M.E. Epidemiology and Causal Theories

Clusters

Levine PH, Fears TR, Cummings P, Hoover RN. Cancer and a fatiguing illness in Northern Nevada--a causal hypothesis. Ann Epidemiol. 1998 May;8(4):245-9. PMID: 9590603

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.

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Levine PH, Snow PG, Ranum BA, Paul C, Holmes MJ. Epidemic neuromyasthenia and chronic fatigue syndrome in west Otago, New Zealand. A 10-year follow-up. Arch Intern Med. 1997 Apr 14;157(7):750-4. PMID: 9125006

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.

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Levine PH, Atherton M, Fears T, Hoover R. An approach to studies of cancer subsequent to clusters of chronic fatigue syndrome: use of data from the Nevada State Cancer Registry. Clin Infect Dis. 1994 Jan;18 Suppl 1:S49-53. PMID: 8148453

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.

*

Briggs NC, Levine PH. A comparative review of systemic and neurological symptomatology in 12 outbreaks collectively described as chronic fatigue syndrome, epidemic neuromyasthenia, and myalgic encephalomyelitis. Clin Infect Dis. 1994 Jan;18 Suppl 1:S32-42. PMID: 8148451

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.

*

Levine PH, Jacobson S, Pocinki AG, Cheney P, Peterson D, Connelly RR, Weil R, Robinson SM, Ablashi DV, Salahuddin SZ, et al. Clinical, epidemiologic, and virologic studies in four clusters of the chronic fatigue syndrome. Arch Intern Med. 1992 Aug;152(8):1611-6. PMID: 1323246

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

*

Levine PH, Peterson D, McNamee FL, O'Brien K, Gridley G, Hagerty M, Brady J, Fears T, Atherton M, Hoover R. Does chronic fatigue syndrome predispose to non-Hodgkin's lymphoma? Cancer Res. 1992 Oct 1;52(19 Suppl):5516s-5518s; discussion 5518s-5521s. PMID: 1394166

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

*

Daugherty SA, Henry BE, Peterson DL, Swarts RL, Bastien S, Thomas RS. Chronic fatigue syndrome in northern Nevada. Rev Infect Dis. 1991 Jan-Feb;13 Suppl 1:S39-44. PMID: 1850542

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

Johnston S, Brenu EW, Staines D, Marshall-Gradisnik S. The prevalence of chronic fatigue syndrome/ myalgic encephalomyelitis: a meta-analysis. Clin Epidemiol. 2013;5:105-10. PMID: 23576883

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

*

Vincent A, Brimmer DJ, Whipple MO, Jones JF, Boneva R, Lahr BD, Maloney E, St Sauver JL, Reeves WC. Prevalence, incidence, and classification of chronic fatigue syndrome in Olmsted County, Minnesota, as estimated using the Rochester Epidemiology Project. Mayo Clin Proc. 2012 Dec;87(12):1145-52. PMID: 23140977

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.

*

Hamaguchi M, Kawahito Y, Takeda N, Kato T, Kojima T. Characteristics of chronic fatigue syndrome in a Japanese community population : Chronic fatigue syndrome in Japan. Clin Rheumatol. 2011 Feb 8. PMID: 21302125

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

*

Nacul LC, Lacerda EM, Pheby D, Campion P, Molokhia M, Fayyaz S, Leite JC, Poland F, Howe A, Drachler ML. Prevalence of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) in three regions of England: a repeated cross-sectional study in primary care. BMC Med. 2011 Jul 28;9(1):91. PMID: 21794183

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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Nijhof SL, Maijer K, Bleijenberg G, Uiterwaal CS, Kimpen JL, van de Putte EM. Adolescent chronic fatigue syndrome: prevalence, incidence, and morbidity. Pediatrics. 2011 May;127(5):e1169-75. PMID: 21502228

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.

*

van't Leven M, Zielhuis GA, van der Meer JW, Verbeek AL, Bleijenberg G. Fatigue and chronic fatigue syndrome-like complaints in the general population. Eur J Public Health. 2010 Jun;20(3):251-7. PMID: 19689970

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.

*

Smith MS, Buchwald DS, Bogart A, Goldberg J, Smith WR, Afari N. Adolescent offspring of mothers with chronic fatigue syndrome. J Adolesc Health. 2010 Mar;46(3):284-91. PMID: 20159507

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).

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Jones JF, Nisenbaum R, Solomon L, Reyes M, Reeves WC. Chronic fatigue syndrome and other fatiguing illnesses in adolescents: a population-based study. J Adolesc Health. 2004 Jul;35(1):34-40. PMID: 15193572

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.

*

Huibers MJ, Kant IJ, Swaen GM, Kasl SV. Prevalence of chronic fatigue syndrome-like caseness in the working population: results from the Maastricht cohort study. Occup Environ Med. 2004 May;61(5):464-6. PMID: 15090670

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%).

*

Bierl C, Nisenbaum R, Hoaglin DC, Randall B, Jones AB, Unger ER, Reeves WC. Regional distribution of fatiguing illnesses in the United States: a pilot study. Popul Health Metr. 2004 Feb 4;2(1):1. PMID: 14761250

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.

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Reyes M, Nisenbaum R, Hoaglin DC, Unger ER, Emmons C, Randall B, Stewart JA, Abbey S, Jones JF, Gantz N, Minden S, Reeves WC. Prevalence and incidence of chronic fatigue syndrome in Wichita, Kansas. Arch Intern Med. 2003 Jul 14;163(13):1530-6. PMID: 12860574

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.

*

Jason LA, Wagner L, Rosenthal S, Goodlatte J, Lipkin D, Papernik M, Plioplys S, Plioplys AV. Estimating the prevalence of chronic fatigue syndrome among nurses. Am J Med. 1998 Sep 28;105(3A):91S-93S. PMID: 9790488

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.

*

Reyes M, Gary HE Jr, Dobbins JG, Randall B, Steele L, Fukuda K, Holmes GP, Connell DG, Mawle AC, Schmid DS, Stewart JA, Schonberger LB, Gunn WJ, Reeves WC. Surveillance for chronic fatigue syndrome--four U.S. cities, September 1989 through August 1993. MMWR CDC Surveill Summ. 1997 Feb 21;46(2):1-13. PMID: 12412768

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.

*

Minowa M, Jiamo M. Descriptive epidemiology of chronic fatigue syndrome based on a nationwide survey in Japan. J Epidemiol. 1996 Jun;6(2):75-80. PMID: 8795946

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

*

Jason LA, Taylor R, Wagner L, Holden J, Ferrari JR, Plioplys AV, Plioplys S, Lipkin D, Papernik M. Estimating rates of chronic fatigue syndrome from a community-based sample: a pilot study. Am J Community Psychol. 1995 Aug;23(4):557-68. PMID: 8546110

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.

*

Jason LA, Taylor SL, Johnson S, Goldston SE, Salina D, Bishop P, Wagner L. Prevalence of chronic fatigue syndrome-related symptoms among nurses. Eval Health Prof. 1993 Dec;16(4):385-99. PMID: 10130552

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

*

Bates DW, Schmitt W, Buchwald D, Ware NC, Lee J, Thoyer E, Kornish RJ, Komaroff AL. Prevalence of fatigue and chronic fatigue syndrome in a primary care practice. Arch Intern Med. 1993 Dec 27;153(24):2759-65. PMID: 8257251

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

Maes M, Twisk FN. Why myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) may kill you: disorders in the inflammatory and oxidative and nitrosative stress (IO&NS) pathways may explain cardiovascular disorders in ME/CFS. Neuro Endocrinol Lett. 2009;30(6):677-93. PMID: 20038921

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.

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Jason LA, Corradi K, Gress S, Williams S, Torres-Harding S. Causes of death among patients with chronic fatigue syndrome. Health Care Women Int. 2006 Aug;27(7):615-26. PMID: 16844674

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

Huibers MJ, Kant IJ, Knottnerus JA, Bleijenberg G, Swaen GM, Kasl SV. Development of the chronic fatigue syndrome in severely fatigued employees: predictors of outcome in the Maastricht cohort study. J Epidemiol Community Health. 2004 Oct;58(10):877-82. PMID: 15365116

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

**

Schacterle RS, Komaroff AL. A comparison of pregnancies that occur before and after the onset of chronic fatigue syndrome. Arch Intern Med. 2004 Feb 23;164(4):401-4. PMID: 14980991

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.

*

Hickie IB, Bansal AS, Kirk KM, Lloyd AR, Martin NG. A twin study of the etiology of prolonged fatigue and immune activation. Twin Res. 2001 Apr;4(2):94-102. PMID:11665341

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.

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Söderlund A, Skoge AM, Malterud K. "I could not lift my arm holding the fork...". Living with chronic fatigue syndrome. Scand J Prim Health Care. 2000 Sep;18(3):165-9. PMID: 11097102

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.

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Buchwald D, Pearlman T, Umali J, Schmaling K, Katon W. Functional status in patients with chronic fatigue syndrome, other fatiguing illnesses, and healthy individuals. Am J Med. 1996 Oct;101(4):364-70. PMID: 8873506

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.

*

Komaroff AL. Clinical presentation of chronic fatigue syndrome. Ciba Found Symp. 1993;173:43-54; discussion 54-61. PMID: 8491106

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

Jason LA, Taylor RR, Carrico AW. A community-based study of seasonal variation in the onset of chronic fatigue syndrome and idiopathic chronic fatigue. Chronobiol Int. 2001 Mar;18(2):315-9. PMID: 11379670

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

*

Zhang QW, Natelson BH, Ottenweller JE, Servatius RJ, Nelson JJ, De Luca J, Tiersky L, Lange G. Chronic fatigue syndrome beginning suddenly occurs seasonally over the year. Chronobiol Int. 2000 Jan;17(1):95-9. PMID: 10672437

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

*

Terman M, Levine SM, Terman JS, Doherty S. Chronic fatigue syndrome and seasonal affective disorder: comorbidity, diagnostic overlap, and implications for treatment. Am J Med. 1998 Sep 28;105(3A):115S-124S. PMID: 9790493

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

Paradigm Change

Environmental Toxins & Loss of Tolerance

Mostafalou S, Abdollahi M. Pesticides and human chronic diseases: evidences, mechanisms, and perspectives. Toxicol Appl Pharmacol. 2013 Apr 15;268(2):157-77. PMID: 23402800

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

*

Guillard O, Fauconneau B, Pineau A, Marrauld A, Bellocq JP, Chenard MP. Aluminium overload after 5 years in skin biopsy following post-vaccination with subcutaneous pseudolymphoma. J Trace Elem Med Biol. 2012 Oct;26(4):291-3. PMID: 22425036

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.

*

Jason LA, Sorenson M, Porter N, Belkairous N. An Etiological Model for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Neurosci Med. 2011 Mar 1;2(1):14-27. PMID: 21892413

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).

*

De Luca C, Raskovic D, Pacifico V, Thai JC, Korkina L. The search for reliable biomarkers of disease in multiple chemical sensitivity and other environmental intolerances. Int J Environ Res Public Health. 2011 Jul;8(7):2770-97. PMID: 21845158

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.

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De Luca C, Raskovic D, Pacifico V, Thai JC, Korkina L. The search for reliable biomarkers of disease in multiple chemical sensitivity and other environmental intolerances. Int J Environ Res Public Health. 2011 Jul;8(7):2770-97. PMID: 21845158

The role of environmental toxins in CFS is discussed.

*

Empting LD. Neurologic and neuropsychiatric syndrome features of mold and mycotoxin exposure. Toxicol Ind Health. 2009 Oct-Nov;25(9-10):577-81. PMID: 19854819

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.

*

Pall ML. Post-radiation syndrome as a NO/ONOO- cycle, chronic fatigue syndrome-like disease. Med Hypotheses. 2008 Oct;71(4):537-41. PMID: 18667279

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

*

Arnold Llamosas PA, Arrizabalaga Clemente P, Bonet Agusti M, de la Fuente Brull X. Multiple chemical sensitivity in sick-building syndrome. Med Clin (Barc). 2006 May 27;126(20):774-8. PMID: 16883665

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

*

Gharibzadeh S, Hoseini SS. Is there any relation between moldy building exposure and chronic fatigue syndrome? Med Hypotheses. 2006;66(6):1243-4. PMID: 16527430

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

*

Bell IR, Brooks AJ, Baldwin CM, Fernandez M, Figueredo AJ, Witten ML. JP-8 jet fuel exposure and divided attention test performance in 1991 Gulf War veterans. Aviat Space Environ Med. 2005 Dec;76(12):1136-44. PMID: 16385767

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.

*

Miller R. Thimerosal, micromercurialism and chronic fatigue syndrome. Med Hypotheses. 2005;64(5):1063-4. PMID: 15780514

The author considers the role of mercury poisoning in CFS.

*

Lange G, Steffener J, Cook DB, Bly BM, Christodoulou C, Liu WC, Deluca J, Fernández-Solà J, Lluís Padierna M, Nogué Xarau S, Munné Mas P. Chronic fatigue syndrome and multiple chemical hypersensitivity after insecticide exposure. Med Clin (Barc). 2005 Apr 2;124(12):451-3. PMID: 15826581

CFS and multiple chemical hypersensitivity can follow insecticide exposure.

*

Staines DR. Is chronic fatigue syndrome an autoimmune disorder of endogenous neuropeptides, exogenous infection and molecular mimicry? Med Hypotheses. 2004;62(5):646-52. PMID: 15082083

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.

*

Khan F, Kennedy G, Spence VA, Newton DJ, Belch JJ. Peripheral cholinergic function in humans with chronic fatigue syndrome, Gulf War syndrome and with illness following organophosphate exposure. Clin Sci (Lond). 2004 Feb;106(2):183-9. PMID: 14503920

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.

*

Tahmaz N, Soutar A, Cherrie JW. Chronic fatigue and organophosphate pesticides in sheep farming: a retrospective study amongst people reporting to a UK pharmacovigilance scheme. Ann Occup Hyg. 2003 Jun;47(4):261-7. PMID: 12765866

Pesticide exposure can trigger CFS.

*

Hokama Y, Uto GA, Palafox NA, Enlander D, Jordan E, Cocchetto A. Chronic phase lipids in sera of chronic fatigue syndrome (CFS), chronic ciguatera fish poisoning (CCFP), hepatitis B, and cancer with antigenic epitope resembling ciguatoxin, as assessed with MAb-CTX. J Clin Lab Anal. 2003;17(4):132-9. PMID: 12784262

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.

*

Brunet JL, Fatoohi F, Liaudet AP, Cozon GJ. Role of pathological delayed-type hypersensitivity in chronic fatigue syndrome: importance of the evaluation of lymphocyte activation by flow cytometry and the measurement of urinary neopterin. Allerg Immunol (Paris). 2002 Feb;34(2):38-44. PMID: 11933752

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.

*

Kowal K, Schacterele RS, Schur PH, Komaroff AL, DuBuske LM. Prevalence of allergen-specific IgE among patients with chronic fatigue syndrome. Allergy Asthma Proc. 2002 Jan-Feb;23(1):35-9. PMID:11894732

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.

*

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.

*

Brunet JL, Liaudet AP, Later R, Peyramond D, Cozon GJ. Delayed-type hypersensitivity and chronic fatigue syndrome: the usefulness of assessing T-cell activation by flow cytometry--preliminary study. Allerg Immunol (Paris). 2001 Apr;33(4):166-72. PMID: 11434196

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.

*

Racciatti D, Vecchiet J, Ceccomancini A, Ricci F, Pizzigallo E. Chronic fatigue syndrome following a toxic exposure. Sci Total Environ. 2001 Apr 10;270(1-3):27-31. PMID: 11327394

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.

*

Skowera A, Peakman M, Cleare A, Davies E, Deale A, Wessely S. High prevalence of serum markers of coeliac disease in patients with chronic fatigue syndrome. J Clin Pathol. 2001 Apr;54(4):335-6. PMID: 11304857

Coeliac disease is common in CFS.

*

Ting JY, Brown AF. Ciguatera poisoning: a global issue with common management problems. Eur J Emerg Med. 2001 Dec;8(4):295-300. PMID: 11785597

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

*

Miller CS.Toxicant-induced loss of tolerance.Addiction. 2001 Jan;96(1):115-37. PMID: 11177524

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

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Racciatti D, Vecchiet J, Ceccomancini A, Ricci F, Pizzigallo E. Chronic fatigue syndrome following a toxic exposure. Sci Total Environ. 2001 Apr 10;270(1-3):27-31. PMID: 11327394

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+).

*

Nawab SS, Miller CS, Dale JK, Greenberg BD, Friedman TC, Chrousos GP, Straus SE, Rosenthal NE. Self-reported sensitivity to chemical exposures in five clinical populations and healthy controls. Psychiatry Res. 2000 Jul 24;95(1):67-74. PMID: 10904124

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.

*

Marcusson JA, Lindh G, Evengård B. Chronic fatigue syndrome and nickel allergy. Contact Dermatitis. 1999 May;40(5):269-72. PMID: 10344482

CFS patients are very frequently allergic to nickel.

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Bell IR, Baldwin CM, Schwartz GE. Illness from low levels of environmental chemicals: relevance to chronic fatigue syndrome and fibromyalgia. Am J Med. 1998 Sep 28;105(3A):74S-82S. PMID: 9790486

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.

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Pearn JH. Chronic fatigue syndrome: chronic ciguatera poisoning as a differential diagnosis. Med J Aust. 1997 Mar 17;166(6):309-10. PMID: 9087189

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

*

Chester AC, Levine PH. The natural history of concurrent sick building syndrome and chronic fatigue syndrome. J Psychiatr Res. 1997 Jan-Feb;31(1):51-7. PMID: 9201647

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.

*

Shefer A, Dobbins JG, Fukuda K, Steele L, Koo D, Nisenbaum R, Rutherford GW. Fatiguing illness among employees in three large state office buildings, California, 1993: was there an outbreak? J Psychiatr Res. 1997 Jan-Feb;31(1):31-43. PMID: 9201645

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.

**

Chester AC, Levine PH. Concurrent sick building syndrome and chronic fatigue syndrome: epidemic neuromyasthenia revisited. Clin Infect Dis. 1994 Jan;18 Suppl 1:S43-8. PMID: 8148452

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.

*

Dechene L. Chronic fatigue syndrome: influence of histamine, hormones and electrolytes. Med Hypotheses. 1993 Jan;40(1):55-60. PMID: 8455468

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

Prinsen H, de Vries IJ, Torensma R, Pots JM, Mulder SF, van Herpen CM, Elving LD, Bleijenberg G, Stelma FF, van Laarhoven HW. Humoral and cellular immune responses after influenza vaccination in patients with chronic fatigue syndrome. BMC Immunol. 2012 Dec 17;13:71. PMID: 23244635

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

*

Rosenblum H, Shoenfeld Y, Amital H. The Common Immunogenic Etiology of Chronic Fatigue Syndrome: From Infections to Vaccines via Adjuvants to the ASIA Syndrome. Infect Dis Clin North Am. 2011 Dec;25(4):851-63. PMID: 22054760

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.

*

Exley C, Swarbrick L, Gherardi RK, Authier FJ. A role for the body burden of aluminium in vaccine-associated macrophagic myofasciitis and chronic fatigue syndrome. Med Hypotheses. 2009 Feb;72(2):135-9. PMID: 19004564

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

*

Magnus P, Brubakk O, Nyland H, Wold BH, Gjessing HK, Brandt I, Eidem T, Nøkleby H, Stene-Larsen G. Vaccination as teenagers against meningococcal disease and the risk of the chronic fatigue syndrome. Vaccine. 2009 Jan 1;27(1):23-7. PMID: 18984023

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.

*

Appel S, Chapman J, Shoenfeld Y. Infection and vaccination in chronic fatigue syndrome: myth or reality? Autoimmunity. 2007 Feb;40(1):48-53. PMID: 17364497

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.

*

Ablin JN, Shoenfeld Y, Buskila D. Fibromyalgia, infection and vaccination: two more parts in the etiological puzzle. J Autoimmun. 2006 Nov;27(3):145-52. PMID: 17071055

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.

*

Sleigh KM, Danforth DG, Hall RT, Fleming JA, Stiver HG. Double-blind, randomized study of the effects of influenza vaccination on the specific antibody response and clinical course of patients with chronic fatigue syndrome. Can J Infect Dis. 2000 Sep;11(5):267-73. PMID: 18159300

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.

*

Vedhara K, Llewelyn MB, Fox JD, Jones M, Jones R, Clements GB, Wang EC, Smith AP, Borysiewicz LK. Consequences of live poliovirus vaccine administration in chronic fatigue syndrome. J Neuroimmunol. 1997 May;75(1-2):183-95. PMID: 9143253

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.

*

----. Report of the working group on the possible relationship between hepatitis B vaccination and the chronic fatigue syndrome. CMAJ. 1993 Aug 1;149(3):314-9. PMID: 8339178

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Delage G, Salit I, Pennie R, Alary M, Duval B, Ward B. The possible relation between hepatitis B vaccination and chronic fatigue syndrome. Union Med Can. 1993 Jul-Aug;122(4):278-9. PMID: 8367918

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-----. Report of the working group on the possible relationship between hepatitis B vaccination and the chronic fatigue syndrome. Can Commun Dis Rep. 1993 Feb 28;19(4):25-8. PMID: 8453393

Trauma and Stress

Kempke S, Luyten P, Claes S, Van Wambeke P, Bekaert P, Goossens L, Van Houdenhove B. The prevalence and impact of early childhood trauma in Chronic Fatigue Syndrome. J Psychiatr Res. 2013 May;47(5):664-9. PMID: 23421962

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.

*

Dansie EJ, Heppner P, Furberg H, Goldberg J, Buchwald D, Afari N. The Comorbidity of Self-Reported Chronic Fatigue Syndrome, Post-Traumatic Stress Disorder, and Traumatic Symptoms. Psychosomatics. 2012 Jan 31. PMID: 22296866

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

*

Nater UM, Maloney E, Heim C, Reeves WC. Cumulative life stress in chronic fatigue syndrome. Psychiatry Res. 2011 Sep 30;189(2):318-20. PMID: 21840607

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.

*

Heim C, Nater UM, Maloney E, Boneva R, Jones JF, Reeves WC. Childhood trauma and risk for chronic fatigue syndrome: association with neuroendocrine dysfunction. Arch Gen Psychiatry. 2009 Jan;66(1):72-80. PMID: 19124690

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.

*

Maloney EM, Boneva R, Nater UM, Reeves WC. Chronic fatigue syndrome and high allostatic load: results from a population-based case-control study in Georgia. Psychosom Med. 2009 Jun;71(5):549-56. PMID: 19414615

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.

*

Heim C, Wagner D, Maloney E, Papanicolaou DA, Solomon L, Jones JF, Unger ER, Reeves WC. Early adverse experience and risk for chronic fatigue syndrome: results from a population-based study. Arch Gen Psychiatry. 2006 Nov;63(11):1258-66. PMID: 17088506

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.

*

Heim C, Bierl C, Nisenbaum R, Wagner D, Reeves WC. Regional prevalence of fatiguing illnesses in the United States before and after the terrorist attacks of September 11, 2001. Psychosom Med. 2004 Sep-Oct;66(5):672-8. PMID: 15385690

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.

*

Hatcher S, House A. Life events, difficulties and dilemmas in the onset of chronic fatigue syndrome: a case-control study. Psychol Med. 2003 Oct;33(7):1185-92. PMID: 14580073

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.

*

Taylor RR, Jason LA. Sexual abuse, physical abuse, chronic fatigue, and chronic fatigue syndrome: a community-based study. J Nerv Ment Dis. 2001 Oct;189(10):709-15. PMID:11708672

Compared with healthy controls, childhood sexual abuse was significantly more likely to be associated with outcomes of idiopathic chronic fatigue, chronic fatigue explained by a psychiatric condition, and chronic fatigue explained by a medical condition. None of the abuse history types were significant predictors of chronic fatigue syndrome.

Other Risk Factors

Vallings R. A case of chronic fatigue syndrome triggered by influenza H1N1 (swine influenza). J Clin Pathol. 2010 Feb;63(2):184-5. PMID: 19858526

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

*

Katz BZ, Shiraishi Y, Mears CJ, Binns HJ, Taylor R. Chronic fatigue syndrome after infectious mononucleosis in adolescents. Pediatrics. 2009 Jul;124(1):189-93. PMID:19564299

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.

*

Harvey SB, Wadsworth M, Wessely S, Hotopf M. Etiology of chronic fatigue syndrome: testing popular hypotheses using a national birth cohort study. Psychosom Med. 2008 May;70(4):488-95. PMID: 18378866

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

*

Jason LA, Plioplys AV, Torres-Harding S, Corradi K. Comparing symptoms of chronic fatigue syndrome in a community-based versus tertiary care sample. J Health Psychol. 2003 Jul;8(4):459-64. PMID: 19127712

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.

*

Jason LA, Taylor RR, Kennedy CL, Jordan KM, Song S, Johnson D, Torres-Harding S. Chronic fatigue syndrome: symptom subtypes in a community based sample. Women Health. 2003;37(1):1-13. PMID: 12627607

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.

*

Jason LA, Taylor RR, Kennedy CL, Jordan K, Song S, Johnson DE, Torres SR. Chronic fatigue syndrome: sociodemographic subtypes in a community-based sample. Eval Health Prof. 2000 Sep;23(3):243-63. PMID: 11067190

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.

*

Jason LA, Taylor RR, Kennedy CL. Chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities in a community-based sample of persons with chronic fatigue syndrome-like symptoms. Psychosom Med. 2000 Sep-Oct;62(5):655-63. PMID:11020095

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.

*

Jason LA, Richman JA, Rademaker AW, Jordan KM, Plioplys AV, Taylor RR, McCready W, Huang CF, Plioplys S. A community-based study of chronic fatigue syndrome. Arch Intern Med. 1999 Oct 11;159(18):2129-37. PMID: 10527290

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.

*

MacDonald KL, Osterholm MT, LeDell KH, White KE, Schenck CH, Chao CC, Persing DH, Johnson RC, Barker JM, Peterson PK. A case-control study to assess possible triggers and cofactors in chronic fatigue syndrome. Am J Med. 1996 May;100(5):548-54. PMID: 8644768

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.

*

Lutgendorf SK, Antoni MH, Ironson G, Fletcher MA, Penedo F, Baum A, Schneiderman N, Klimas N. Physical symptoms of chronic fatigue syndrome are exacerbated by the stress of Hurricane Andrew. Psychosom Med. 1995 Jul-Aug;57(4):310-23. PMID: 7480560

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

Concurrent Illness

Sáez-Francàs N, Alegre J, Calvo N, Antonio Ramos-Quiroga J, Ruiz E, Hernández-Vara J, Casas M. Attention-deficit hyperactivity disorder in chronic fatigue syndrome patients. Psychiatry Res. 2012 Dec 30;200(2-3):748-53. PMID: 22648008

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.

*

Sarzi-Puttini P, Atzeni F, Di Franco M, Buskila D, Alciati A, Giacomelli C, Rossi A, Bazzichi L. Dysfunctional syndromes and fibromyalgia: a 2012 critical digest. Clin Exp Rheumatol. 2012 Nov-Dec;30(6 Suppl 74):143-51. PMID: 23261014

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

*

Check JH, Cohen R. Sympathetic neural hyperalgesia edema syndrome, a frequent cause of pelvic pain in women, mistaken for Lyme disease with chronic fatigue. Clin Exp Obstet Gynecol. 2011;38(4):412-3. PMID: 22268288

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.

*

Proal AD, Albert PJ, Marshall TG, Blaney GP, Lindseth IA. Immunostimulation in the treatment for chronic fatigue syndrome/myalgic encephalomyelitis. Immunol Res. 2013 Apr 11. PMID: 23576059

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.

*

Morris G, Maes M. A neuro-immune model of Myalgic Encephalomyelitis/Chronic fatigue syndrome. Metab Brain Dis. 2012 Jun 21. PMID: 22718491

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.

*

Agliari E, Barra A, Vidal KG, Guerra F. Can persistent Epstein-Barr virus infection induce chronic fatigue syndrome as a Pavlov reflex of the immune response? J Biol Dyn. 2012;6(2):740-62. PMID: 22873615

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.

*

Lackeyram D, Mine Y, Widowski T, Archbold T, Fan MZ. The in vivo infusion of hydrogen peroxide induces oxidative stress and differentially affects the activities of small intestinal carbohydrate digestive enzymes in the neonatal pig. J Anim Sci. 2012 Dec;90 Suppl 4:418-20. PMID: 23365398

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.

*

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.

*

Morris G, Maes M. Increased nuclear factor-κB and loss of p53 are key mechanisms in Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS). Med Hypotheses. 2012 Nov;79(5):607-13. PMID: 22951418

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.

*

Hooper PL, Hightower LE, Hooper PL. Loss of stress response as a consequence of viral infection: implications for disease and therapy. Cell Stress Chaperones. 2012 Jul 14. PMID: 22797944

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

*

Pacini S, Fiore MG, Magherini S, Morucci G, Branca JJ, Gulisano M, Ruggiero M. Could cadmium be responsible for some of the neurological signs and symptoms of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Med Hypotheses. 2012 Sep;79(3):403-7. PMID: 22795611

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.

*

Pukhal'skiĭ AL, Shmarina GV, Aleshkin VA. Regulatory T-cells: modern approaches to optimization of their numbers. Vestn Ross Akad Med Nauk. 2011;(8):24-33. PMID: 21950132

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

*

Komaroff AL, Cho TA. Role of infection and neurologic dysfunction in chronic fatigue syndrome. Semin Neurol. 2011 Jul;31(3):325-37. PMID: 21964849

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.

*

Ortega-Hernandez OD, Shoenfeld Y. Infection, vaccination, and autoantibodies in chronic fatigue syndrome, cause or coincidence? Ann N Y Acad Sci. 2009 Sep;1173:600-9. PMID: 19758205

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).

*

Perrin RN. Lymphatic drainage of the neuraxis in chronic fatigue syndrome: a hypothetical model for the cranial rhythmic impulse. J Am Osteopath Assoc. 2007 Jun;107(6):218-24. PMID: 17635902

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

*

Emmert-Streib F. The chronic fatigue syndrome: a comparative pathway analysis. J Comput Biol. 2007 Sep;14(7):961-72. PMID: 17803373

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

*

Staines DR. Do vasoactive neuropeptides and heat shock proteins mediate fatigue-related autoimmune disorders? Med Hypotheses. 2005;64(3):539-42. PMID: 15617862

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

*

Nijs J, De Meirleir K, Englebienne P, McGregor N. Chronic fatigue syndrome: a risk factor for osteopenia? Med Hypotheses. 2003 Jan;60(1):65-8. PMID: 12450768

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.

*

Evengård B, Jonzon E, Sandberg A, Theorell T, Lindh G. Differences between patients with chronic fatigue syndrome and with chronic fatigue at an infectious disease clinic in Stockholm, Sweden. Psychiatry Clin Neurosci. 2003 Aug;57(4):361-8. PMID: 12839515

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.

*

Kavelaars A, Kuis W, Knook L, Sinnema G, Heijnen CJ. Disturbed neuroendocrine-immune interactions in chronic fatigue syndrome. J Clin Endocrinol Metab. 2000 Feb;85(2):692-6. PMID: 10690878

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.

*

van der Steen WJ. Chronic fatigue syndrome: a matter of enzyme deficiencies? Med Hypotheses. 2000 May;54(5):853-4. PMID: 10859701

Enzyme deficiencies may play a role in CFS.

*

Bounous G, Molson J. Competition for glutathione precursors between the immune system and the skeletal muscle: pathogenesis of chronic fatigue syndrome. Med Hypotheses. 1999 Oct;53(4):347-9. PMID: 10608272

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

*

Corrigan FM, MacDonald S, Brown A, Armstrong K, Armstrong EM. Neurasthenic fatigue, chemical sensitivity and GABAa receptor toxins. Med Hypotheses. 1994 Oct;43(4):195-200. PMID: 7838000

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

*

Downey DC. Fatigue syndromes revisited: the possible role of porphyrins. Med Hypotheses. 1994 May;42(5):285-90. PMID: 7935069

The author suggests that abnormal porphyrin metabolism may be a factor in chronic fatigue.

Paradigm Change

M.E. 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

http://www.examiner.com/article/chronic-fatigue-seen-many-previously-infected-with-q-fever-the-netherlands

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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

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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

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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

http://www.dailymail.co.uk/health/article-2061267/Schoolgirl-Lucy-Hinks-left-waking-coma-severe-reaction-cervical-cancer-jab.html

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

http://www.latimes.com/news/opinion/commentary/la-oe-levy-chronic-fatigue-syndrome-20110930,0,4021674.story

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