stress and TNF-alpha levels in the brain.

*



Paradigm Change

Vij G, Gupta A, Chopra K. Modulation of antigen-induced chronic fatigue in mouse model of water immersion stress by naringin, a polyphenolic antioxidant. *Fundam Clin Pharmacol.* 2009 Jun;23(3):331-7. PMID: 19469804

In a mouse model of CFS, the natural polyphenol naringin was successful in attenuating oxidative stress as well as TNF-alpha levels.

*

Sachdeva AK, Kuhad A, Tiwari V, Chopra K. Epigallocatechin gallate ameliorates chronic fatigue syndrome in mice: behavioral and biochemical evidence. *Behav Brain Res.* 2009 Dec 28;205(2):414-20. PMID: 19643148

In a mouse model of CFS, epigallocatechin gallate was effective at reversing behavioral deficits and oxidative-nitrosative stress.

*

Lyle N, Gomes A, Sur T, Munshi S, Paul S, Chatterjee S, Bhattacharyya D. The role of antioxidant properties of *Nardostachys jatamansi* in alleviation of the symptoms of the chronic fatigue syndrome. *Behav Brain Res.* 2009 Sep 14;202(2):285-90. PMID: 19375459

In a rat model of CFS, *Nardostachys jatamansi* extract normalized lipid peroxidation, nitrite, superoxide dismutase, catalase and overall behavior.

*

Kumar A, Garg R. Protective effects of antidepressants against chronic fatigue syndrome-induced behavioral changes and biochemical alterations. *Fundam Clin Pharmacol.* 2009 Feb;23(1):89-95. PMID: 19207541

In a mouse model of CFS, the antidepressant drugs imipramine, desipramine and citalopram helped with anxiety and oxidative stress, improved locomotor activity, and reduced immobility time.

*

Gupta A, Vij G, Sharma S, Tirkey N, Rishi P, Chopra K. Curcumin, a polyphenolic antioxidant, attenuates chronic fatigue syndrome in murine water immersion stress model. *Immunobiology.* 2009;214(1):33-9. PMID: 19159825



Paradigm Change

In a mouse model of CFS, treatment with curcumin resulted in decreased oxidative stress, decreased TNF-alpha levels, and decreased immobility time.

*

Kuo YH, Tsai WJ, Loke SH, Wu TS, Chiou WF. Astragalus membranaceus flavonoids (AMF) ameliorate chronic fatigue syndrome induced by food intake restriction plus forced swimming. *J Ethnopharmacol.* 2009 Feb 25;122(1):28-34. PMID: 19103273

In a rat simulation of CFS, astragalus membranaceus flavonoids helped to normalize cytokines.

*

Chen R, Moriya J, Luo X, Yamakawa J, Takahashi T, Sasaki K, Yoshizaki F. Hochu-ekki-to combined with interferon-gamma moderately enhances daily activity of chronic fatigue syndrome mice by increasing NK cell activity, but not neuroprotection. *Immunopharmacol Immunotoxicol.* 2009 Jun;31(2):238-45. PMID: 18791913

In a mouse model of CFS, Hochu-ekki-to (TJ-41) combined with interferon-gamma (IFN gamma) appeared to have a protective effect on host immune responses, but did not seem neuroprotective.

*

Kumar A, Garg R, Kumar P. Nitric oxide modulation mediates the protective effect of trazodone in a mouse model of chronic fatigue syndrome. *Pharmacol Rep.* 2008 Sep-Oct;60(5):664-72. PMID: 19066412

In a mouse model of CFS, trazodone was protective against oxidative damage, especially when preceded with treatment with L-NAME. Pre-treatment with L-arginine removed the protective effect of the trazodone.

*

Takahashi T, Yu F, Zhu SJ, Moriya J, Sumino H, Morimoto S, Yamaguchi N, Kanda T. Beneficial effect of brewers' yeast extract on daily activity in a murine model of chronic fatigue syndrome. *Evid Based Complement Alternat Med.* 2006 Mar;3(1):109-15. PMID: 16550231

In a mouse model of CFS, brewers' yeast extract seemed to be protective.



Paradigm Change

*

Singal A, Kaur S, Tirkey N, Chopra K. Green tea extract and catechin ameliorate chronic fatigue-induced oxidative stress in mice. *J Med Food*. 2005 Spring;8(1):47-52. PMID:15857209

In a mouse model of CFS, green tea extract and catechin were effective at decreasing oxidative stress.

Stress Reduction

Jason LA, Brown M, Brown A, Evans M, Flores S, Grant-Holler E, Sunquist M. Energy Conservation/Envelope Theory Interventions to Help Patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Fatigue*. 2013 Jan 14;1(1-2):27-42. PMID: 23504301

Studies show that the energy envelope approach, which involves rehabilitation methods, helps patients with ME/CFS pace activities and manage symptoms and can significantly improve their quality of life.

*

Jason LA, Brown MM. Sub-typing daily fatigue progression in chronic fatigue syndrome. *J Ment Health*. 2013 Feb;22(1):4-11. PMID: 22548385

Activity logs can provide investigators and clinicians with valuable sources of data for understanding patterns of fatigue and activity among patients with CFS.

*

Brown AA, Evans MA, Jason LA. Examining the energy envelope and associated symptom patterns in chronic fatigue syndrome: does coping matter? *Chronic Illn*. 2013 Apr 12. PMID: 23585632

Although energy maintenance may be associated with improved functioning and less severe symptoms for some CFS patients, a subsegment of patients was severely limited in functioning despite using adaptive coping strategies.

*



Paradigm Change

Goudsmit EM, Nijs J, Jason LA, Wallman KE. Pacing as a strategy to improve energy management in myalgic encephalomyelitis/chronic fatigue syndrome: a consensus document. *Disabil Rehabil.* 2012;34(13):1140-7. PMID: 22181560

Based on various studies, it is proposed that pacing can help to stabilize the condition of CFS and avoid post-exertional malaise.

*

Jason LA, Roesner N, Porter N, Parenti B, Mortensen J, Till L. Provision of social support to individuals with chronic fatigue syndrome. *J Clin Psychol.* 2010 Mar;66(3):249-58. PMID: 19902489

CFS patients who had a “student buddy” to help out with tasks had significantly greater reductions in fatigue severity and increases in vitality than individuals in the control condition.

*

Reynolds NL, Brown MM, Jason LA. The relationship of Fennell phases to symptoms among patients with chronic fatigue syndrome. *Eval Health Prof.* 2009 Sep;32(3):264-80. PMID: 19696083

CFS patients who use a crisis approach to coping are less functional than other patients.

*

Bjørkum T, Wang CE, Waterloo K. Patients' experience with treatment of chronic fatigue syndrome. *Tidsskr Nor Laegeforen.* 2009 Jun 11;129(12):1214-6. PMID: 19521443

Pacing was evaluated as useful by 96% of the participants, rest by 97%, and 96% of the participants considered complete shielding and quietness to be useful. 57% of the participants who had received help to identify and challenge negative thought patterns regarded this useful. 79% of the participants with experience from graded training regarded this to worsen their health status.

*

Wells DL. Associations between pet ownership and self-reported health status in people suffering from chronic fatigue syndrome. *J Altern Complement Med.* 2009 Apr;15(4):407-13. PMID: 19388863



Paradigm Change

Findings suggest no statistically significant association between pet ownership and self-reported health in people with CFS.

*

Sampalli T, Berlasso E, Fox R, Petter M. A controlled study of the effect of a mindfulness-based stress reduction technique in women with multiple chemical sensitivity, chronic fatigue syndrome, and fibromyalgia. *J Multidiscip Healthc.* 2009 Apr 7;2:53-9. PMID: 21197347

CFS patients who were trained in a stress reduction technique demonstrated improvements.

*

Bogaerts K, Hubin M, Van Diest I, De Peuter S, Van Houdenhove B, Van Wambeke P, Crombez G, Van den Bergh O. Hyperventilation in patients with chronic fatigue syndrome: the role of coping strategies. *Behav Res Ther.* 2007 Nov;45(11):2679-90. PMID: 17719001

A “hostile resistance” coping strategy seems to trigger both physiological and symptom perception processes contributing to the clinical picture of CFS.

*

Van Damme S, Crombez G, Van Houdenhove B, Mariman A, Michielsen W. Well-being in patients with chronic fatigue syndrome: the role of acceptance. *J Psychosom Res.* 2006 Nov;61(5):595-9. PMID: 17084136

Patients who accept their condition rather than trying to control their symptoms feel less fatigued and more emotionally stable.

*

Taylor RR. Quality of life and symptom severity for individuals with chronic fatigue syndrome: findings from a randomized clinical trial. *Am J Occup Ther.* 2004 Jan-Feb;58(1):35-43. PMID: 14763634

The effects of an integrative, consumer-driven rehabilitation program on quality of life and symptom severity for individuals with chronic fatigue syndrome were examined.



Paradigm Change

M.E. TREATMENTS

MEDIA COVERAGE

“I Was a Zombie for Years, Then A Massage Brought Me Back to Life: ME Treatment
November 12, 2011
Daily Mail (UK)
Which GP’s Don’t Know About”
By Alex Terry

<http://www.dailymail.co.uk/health/article-2060818/I-zombie-years-massage-brought-life-ME-treatment-GPs-dont-know-about.html>

*

August 2011
Ladies’ Home Journal
What Ever Happened to Chronic Fatigue Syndrome
By Margery D. Rosen

<http://www.lhj.com/health/news/chronic-fatigue-syndrome/>

*

May 14, 2011
KSL-TV
Fibromyalgia to Cause “Bone-Crushing Fatigue”
By Wendy Leonard

<http://www.ksl.com/?nid=960&sid=15534055>

*

October 27, 2009
The Washington Post
Don’t Wait for a Cure to Appear
As Someone with Chronic Fatigue Syndrome, I Had to Change My Life to Get Relief
By Zachary Sklar



Paradigm Change

<http://pqasb.pqarchiver.com/washingtonpost/access/1887013121.html?FMT=ABS&FMTS=ABS:FT&date=Oct+27%2C+2009&author=Zachary+Sklar&pub=The+Washington+Post&edition=&startpage=E.5&desc=Don%27t+wait+for++a+cure+to+appear%3B+As+so+meone+with+chronic+fatigue+syndrome%2C+I+had+to+change+my+life+to+get+relief>

*

December 3, 2009
Woman's Day
Understanding Chronic Fatigue
By Barbara Brody

<http://www.womansday.com/Articles/Health-Fitness/Conditions-Diseases/Understanding-Chronic-Fatigue.html>

*

January 3, 1999
The New York Times
Q&A: A Doctor Tackles the Mysteries of Fatigue
By Karen DeMasters

<http://www.nytimes.com/1999/01/03/nyregion/q-a-a-doctor-tackles-the-mysteries-of-fatigue.html?scp=153&sq=%22chronic+fatigue+syndrome%22&st=nyt&gwh=4AAAA1ED49B0EC3D183272794D7BE33B>

*

October 2, 1991
The New York Times
Test Drug Seen as Promising in Study on Chronic Fatigue
By Lawrence K. Altman

<http://www.nytimes.com/1991/10/02/us/test-drug-seen-as-promising-in-study-on-chronic-fatigue.html>

*

April 30, 1991
The New York Times
Magnesium May Play Role in Chronic Fatigue Syndrome



Paradigm Change

<http://www.nytimes.com/1991/04/30/news/magnesium-may-play-role-in-chronic-fatigue.html?scp=231&sq=%22chronic+fatigue+syndrome%22&st=nyt&gwh=092561814CDE514F58C8464F60A3B449>

Rituximab:

May 2013
Discover Magazine
Are B-Cells to Blame for Chronic Fatigue Syndrome?
By Jill Neimark

<http://discovermagazine.com/2013/may/01-are-b-cells-to-blame-for-chronic-fatigue-syndrome#.UaWQIY5OTzI>

*

December 23, 2011
Irish Central (UK)
Irish Doctor Opens New Chronic Fatigue Syndrome Clinic in NYC
By Molly Muldoon

<http://www.irishcentral.com/news/Irish-doctor-opens-new-chronic-fatigue-syndrome-clinic-in-NYC-136017443.html>

*

December 22, 2011
Lab Canada
Plans Unveiled For New Complex Chronic Disease Clinic

<http://www.labcanada.com/news/plans-unveiled-for-new-complex-chronic-disease-clinic/1000779921/>

*

December 6, 2011
The Vancouver Sun
BC Women's Hospital Named New Medical Centre For Lyme, Chronic Fatigue and Other Complex Diseases
By Pamela Fayerman



Paradigm Change

<http://blogs.vancouversun.com/2011/12/06/bc-womens-hospital-named-new-medical-centre-for-lyme-chronic-fatigue-and-other-complex-diseases/>

*

October 26, 2011
Huffington Post
Chronic Fatigue Syndrome -- A Treatable Autoimmune Disease
By Matthew Edlund, M.D.

http://www.huffingtonpost.com/matthew-edlund-md/chronic-fatigue-syndrome_b_1028341.html

*

October 24, 2011
ABC News
Chronic Fatigue Syndrome: Study Supports Autoimmune Disease Theory
By Katie Moisse

<http://abcnews.go.com/Health/Wellness/chronic-fatigue-syndrome-study-supports-autoimmune-disease-theory/story?id=14801908>

*

October 24, 2011
Daily Mail (UK)
Cancer Drug 'Key to Treating Chronic Fatigue' As Experts Say Syndrome May be Caused By Defective Immune System
By Claire Bates

<http://www.dailymail.co.uk/health/article-2052738/Chronic-fatigue-Cancer-drug-key-treating-M-E-experts-say-disorder-caused-defective-immune-system.html>

*

October 23, 2011
BBC
Immune System May Cause ME
By James Gallagher



Paradigm Change

<http://www.bbc.co.uk/news/health-15401746>

*

October 20, 211
NewScientist
Chronic Fatigue Syndrome Eased By Cancer Drug
By Andy Coghlan

<http://www.newscientist.com/article/dn21065-chronic-fatigue-syndrome-eased-by-cancer-drug.html>



Paradigm Change

“Cure Together” Treatment Ratings

The Cure Together website offers surveys allowing patients with various diseases to rate whether specific treatments were helpful or harmful to them. As of 5/28/13, more than 500 patients had responded to the survey about “Chronic Fatigue Syndrome (CFS).”

Listed here are the percentages of people (out of those who tried it) who found each treatment to be of moderate or major effectiveness.

Also listed are treatments in which 20% or more (out of those who tried it) reported that it had made their condition much or moderately worse.

Treatments with fewer than 20 people responding are not included on this list.

70%+ Effectiveness:

Lifestyle:

- * Spend time in low stimulation environment. 72%
- * Take frequent rest breaks. 71%
- * Wheelchair. 71%

60%+ Effectiveness:

Lifestyle:

- * Rest. 64%
- * Personal development (learn to say no). 63%

Hormones:

- * T3. 65%

Drugs:

- * Low Dose Naltrexone (LDN). 62%

50%+ Effectiveness:



Paradigm Change

Avoidance:

- * Avoid allergens. 59%
- * Avoid biotoxins. 57%

Lifestyle:

- * Ignore people who think ME/CFIDS is not real. 54%
- * Mindfulness. 54%
- * Meditation. 53%
- * Change job. 50%

Diet/Nutrition:

- * Diet changes. 52%
- * Treat methylation. 51%

Bodywork:

- * Invert body position. 56%
- * Qi Gong. 52%

Drugs:

- * Klonopin. 51%

40%+ Effectiveness:

Avoidance:

- * Avoid mold. 49%
- * Reduce sugar. 49%
- * Avoid gluten. 46%
- * Avoid dairy. 44%
- * Avoid alcohol. 43%

Bodywork:

- * Massage. 49%
- * FIR sauna. 47%
- * Diaphragmatic breathing. 45%
- * Lymphatic Massage. 44%
- * Stretching. 43%
- * Cranial Sacral. 42%
- * Yoga. 41%
- * Chiropractic. 40%



Paradigm Change

Drugs:

- * Stimulants. 49%
- * Tramadol. 49%
- * Ritalin. 47%
- * Antivirals. 45%
- * Xanax. 42%
- * Baclofen. 41%
- * Ibuprofen. 41%

Infections:

- * Treat yeast. 49%
- * Sinus treatments. 43%

Supplements/Nutrition:

- * B12 Injections. 46%
- * Probiotics. 42%
- * Betaine Hcl. 40%
- * Electrolyte beverages. 40%

Lifestyle:

- * Go to bed early/sleep longer. 43%
- * Amygdala retraining. 41%

Alternative:

- * Ayurveda. 41%

30%+ Effectiveness

Supplements/Nutrition:

- * Oral magnesium. 39%
- * Malic acid. 38%
- * NAC. 38%
- * Stay well-hydrated. 38%
- * Sublingual B12. 36%
- * Topical magnesium. 36%
- * D-Ribose. 34%
- * Myers' Cocktail. 34%
- * Acetyl-L-Carnitine. 32%
- * B Vitamins 32%
- * Chinese herbs. 32%



Paradigm Change

- * Eat more produce. 32%
- * Liposomal glutathione. 32%
- * Anti-Yeast Diet. 31%
- * Vitamin D. 31%
- * Omega 3. 31%
- * Cerefolin. 31%
- * Ionized water. 30%
- * MSM. 30%

Hormones:

- * Testosterone. 37%
- * Bioidentical Hormones (e.g. progesterone). 36%
- * Cortef. 35%
- * DHEA. 33%
- * Melatonin. 31%

Antibiotics:

- * Doxycycline. 39%
- * Antibiotics. 37%

Antidepressants:

- * Cymbalta. 38%
- * Wellbutrin. 35%

Bodywork:

- * Osteopathy. 38%
- * Tai Chi. 37%
- * Soak feet in cold water. 36%
- * Cool shower following exertion. 34%
- * Root canal/cavitation removal. 33%
- * Reiki. 32%
- * Acupuncture. 30%

Other Drugs:

- * Guaifenesin. 38%
- * Chelation. 36%
- * Immunovir. 36%
- * Provigil. 35%
- * Antihistamines. 34%
- * Naproxen. 34%
- * Beta Blockers. 31%
- * Neurontin. 31%



Paradigm Change

- * Tylenol. 31%
- * Benadryl. 30%

Lifestyle:

- * Emotional Freedom Technique (EFT). 34%.
- * Distract attention from symptoms. 33%

20%+ Effectiveness:

Antidepressants:

- * Amitriptyline. 29%
- * Trazadone. 28%
- * Celexa. 28%
- * SSRIs. 25%
- * Effexor. 23%

Exercise:

- * Mild/Moderate Exercise. 29%
- * Regular Exercise Program. 25%
- * Orthostatic conditioning. 23%

Supplements/Nutrition:

- * Alpha Lipoic Acid. 28%
- * Licorice Root Extract. 28%
- * CoQ10. 27%
- * L-Carnitine. 27%
- * Inosine. 26%
- * Iodine. 26%
- * 5HTP. 25%
- * Omega 3, 6, 9. 25%
- * Vitamin C (Lypospheric). 24%
- * Glucosamine/Chondroitin. 23%
- * NADH. 22%
- * Undenatured whey. 22%
- * Ginkgo Biloba. 21%
- * Vitamin E. 21%
- * Fresh Juicing/Smoothies. 20%

Alternative:

- * Kinesiology. 28%



Paradigm Change

* Homeopathy. 27%

Other Drugs:

* Aspirin. 27%

* Caffeine. 25%

Lifestyle:

* Psychotherapy. 25%

* Cognitive-Behavioral Therapy (CBT). 24%

Bodywork:

* Rolfing. 21%

Less Than 20% Effectiveness:

Lifestyle:

* Brainwave Audio CD's. 19%

* Neurofeedback. 17%

Supplements:

* Olive Leaf Extract. 19%

* SAM-E. 19%

* Cat's Claw. 17%

* GABA. 17%

* Garlic. 16%

* Vitamin A. 13%

* Monolaurin. 8%

Antidepressants:

* Prozac. 19%

* Zoloft. 16%

* Paroxetine. 15%

Bodywork:

* Skin Brushing. 19%

* Detox Foot Baths. 14%

* Rebounder. 11%

Other Drugs:

* Doxylamine. 18%



Paradigm Change

* Alcohol. 14%

Exercise:

* Graded Exercise Therapy (CBT). 18%

Treatments with 20%+ Reporting Declines:

Exercise:

- * Graded Exercise Therapy (75%)
- * Regular Exercise Program (45%)
- * Mild/Moderate Exercise (43%)
- * Orthostatic Conditioning/Exercise (32%)

Antidepressants:

- * Paxil (59%)
- * Prozac (46%)
- * Zoloft (44%)
- * Effexor (43%)
- * Elavil (43%)
- * SSRI's (43%)
- * Trazodone (40%)
- * Wellbutrin (38%)
- * Cymbalta (36%)
- * Celexa (32%)

Other Drugs:

- * Alcohol (57%)
- * Caffeine (37%)
- * Neurontin (32%)
- * Provigil (31%)
- * Benadryl (28%)
- * SAM-E (23%)

Lifestyle:

* Cognitive/Behavioral Therapy (CBT) 20%

<http://curetogether.com/chronic-fatigue-syndrome/treatments/>



Paradigm Change

Survey Discussion:

Only a relatively small number of different types of treatments were reported as helpful by more than half of those survey respondents who had tried them.

Topping the list were “pacing” activities: spending time in low-stimulation environments, taking rest breaks, learning to say no, ignoring people who didn’t believe in the illness, meditation, mindfulness and changing job (presumably to a less stressful one). A high percentage of the relatively small number of participants (n=55) who had tried a wheelchair found it helpful.

Avoiding “biotoxins” (presumably including toxic mold) was found to be helpful for 57% of respondents. About 59% said that they had been helped by avoiding “allergens” (unspecified, possibly including food). Just over half said that they had been helped by changes in diet (also unspecified).

Only a few drugs were found helpful by more than 50% of patients who had tried them: T3 (a form of thyroid hormone), Low-Dose Naltrexone (an immune modulator) and Klonopin (a benzodiazepine often prescribed for sleep). Treating methylation (presumably with supplements such as activated folate and B12) was found helpful by just over half of respondents.

Two other interventions with more than 50% of participants reporting positive outcomes were qi gong and inversion of body position.

Also rating fairly highly in the survey (with 43-49% reporting benefits) were a variety of other kinds of avoidance activities -- mold, sugar, gluten, dairy and alcohol. (About 140 people responded to the item about “avoiding mold,” compared to only 70 to the item about “avoiding biotoxins.”)

Several bodywork treatments (massage, lymphatic massage, far infrared sauna, stretching, cranial sacral, yoga, chiropractic, diaphragmatic breathing) all were found helpful by more than 40% of those who tried them.

Treating yeast and sinus infections (presumably frequently caused by fungi) were reported as helpful by about 45% of those who had tried this. The alternative treatments of amygdala retraining and ayurveda were found effective by about the same percentage, as was simply going to bed earlier and sleeping longer.

Supplements and drugs found helpful by 40-49% of participants who had tried them included B12 shots; probiotics; betaine Hcl; electrolyte beverages; Xanax; antivirals; Ritalin and other stimulants; and the pain relievers tramadol, baclofen and ibuprofen.



Paradigm Change

Reported as helpful by less than 40% of respondents who had tried them were a vast smorgasbord of other drugs, supplements and alternatives. None of these was reported as having prompted a major improvement by any more than a tiny percentage (less than 5%) of people reporting.

Ironically, two treatment types frequently suggested for CFS by non-specialists -- anti-depressants and exercise -- appear to be by far the least appropriate for the disease, based on this survey. Relatively few respondents (less than 30%) reported being helped by these treatments, and relatively high percentages (30-75%) who had tried them said that they had been harmed by them.

Other treatments that were reported as having had negative effects by substantial numbers of respondents were alcohol (57%), caffeine (37%), neurontin (32%), Provigil (31%), Benadryl (28%), SAM-E (23%) and cognitive-behavioral therapy (20%).

-Lisa Petrison, Ph.D.

Copyright 2013, Paradigm Change/Lisa Petrison, Ph.D.

This document may be distributed freely in its entirety. Quotations may be used without restriction insofar as attribution is provided.

For more information, visit Paradigm Change at www.paradigmchange.me.