ME/CFS Epidemiology and Causal Theories

Clusters


The authors investigated the possibility that chronic fatigue syndrome (CFS) predisposes to cancer by comparing the cancer pattern in an area in northern Nevada, where an outbreak of a fatiguing illness, which included cases of CFS, was reported, to an area in southern Nevada, where no such illness was reported. Higher incidences of NHL and primary brain tumors were noted in the two northern Nevada counties (Washoe and Lyon) in 1986 and 1987 respectively, compared to the southern Nevada (Clark) county.


The authors interviewed of the original 28 patients in the CFS outbreak in West Otago, NZ. Of these, 48% currently met the criteria for CFS; the rest were classified as having prolonged or idiopathic fatigue. The women were more likely to still meet the CFS criteria than the men. Most of the patients had returned to at least moderate levels of activity.


The authors consider whether the decreased natural killer cell function in CFS clusters may be related to brain/CNS tumors and non-Hodgkin’s lymphoma, finding a trend that merits future research.

The authors reviewed 12 outbreaks of CFS, epidemic neuromyasthenia and myalgic encephalomyelitis, finding heterogeneity in the range of neurological features present. Outbreaks were grouped into four levels of increasing neurological involvement.


Of outbreaks in the Nevada-California region, giardiasis appears to have precipitated one of the four clusters.


The authors examined the prevalence of non-Hodgkins lymphoma in epidemic areas for CFS.

The clinical and laboratory findings from studies of CFS patients from northern Nevada from 1984-1988 are summarized. Symptoms include profound fatigue of prolonged duration; cervical lymphadenopathy; recurrent sore throat and/or symptoms of influenza; loss of cognitive function manifested by loss of memory and loss of ability to concentrate; myalgia; impairment of fine motor skills; abnormal findings on magnetic resonance imaging brain scan; depressed level of antibody to Epstein-Barr virus (EBV) nuclear antigen; elevated level of antibody to EBV early antigen restricted component; elevated ratio of CD4 helper to CD8 suppressor cells; and strong evidence of association of this syndrome with infection with human herpesvirus 6. More-serious and longer-lasting neurologic impairments, including seizures, psychosis, and dementia, have also been observed.

**Prevalence**


The pooled prevalence for self-reporting assessment of CFS was 3.28%, while the prevalence for clinical assessment was 0.76%.


A study in Olmsted County, Minnesota, demonstrated an overall prevalence and incidence of chronic fatigue syndrome and insufficient/idiopathic fatigue of 71.34 per 100,000 persons.

Prevalence of CFS in a Japanese community was 1%. Amongst these patients, unrefreshing sleep was a common problem.

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The estimated minimum prevalence rate of ME/CFS was 0.2% for cases meeting any of the study case definitions, 0.19% for the CDC-1994 definition, 0.11% for the Canadian definition and 0.03% for the ECD. The overall estimated minimal yearly incidence was 0.015%. The highest rates were found in London and the lowest in East Yorkshire.

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Prevalence was calculated as 111 per 100 000 adolescents and incidence as 12 per 100 000 adolescents per year. The primary adverse impact of CFS is extreme disability associated with considerable school absence.

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Study data suggests that 1% of the population of Nijmegen (in the Netherlands) suffers from CFS. A large part of this group remains unrecognized by the general practitioner.

The higher prevalence of fatiguing states in offspring of CFS mothers, despite the lack of statistical significance, suggests that familial factors may potentially play a role in developing chronically fatiguing states.

* Njoku MG, Jason LA, Torres-Harding SR. The prevalence of chronic fatigue syndrome in Nigeria. J Health Psychol. 2007 May;12(3):461-74. PMID: 17439996

Adult rates of chronic fatigue syndrome (CFS) in Nigeria that were somewhat higher than rates from community-based CFS epidemiological studies in the USA.

* Reeves WC, Jones JF, Maloney E, Heim C, Hoaglin DC, Boneva RS, Morrissey M, Devlin R. Prevalence of chronic fatigue syndrome in metropolitan, urban, and rural Georgia. Popul Health Metr. 2007 Jun 8;5:5.PMID: 17559660

A study of a Georgia population suggested that 2.54% of persons 18 to 59 years of age suffered from CFS. There were no significant differences in prevalence of CFS between metropolitan, urban or rural populations or between white and black residents of the three regions. However, there were significant differences in female-to-male ratios of prevalence across the strata (metropolitan female: male 11.2 : 1, urban 1.7 : 1, rural 0.8 : 1).


A survey of the residents of Wichita, Kansas, suggests that prevalence of CFS among adolescents was considerably lower than among adults. The baseline weighted prevalence of CFS-like illness was 338 per 100,000. Significant differences existed between parental and adolescents' descriptions of illness.

The prevalence of CFS-like cases (3.6%) in the Netherlands was considerably higher than the prevalence of CFS reported in previous studies (0.006-3%).


The authors conducted a pilot random-digit-dialing survey to estimate the prevalence of fatiguing illnesses in different geographic regions and in urban and rural populations of the United States. The prevalence did not differ meaningfully among the four regions surveyed, and no significant geographic trends were observed. This investigation estimated that nearly 2.2 million American adults suffer from CFS-like illness.


In a population from Wichita, Kansas, prevalence of CFS was 235 per 100,000 persons. The prevalence of CFS was higher among women, 373 per 100,000 persons, than among men, 83 per 100,000 persons. Among subjects nonfatigued and fatigued for less than 6 months, the 1-year incidence of CFS was 180 per 100,000 persons.

The prevalence of CFS was found to be 1,088 per 100,000 in a population of nurses. These findings suggest that nurses might represent a high-risk group for this illness.


This report summarizes CFS surveillance data collected in four U.S. cities (Atlanta, Georgia; Wichita, Kansas; Grand Rapids, Michigan; and Reno, Nevada) from September 1989 through August 1993.


A survey in Japan in 1992 suggested that the prevalence of CFS was 0.85 per 100,000.


A random community sample (N = 1,031) was interviewed by telephone in order to identify and comprehensively evaluate individuals with symptoms of CFS and those who self-report having CFS. Higher rates (0.2%) of CFS were found than in previous studies.

This study is the first to assess the prevalence of Chronic Fatigue Syndrome-related symptoms in a sample of nurses.


While chronic, debilitating fatigue is common in medical outpatients, CFS is relatively uncommon. Prevalence varied between 0.3% and 1%, depending on the case definition used.

**Deaths**


CFS patients dying of heart failure do so at a significantly lower age than non-patients (59 years vs. 83 years). Abnormalities that may be responsible include: a) chronic low grade inflammation; b) increased O&NS; c) decreased levels of specific antioxidants; d) bacterial translocation as a result of leaky gut; e) decreased omega-3 and increased omega-6 levels; and f) viral and bacterial infections and psychological stressors.


The causes of death of a population of CFS patients was examined. The three most prevalent causes of death were heart failure, suicide, and cancer, which accounted for 59.6% of all deaths. The mean age of those who died from cancer and suicide was 47.8 and 39.3 years, respectively, which is considerably younger than those who died from cancer and suicide in the general population. The mean age of patients dying from heart
failure (58.7 years), is significantly lower than the age of those dying from heart failure in the general US population (83.1 years).

Presentation


Unexplained fatigue among employees in some instances is a precursor of the development of CFS.


Pregnancy did not consistently worsen the symptoms of CFS. Most maternal and infant outcomes were not systematically worse in pregnancies occurring after the onset of CFS. The higher rates of spontaneous abortions and of developmental delays in offspring that we observed could be explained by maternal age or parity differences.


A study was done of CFS patients and their twins. Relevant etiologic factors included: a common genetic factor accounting for 48% of the variance in fatigue which also accounted for 4%, 6% and 8% reductions in immune activation; specific genetic factors for each of the in vitro immune measures; a shared environment factor influencing the three immune activation measures; and, most interestingly, unique environmental influences which increased fatigue but also increased markers of immune activation.

CFS patients reported reduced muscular strength, continuous weakness and recurrent pain, problems related to memory and concentration, sleep disturbances and excessive sensitivity towards smell, light and sound. Learning abilities had deteriorated, and housework, conversation, reading and watching TV were characterised as exhausting, leading to an unpredictability of everyday life-disturbing social relations.

Chester AC. Chronic fatigue syndrome criteria in patients with other forms of unexplained chronic fatigue. J Psychiatr Res. 1997 Jan-Feb;31(1):45-50. PMID: 9201646

People with unexplained chronic fatigue often have other CFS criteria.


Compared to patients with plain unexplained fatigue, CFS patients had significantly lower scores on physical functioning, role functioning and body pain subscales. The presence of fibromyalgia, being unemployed, and increasing fatigue severity all were associated with additional functional limitations.


CFS can include an 'infectious-like' illness, intermittent unexplained fevers, arthralgias and 'gelling' (stiffness), sore throats, cough, photophobia, night sweats, and post-
exertional malaise with systemic symptoms. The illness can last for years and is associated with marked impairment of functional health status.

**Seasonal Variation**


Greater numbers of participants than expected reported an onset of CFS or Idiopathic Chronic Fatigue during January.

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Date of illness onset in CFS was distinctly nonrandom. It peaked from November through January and was at its lowest from April through May.

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A subgroup of patients with CFS shows seasonal variation in symptoms resembling those of SAD, with winter exacerbation.

**Environmental Toxins & Loss of Tolerance**

The possible role of pesticides in chronic diseases, including CFS, is discussed.


The authors consider the possible contributions of aluminum hydroxide (used as an adjuvant in vaccines) as a contributor to CFS, looking at a particular patient case study.


Kindling (which occurs when an organism is exposed repeatedly to an initially sub-threshold stimulus resulting in hypersensitivity and spontaneous seizure-like activity) might represent a heuristic model for understanding the etiology of Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS).


Multiple chemical sensitivity (MCS), fibromyalgia, chronic fatigue syndrome, electric hypersensitivity and amalgam disease share the features of poly-symptomatic multi-organ cutaneous and systemic manifestations, with postulated inherited/acquired impaired metabolism of chemical/physical/nutritional xenobiotics, triggering adverse reactions at exposure levels far below toxicologically-relevant values. The finding of relevant alterations of catalase, glutathione-transferase and peroxidase detoxifying activities significantly correlating with clinical manifestations of MCS, has recently registered some progress towards the identification of reliable biomarkers of disease onset, progression, and treatment outcomes.

The role of environmental toxins in CFS is discussed.


Human exposure to molds, mycotoxins, and water-damaged buildings can cause neurologic and neuropsychiatric signs and symptoms similar to many of those in diseases such as CFS.

Dietert RR, Dietert JM. Possible role for early-life immune insult including developmental immunotoxicity in chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME). Toxicology. 2008 May 2;247(1):61-72. PMID: 18336982

Toxic insults early in life may have an effect on the immune system and make people more likely to get CFS.


Post-radiation syndrome is proposed to be chronic fatigue syndrome (CFS) or a chronic fatigue syndrome-like illness, initiated by exposure to ionizing radiation.

A case study of an individual in a sick building who developed CFS.


The authors consider the relationship between toxic mold illness and CFS.


Unhealthy Gulf veterans show an acceleration of divided attention task performance over the course of repeated low-level JP-8 exposures. The present faster reaction times are consistent with rat neurobehavioral studies on environmental toxicant cross-sensitization and nonlinear dose-response patterns with stimulant drugs, as well as some previous civilian studies using other exposure agents.


The author considers the role of mercury poisoning in CFS.


CFS and multiple chemical hypersensitivity can follow insecticide exposure.

This paper describes a biologically plausible mechanism for the development of CFS based on loss of immunological tolerance to the vasoactive neuropeptides following infection, significant physical exercise or de novo. It is proposed that release of these substances is accompanied by a loss of tolerance either to them or their receptor binding sites in CFS.


The results indicate peripheral cholinergic abnormalities in the vascular endothelium of only patients with CFS, suggesting that this syndrome has a different aetiology, which might involve inhibition of vascular cholinesterase.


Pesticide exposure can trigger CFS.


Clinical reports and descriptions of chronic fatigue syndrome (CFS) and chronic ciguatera fish poisoning (CCFP) show great similarities in clinical symptomology. A
significant increase (P<0.001) in the chronic phase lipids (CPLs) was shown in CFS patients relative to the normal group.

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This article describes the detection of delayed-type hypersensitive responses to certain common environmental antigens in almost fifty per cent of patients with CFS. Such hypersensitivity can be detected by the intradermal administration of antigens derived from commensal organisms like the yeast Candida albicans, and then monitoring for a systemic reaction over the following six to forty eight hours.

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Allergy testing was done for CFS patients. Among the 22% of CFS patients having a total IgE > 100 IU/mL, 73% had a positive test for allergen-specific IgE for one or more allergens. The most commonly positive allergens were dust mites (24-26%), whereas molds (0-6%) and foods (0-4%) were rarely positive.

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Bested AC, Saunders PR, Logan AC. Chronic fatigue syndrome: neurological findings may be related to blood--brain barrier permeability. Med Hypotheses. 2001 Aug;57(2):231-7. PMID: 11461179

The authors hypothesize that altered permeability of the blood-brain barrier (BBB) is a contributor to CFS.

The authors describe the detection of delayed-type hypersensitive responses to certain common environmental antigens in almost fifty per cent of patients with this syndrome.


Toxic exposures to ciguatoxin or solvents may result in some of the same abnormalities (decreased levels of NK cells, abnormal CD4/CD8 ratios and disturbed hypothalmic function) seen in CFS.


Coeliac disease is common in CFS.


Ciguatera poisoning has constitutional symptoms may be misdiagnosed as chronic fatigue syndrome.

TILT, or toxicant-induced loss of tolerance, bridges the gap between addiction and abduction and has the potential to explain CFS. This paper argues that both addiction and chemical intolerance involve a fundamental breakdown in innate tolerance, resulting in an amplification of various biological effects.


The authors examined five patients who developed the clinical features of CFS several months after the exposure to environmental toxic factors: ciguatera poisoning in two cases, and exposure to solvents in the other three cases. Patients exposed to toxic factors had disturbances of hypothalamic function similar to those in controls and, above all, showed more severe dysfunction of the immune system with an abnormal CD4/CD8 ratio, and in three of such cases with decreased levels of NK cells (CD56+).


Chemical sensitivity may be a relevant area to explore in CFS.

*Vojdani A, Lapp CW. Interferon-induced proteins are elevated in blood samples of patients with chemically or virally induced chronic fatigue syndrome. Immunopharmacol Immunotoxicol. 1999 May;21(2):175-202. PMID: 10319275*

Certain toxic chemicals (MTBE’s and benzenes) and certain viruses (HHV6) produce the same kinds of inflammatory effects (2-5A Synthetase and Protein Kinase RNA (PKR)). This was the case with study subjects and in cell lines. Anti IFN beta inhibited the reactions.

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CFS patients are very frequently allergic to nickel.


Severe chemical intolerance is a characteristic of 20-47% of individuals with apparent CFS and/or fibromyalgia and approximately 4-6% of the general population. The authors suggest the limbic system of the brain may be responsible for this.


The authors discuss similarities and differences between CFS and chronic ciguatera illness.


Individuals who got CFS in association with sick building syndrome were interviewed. Three years later, most were substantially improved or fatigue free. Many of those who continued to have fatigue also had upper respiratory symptoms (nasal and sinus problems, sore throats), swollen cervical lymph nodes, and headaches.

The researchers looked at whether a CFS-like illness had occurred among employees in two large state office buildings in northern California. 2.3% had symptoms compatible with a CFS-like illness. Female sex was the only independent risk factor found for those persons classified as having a CFS-like illness. The prevalence was not significantly different than that for a comparable control building.


The authors look at outbreaks of CFS in Truckee, California; Elk Grove, California; and Washington, D.C. They conclude that CFS is often associated with Sick Building Syndrome but is not exactly the same thing because it also includes neurological complaints.


The authors propose that much of the symptomatology of CFS can be explained by all four types of hypersensitivity (Gell and Coombs classification) in reaction to a pathogen, electrolyte disturbances which include sometimes permanent changes in cell membranes' ability to pass electrolytes, sometimes permanent biochemical changes in mitochondrial function, and disturbances of insulin and T3-thyroid hormone functions.

**Vaccines**


This study compares the humoral and cellular immune responses upon influenza vaccination in CFS patients and healthy controls, finding no difference.

The authors propose an AISA (autoimmune/inflammatory syndrome induced by adjuvants) syndrome, indicating the possible contribution of adjuvants and vaccines to the development of autoimmunity.


CFS may be caused by adverse reactions to aluminium-containing adjuvants in vaccines.


No statistically significant association between vaccination against meningococcal disease in teenagers and occurrence of CFS in a UK population was observed.

* Nancy AL, Shoenfeld Y. Chronic fatigue syndrome with autoantibodies--the result of an augmented adjuvant effect of hepatitis-B vaccine and silicone implant. Autoimmun Rev. 2008 Oct;8(1):52-5. PMID: 18725327

The relevance of the rupture of a silicone implant along with a Hepatitis B vaccine in the development of a CFS case is considered.

The current concept is that CFS pathogenesis is a multi factorial condition in which an infective agent cause an aberrant immune response characterized by a shift to Th-2 dominant response. When the response fails to be switched-off, a chronic immune activation occurs and clinically expressed as the symptomatology of CFS. Vaccinations may stimulate the immune system to induce a persistent immunity against the favorable antigens.

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The authors propose a model wherein vaccinations function as co-triggers for the development of functional disorders including CFS, in conjunction with additional contributing factors.

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In a population of patients with CFS, influenza immunization was not associated with any excess early reactions and stimulated an immunizing response comparable with that of healthy volunteers.

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Upon the administration of a polio vaccine to CFS sufferers, the researchers found increased poliovirus isolation, earlier peak proliferative responses, lower T-cell subsets
on certain days post vaccination and a trend for reduced gamma-interferon compared to a control group. This suggests altered immune reactivity and virus clearance.


**Trauma and Stress**


More than half of the CFS patients studied had experienced at least one type of early trauma, with the majority of these patients reporting multiple traumas. Total trauma scores and emotional abuse significantly predicted higher levels of daily fatigue and pain over the 14-day period, even when controlling for demographic features and depressed mood.

The results suggest that a lifetime diagnosis of CFS is associated with both lifetime PTSD and current traumatic symptoms.


The authors found that exposure to stressors was significantly more common in persons with CFS compared to NF controls; those with CFS reported experiencing significantly higher levels of psychological distress. Also, post-traumatic stress disorder was significantly more common in people with CFS.


This was a case-control study of 113 persons with CFS and 124 well control subjects identified from a general population sample of 19 381 adult residents of Georgia. Individuals with CFS reported significantly higher levels of childhood trauma and psychopathological symptoms than control subjects. Exposure to childhood trauma was associated with a 6-fold increased risk of CFS. Sexual abuse, emotional abuse, and emotional neglect were most effective in discriminating CFS cases from controls. There was a graded relationship between exposure level and CFS risk. The risk of CFS conveyed by childhood trauma further increased with the presence of posttraumatic stress disorder symptoms.

Compared with well controls, persons with CFS were significantly more likely to have a high allostatic load (cumulative physiologic effect of demands to adapt to stress).

* Goertzel BN, Pennachin C, de Souza Coelho L, Maloney EM, Jones JF, Gurbaxani B. Allostatic load is associated with symptoms in chronic fatigue syndrome patients. Pharmacogenomics. 2006 Apr;7(3):485-94. PMID: 16610958

Among CFS patients, but not controls, a high level of allostatic load was significantly associated with worse bodily pain, physical functioning and general symptom frequency/intensity.


CFS cases reported significantly higher levels of childhood trauma and psychopathology compared with the controls. Exposure to childhood trauma was associated with a 3- to 8-fold increased risk for CFS across different trauma types. There was a graded relationship between the degree of trauma exposure and CFS risk. Childhood trauma was associated with greater CFS symptom severity and with symptoms of depression, anxiety, and posttraumatic stress disorder. The risk for CFS conveyed by childhood trauma increased with the presence of concurrent psychopathology.


The authors found decreased regional prevalence of fatiguing illnesses such as CFS in the aftermath of the terrorist attacks on September 11, 2001. The causes of this effect are unknown.
Chronic fatigue syndrome is associated with stressful events and difficulties prior to onset. Those events and difficulties characterized as being dilemmas seem to be particularly important.

Other Risk Factors


This case report describes an adolescent boy who was diagnosed as suffering from chronic fatigue syndrome 5 months after infection with H1N1 influenza.

Infectious mononucleosis may be a risk factor for chronic fatigue syndrome in adolescents. Female gender and greater fatigue severity, but not reported steroid use
during the acute illness, were associated with the development of chronic fatigue syndrome in adolescents.


Individuals who exercise frequently are more likely to report a diagnosis of CFS in later life.


Underserved minorities, who not only tend to manifest higher levels of chronic illness, but are also less likely to seek and receive adequate medical care, have not been adequately represented in CFS studies. The present study compared two groups of individuals with CFS, one from a community-based sample and another from a tertiary-based sample. Findings indicate that patients with CFS from tertiary care settings have a higher frequency of symptoms than those in the general population who have CFS.


People diagnosed with CFS were subclassified based on frequency of symptoms, and important differences emerged on measures of sociodemographics and disability. The implications of these findings and others are discussed.

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Women, minorities, and nonworking individuals with CFS reported greater levels of functional disability, symptom severity, and poorer psychosocial functioning than men, Caucasians, and working individuals, suggesting sociodemographic characteristics may be associated with poorer outcomes in urban, community-based samples of CFS individuals.

People with CFS, MCS, or FM endure significant disability in terms of physical, occupational, and social functioning, and those with more than one of these diagnoses also report greater severity of physical and mental fatigue.

Chronic fatigue syndrome is a common chronic health condition, especially for women, occurring across ethnic groups. Earlier findings suggesting that CFS is a syndrome primarily affecting white, middle-class patients were not supported.

CFS patients were found to be especially likely to have exercised regularly prior to onset of the illness. Female CFS sufferers were especially likely to have been childless prior to onset.


CFS patients who were hit by Hurricane Andrew in South Florida suffered health declines.

Concurrent Illness


Forty-seven of 158 CFS patients (29.7%) were diagnosed of childhood ADHD and in 33 (20.9%), the condition persisted into adulthood. CFS patients with adult ADHD had an earlier CFS onset, more severe anxiety and depression symptoms, and a higher risk of suicide than CFS patients without ADHD.


This review discusses the recent literature concerning fibromyalgia syndrome, myalgic encephalomyelitis/chronic fatigue syndrome, and irritable bowel syndrome.

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Sympathetic neural hyperalgesia edema syndrome can be mistakenly diagnosed as Lyme disease or CFS.

**Causal Theories**

Lucas K, Maes M. Role of the Toll Like Receptor (TLR) Radical Cycle in Chronic Inflammation: Possible Treatments Targeting the TLR4 Pathway. Mol Neurobiol. 2013 Feb 26. PMID: 23436141

The authors discuss the idea that activation of the Toll-like receptor 4 (TLR4) complex, a receptor of the innate immune system, may underpin the pathophysiology of many human diseases associated with “civilization,” including CFS.


The authors put forth a model describing how multiple species-bacterial, viral, and fungal-can cumulatively dysregulate expression by the VDR nuclear receptor in order to survive and thus drive a disease process, and suggest that this may be of relevance to understanding CFS.


This paper proposes a neuro-immune model for Myalgic Encephalomyelitis/Chronic fatigue syndrome (ME/CFS), whereby the initial infection and immune activation caused by a number of possible pathogens leads to a state of chronic peripheral immune
activation driven by activated O&NS pathways that lead to progressive damage of self epitopes even when the initial infection has been cleared.

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The authors use statistical mechanics techniques to show how a persistent acute mononucleosis infection may drive the immune system towards an out-of-equilibrium metastable state displaying chronic activation of both humoral and cellular responses.

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The authors propose that a decrease in key carbohydrate-digesting enzyme activity in the gut is a major biological mechanism for why formula-fed neonatal pigs might acquire the high amount of oxidative stress that leads to chronic fatigue syndrome.

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Arnett SV, Clark IA. Inflammatory fatigue and sickness behaviour - lessons for the diagnosis and management of chronic fatigue syndrome. J Affect Disord. 2012 Dec 10;141(2-3):130-42. PMID: 22578888

This review explores current models of how inflammatory mediators act on the central nervous system to produce fatigue and sickness behaviour, as well as evidence indicating chronic fatigue syndrome may have important pathophysiological similarities with cytokine mediated sickness behavior.
Rovigatti U. Chronic Fatigue Syndrome (CFS) and Cancer Related Fatigue (CRF): two "fatigue" syndromes with overlapping symptoms and possibly related aetiologies. Neuromuscul Disord. 2012 Dec;22 Suppl 3:S235-41. PMID: 23182646

The possibility that an RNA virus, Micro-Foci inducing Virus, may be associated with CFS is discussed.


The authors hypothesize that increased NF-κB together with a loss of p53 are key phenomena in ME/CFS that explain ME/CFS symptoms, such as fatigue and neurocognitive dysfunction, and explain ME symptoms, such as post-exertional malaise following mental and physical activities.


The authors propose that viral infection can induce a deficient cell stress response and thereby impairs stress tolerance and makes tissues vulnerable to damage.


The authors hypothesize that cadmium may be responsible for some of the dysfunctions in CFS, especially with regard to cognitive issues related to the cerebral cortex.
Moss JI. Gulf War illnesses are autoimmune illnesses caused by reactive oxygen species which were caused by nerve agent prophylaxis. Med Hypotheses. 2012 Aug; 79(2):283-4. PMID: 22632735

A suspected cause for GWI, the drug pyridostigmine bromide (PB), has been shown to cause neuronal damage from reactive oxygen species (ROS). Similar mechanisms may apply to other autoimmune illnesses such as CFS.


The functions and dysfunctions of regulatory T-cells (Tregs), which appear to play a role in CFS issues, are discussed.


The authors present a hypothesis that CFS, in some cases, can be triggered and perpetuated by several chronic infections that directly or indirectly affect the nervous system, and that symptoms are a reflection of the immune response to the infection.


The authors suggest that in CFS, there is a possible deregulation of the immune system influenced by specific agents (infections, vaccination, and products, such as silicone).

* Wyller VB, Eriksen HR, Malterud K. Can sustained arousal explain the Chronic Fatigue Syndrome? Behav Brain Funct. 2009 Feb 23;5:10. PMID: 19236717
The authors argue that new data on cardiovascular and thermoregulatory regulation indicate a state of permanent arousal responses - sustained arousal - originating from different precipitating factors (infections, psychosocial challenges) and interacting with predisposing factors (genetic traits, personality) and learned expectancies (classical and operant conditioning).


The authors argue that a disturbed, palpable, and visible neurolymphatic process leads to chronic fatigue syndrome.


The authors introduce a method to detect pathological pathways of CFS.


Autoimmune dysfunction of certain vasoactive neuropeptides may be implicated in CFS.


The possibility that CFS patients have problems with bone density is discussed.
Englebienne P, Verhas M, Herst CV, De Meirleir K. Type I interferons induce proteins susceptible to act as thyroid receptor (TR) corepressors and to signal the TR for destruction by the proteasome: possible etiology for unexplained chronic fatigue. Med Hypotheses. 2003 Feb;60(2):175-80. PMID: 12606231

The authors raise the hypothesis that the 2-5OASL proteins are TRIPs capable of, respectively, repressing TR transactivation and/or signaling the receptor for destruction by the proteasome. Such molecular mechanisms could explain the development of a clinical hypothyroid state in presence of a normal thyroid function.


Because CFS patients (compared to patients with CF) have more somatic symptoms, more often report an infectious, sudden onset and have less psychiatric comorbidity, and CF patients seem to have more of an emotional, burn-out-like component one could speculate about the existence of different pathogenetic backgrounds behind the two diagnoses.


The authors investigate the interaction between neuroendocrine mediators and the immune system in CFS and suggest that it should be viewed as a disease of deficient neuroendocrine-immune communication.


Enzyme deficiencies may play a role in CFS.

In CFS, protracted challenge of the immunocytes may lead to cellular GSH depletion.


The authors propose that CFS and fatigue syndromes in general may be secondary to altered sensitivity of the GABAa receptor.


The author suggests that abnormal porphyrin metabolism may be a factor in chronic fatigue.
Paradigm Change
ME/CFS EPIDEMIOLOGY AND CAUSAL THEORIES

MEDIA ARTICLES:

May 14, 2012
KENS5
Mysterious Illness Links Teenage Girls Along S.A.’s 1-10 Corridor
By Sarah Lucerno

http://www.kens5.com/home/ito-151467795.html

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February 21, 2012
Washington Examiner
Study: Gardasil Risks Outweigh Preventive Benefits
By Barbara Hollingsworth

http://washingtonexaminer.com/opinion/2012/02/study-gardasil-risks-outweigh-preventive-benefits/299536

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February 12, 2012
Examiner
Chronic Fatigue Seen In Many Previously Infected With Q Fever In The Netherlands
By Robert Herriman


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December 21, 2011
The Guardian
“These Are Just Ordinary Women” - How Breast Surgery Has Soared In The UK
By Esther Addley
http://www.guardian.co.uk/society/2011/dec/21/british-women-breast-surgery-rising?newsfeed=true

December 12, 2011
The Guardian
Study Warns of Higher ME Rates Among Pupils
By Denis Campbell

http://www.guardian.co.uk/society/2011/dec/12/chronic-fatigue-syndrome-schools

November 15, 2011
Daily Mail (UK)
Girl, 13, Left in “Waking Coma” and Sleeps for 23 Hours a Day After Severe Reaction to Cervical Cancer Jabs
By Paul Sims


September 30, 2011
L.A. Times
The Mystery of Chronic Fatigue Syndrome
By Jay A. Levy and Daniel L. Peterson


ME/CFS DEATHS:

National CFIDS Foundation
Memorial List