

Authors	Author Address	Title	Publication	Abstract
Aaron LA, Buchwald D.	Department of Medicine, Division of Internal Medicine, Harborview Medical Center, 325 Ninth Avenue, Box 359780, Seattle, WA 98104, USA. laaron@u.washington.edu	A review of the evidence for overlap among unexplained clinical conditions.	Ann Intern Med. 2001 May 1;134(9 Pt 2):868-81.	PURPOSE: Unexplained clinical conditions share features, including symptoms (fatigue, pain), disability out of proportion to physical examination findings, inconsistent demonstration of laboratory abnormalities, and an association with "stress" and psychosocial factors. This literature review examines the nature and extent of the overlap among these unexplained clinical conditions and the limitations of previous research. DATA SOURCES: English-language articles were identified by a search of the MEDLINE database from 1966 to January 2001 by using individual syndromes and their hallmark symptoms as search terms. STUDY SELECTION: Studies that assessed patients with at least one unexplained clinical condition and that included information on symptoms, overlap with other unexplained clinical conditions, or physiologic markers. Conditions examined were the chronic fatigue syndrome, fibromyalgia, the irritable bowel syndrome, multiple chemical sensitivity, temporomandibular disorder, tension headache, interstitial cystitis, and the postconcussion syndrome. DATA EXTRACTION: Information on authorship, patient and control groups, eligibility criteria, case definitions, study methods, and major findings. DATA SYNTHESIS: Many similarities were apparent in case definition and symptoms, and the proportion of patients with one unexplained clinical condition meeting criteria for a second unexplained condition was striking. Tender points on physical examination and decreased pain threshold and tolerance were the most frequent and consistent objective findings. A major shortcoming of all proposed explanatory models is their inability to account for the occurrence of unexplained clinical conditions in many affected patients. CONCLUSIONS: Overlap between unexplained clinical conditions is substantial. Most studies are limited by methodologic problems, such as case definition and the selection and recruitment of case-patients and controls.
Aaron LA, Buchwald D.	Department of Medicine, Harborview Medical Center, 325 Ninth Avenue, Box 359780, Seattle, WA 98104, USA. laaron@u.washington.edu.	Fibromyalgia and other unexplained clinical conditions.	Curr Rheumatol Rep. 2001 Apr;3(2):116-22.	Several unexplained clinical conditions frequently coexist with fibromyalgia; these include chronic fatigue syndrome, irritable bowel syndrome, temporomandibular disorder, tension and migraine headaches, and others. However, only recently have studies directly compared the physiological parameters of these conditions (eg, fibromyalgia vs irritable bowel syndrome) to elucidate underlying pathogenic mechanisms. This review summarizes data from comparative studies and discusses their implications for future research.
Aaron LA, Herrell R, Ashton S, Belcourt M, Schmalig K, Goldberg J, Buchwald D.	Division of General Internal Medicine, Department of Medicine, University of Washington, Seattle, WA 98104, USA. laaron@u.washington.edu	Comorbid clinical conditions in chronic fatigue: a co-twin control study.	J Gen Intern Med. 2001 Jan;16(1):24-31.	OBJECTIVES: Chronically fatiguing illness, defined as fatigue for at least 6 months, has been associated with various physical health conditions. Our objective was to determine whether there is a significant relationship between chronically fatiguing illness and 10 clinical conditions that frequently appear to be associated with fatigue, adjusting for the potentially confounding effects of psychiatric illness. DESIGN: A co-twin control study controlling for genetic and many environmental factors by comparing chronically fatigued twins with their nonfatigued co-twins. SETTING: A nationally distributed volunteer twin registry. PARTICIPANTS: The study included 127 twin pairs in which one member of the pair experienced fatigue of at least 6 months' duration and the co-twin was healthy and denied chronic fatigue. Fatigued twins were classified into 3 levels using increasingly stringent diagnostic criteria. MEASUREMENTS AND MAIN RESULTS: Twins reported on a history of fibromyalgia, irritable bowel syndrome, multiple chemical sensitivities, temporomandibular disorder, interstitial cystitis, postconcussion syndrome, tension headache, chronic low back pain, chronic pelvic pain (women), and chronic nonbacterial prostatitis (men). The prevalence of these comorbid clinical conditions was significantly higher in the fatigued twins compared to their nonfatigued co-twins. Most notably, compared to their nonfatigued co-twins, the chronically fatigued twins had higher rates of fibromyalgia (> 70% vs < 10%) and irritable bowel syndrome (> 50% vs < 5%). The strongest associations were observed between chronic fatigue and fibromyalgia (odds ratios > 20), irritable bowel syndrome, chronic pelvic pain, multiple chemical sensitivities, and temporomandibular disorder (all with odds ratios > or = 4). Regression analysis suggested that the number of comorbid clinical conditions associated with chronic fatigue could not be attributed solely to psychiatric illness. CONCLUSIONS: Chronically fatiguing illnesses were associated with high rates of many other clinical conditions. Thus, patients with chronic fatigue may present a complex clinical picture that poses diagnostic and management challenges. Nonetheless, clinicians should assess such patients for the presence of comorbid clinical conditions. Future research should provide a better understanding of the temporal relationship of the onset of fatigue and these conditions, and develop strategies for early intervention.
Addington AM, Gallo JJ, Ford DE, Eaton WW.	Department of Mental Hygiene, School of Hygiene and Public Health, The Johns Hopkins	Epidemiology of unexplained fatigue and major depression in the community: the Baltimore	Psychol Med. 2001 Aug;31(6):1037-44.	BACKGROUND: Fatigue is a common, non-specific, subjective symptom associated with several medical and psychiatric illnesses. The purpose of this investigation was to explore further the epidemiology of unexplained fatigue in the general population and the relationship between fatigue and depression. METHODS: The design was a prospective population-based study. Subjects included community-dwelling adults who were participants of the

	University, Baltimore, MD 21205, USA.	ECA follow-up, 1981-1994.		Baltimore sample of the Epidemiologic Catchment Area Program in 1981 and who were reinterviewed 13 years later. Lay interviewers using the Diagnostic Interview Schedule interviewed subjects. RESULTS: Number of somatization symptoms and history of a dysphoric episode at baseline were the two strongest predictors of both new onset of fatigue as well as recurrent/chronic fatigue over the 13-year follow-up interval. In addition, individuals who reported a history of unexplained fatigue at baseline as well as during the follow-up, were at markedly increased risk for new onset major depression as compared to those who never reported such fatigue, (RR = 28.4, 95% CI) (11.7, 68.0). Similarly, respondents who developed new fatigue or had remitted fatigue after 1981 were also at increased risk for developing major depression. CONCLUSIONS: Somatization was the strongest predictor of both new and chronic fatigue with unknown cause. In addition, fatigue was both predictive and a consequence of the depression syndrome.
Akagi H, Klimes I, Bass C.	Leeds General Infirmary, Leeds, UK.	Cognitive behavioral therapy for chronic fatigue syndrome in a general hospital--feasible and effective.	Gen Hosp Psychiatry. 2001 Sep-Oct;23(5):254-60.	Cognitive behavior therapy (CBT) has been shown to be effective in recent randomized controlled trials for chronic fatigue syndrome (CFS). We examined the effectiveness of CBT in a general hospital setting in a retrospective questionnaire follow-up study of 94 patients offered CBT by liaison psychiatry services. The questionnaire response rate was 61%. Eighteen percent had returned to normal functioning at follow-up. For the group as a whole, there was a significant improvement in the functional and social impairment and the number of frequently experienced symptoms. Those in work or study at follow-up was 53% (29% pretreatment), and 65% of patients mentioned occupational stress as a contributory factor in their illness. There was a significant reduction in the frequency of attendance at primary care in the year after the end of CBT. We conclude that cognitive behavioral therapy is an acceptable treatment for most patients and can be used in a general hospital outpatient setting by a variety of trained therapists. However, a proportion of patients do not benefit and remain significantly disabled by the condition.
Altemus M, Dale JK, Michelson D, Demitrack MA, Gold PW, Straus SE.	Weill Medical College, Cornell University, Box 244, 1300 York Avenue, New York, NY 10021, USA. maltemus@mail.med.cornell.edu	Abnormalities in response to vasopressin infusion in chronic fatigue syndrome.	Psychoneuroendocrinology. 2001 Feb;26(2):175-88.	Several neuroendocrine studies have suggested hypoactivation of the hypothalamic-pituitary-adrenal axis in chronic fatigue syndrome. One possible determinant of this neuroendocrine abnormality, as well as the primary symptom of fatigue, is reduced hypothalamic secretion of corticotropin-releasing hormone (CRH). Because CRH and vasopressin secreted from the hypothalamus act synergistically at the pituitary to activate ACTH secretion, the ACTH response to peripheral infusion of vasopressin can provide an indirect measure of hypothalamic CRH secretion. We measured the ACTH and cortisol response to a one hour infusion of arginine vasopressin in 19 patients with chronic fatigue syndrome and 19 age and sex matched healthy volunteers. Patients with chronic fatigue syndrome had a reduced ACTH response to the vasopressin infusion and a more rapid cortisol response to the infusion. These results provide further evidence of reduced hypothalamic CRH secretion in patients with chronic fatigue syndrome.
Anderberg UM.	Centrum for miljörelaterad ohälsa och stress (CEOS), institutionen för folkhälso- och vårdvetenskap, enheten för socialmedicin, Uppsala universitet, Akademiska sjukhuset, Uppsala. ullamaria.anderberg@socmed.uu.se	[Stress-related syndromes--contemporary illnesses] [Article in Swedish]	Lakartidningen. 2001 Dec 19;98(51-52):5860-3.	There are many indications that distress within the family as well as at work are strong predictors for developing stress-related disorders. The relatively new diagnoses burnout, chronic fatigue syndrome and fibromyalgia syndrome probably represent different ways of reacting to an overwhelming situation. The boundary between these diseases, on the one hand, and depression, heart disease or infarction on the other is often diffuse, and the new diagnoses may well delineate preliminary stages of more serious diseases such as angina pectoris or myocardial infarction. There is evidence that also other causes of death may be related to stress. These circumstances reflect not only considerable suffering on the part of individuals, but also a substantial economic burden for society.
Anon		DHEA. Monograph.	Altern Med Rev. 2001 Jun;6(3):314-8.	Dehydroepiandrosterone (DHEA) is a steroid hormone secreted primarily by the adrenal glands and to a lesser extent by the brain, skin, testes, and ovaries. It is the most abundant circulating steroid in humans and can be converted into other hormones, including estrogen and testosterone. It has been characterized as a pleiotropic "buffer hormone," with receptor sites in the liver, kidney, and testes, and has a key role in a wide range of physiological responses. Circulating levels of DHEA decline with age and a relationship has been suggested between lower DHEA levels and heart disease, cancer, diabetes, obesity, chronic fatigue syndrome, AIDS, and Alzheimer's disease. Other research suggests that autoimmune diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis, and multiple sclerosis might be associated with declining DHEA levels.
Anon		Bibliography. Current world literature. Nonarticular rheumatism, sports-related injuries, and	Curr Opin Rheumatol. 2001 Mar;13(2):B30-41.	

		related conditions.		
Anon		Defining and managing chronic fatigue syndrome.	Evid Rep Technol Assess (Summ). 2001 Sep;(42):1-4.	
Asbring P.	Centre for Development of Health Services, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden. pia.asbring@smd.sll.se	Chronic illness -- a disruption in life: identity-transformation among women with chronic fatigue syndrome and fibromyalgia.	J Adv Nurs. 2001 May;34(3):312-9.	BACKGROUND: People with chronic illnesses often suffer from identity-loss. Empirical research concerning patients with chronic fatigue syndrome (CFS) or fibromyalgia has not, however, adequately addressed the consequences of these illnesses for identity. AIM: The aim of this article is to describe how women with CFS and fibromyalgia create new concepts of identity after the onset of illness, and how they come to terms with their newly arisen identities. I aim to illuminate the biographical work done by these individuals, which includes a re-evaluation of their former identity and life. This process is illustrated by the following themes: An earlier identity partly lost and Coming to terms with a new identity. METHOD: The study is based on interviews with 25 women in Sweden, 12 with the diagnosis of CFS and 13 diagnosed with fibromyalgia. A grounded theory orientated approach was used when collecting and analysing the data. FINDINGS: The main findings are that: (1) the illnesses can involve a radical disruption in the women's biography that has profound consequences for their identity, particularly in relation to work and social life, (2) biographical disruptions are partial rather than total, calling for different degrees of identity transformation, (3) many of the women also experience illness gains in relation to the new identity. CONCLUSIONS: Thus, the biographical disruption and illness experience comprised both losses and illness gains that had consequences for identity.
Ax S, Gregg VH, Jones D.	Liverpool John Moores University. heasax@yahoo.com	Coping and illness cognitions: chronic fatigue syndrome.	Clin Psychol Rev. 2001 Mar;21(2):161-82.	The chronic fatigue syndrome (CFS) is described, and research on coping with this illness reviewed and analysed. CFS is a severely disabling illness of unknown etiology, which has occurred in epidemic forms all over the world. However, the number of sufferers has dramatically increased over previous years. The heterogeneous symptomatology of CFS was reviewed, and diagnostic criteria were discussed. The difficulty in establishing causality was emphasized. An interaction of factors appears most likely to be associated with illness onset and maintenance. As the mediating factor could be sufferers' coping behavior, the existing coping literature was reviewed. There might be an association between coping and physical and psychological well-being. Finally, recommendations are made for longitudinal research on coping and coping effectiveness, and for the development of therapeutic interventions.
Banks J, Prior L.	Cardiff University School of Social Sciences, Cardiff CF10 3WT, UK.	Doing things with illness. The micro politics of the CFS clinic.	Soc Sci Med. 2001 Jan;52(1):11-23.	This paper focuses on lay and professional ideas about the nature of chronic fatigue syndrome (CFS), and in particular, the ways in which understandings of the disorder are developed in a clinical setting. Our data are drawn from observations of consultations between sufferers and physicians in a UK medical out-patients clinic. We treat the clinic as a political field. That is to say, as an arena in which 'problems' (about the management of illness) are constituted, and alternative approaches and solutions to such problems are pressed. We note that in the realms of symptoms, aetiology and treatment evaluation, lay people in the CFS clinic have quite distinct ideas about what their problems are and how they might be analysed and managed--ideas that are often in conflict with those of medical professionals. Thus, lay sufferers, for example, operate within a different conceptual terrain from that of many professional experts. They are more likely to refer to a disease (myalgic encephalomyelitis or ME), rather than a syndrome. They call upon different kinds of hypotheses to explain their symptoms. They hold to conflicting ideas about the order of causal sequences, and they give emphasis to different kinds of phenomena in their accounts of illness. As a consequence, clinical consultations can often take on the form of a political contest between physician and patient to define the true and real nature of the patient's disorder--a micro political struggle in which neurological symptoms can be re-framed as psychiatric symptoms, and psychiatric symptoms as neurological. In short, a contest in which the demarcation lines between mind and body are continually assessed and re-defined, and the tenets of 'biomedicine' are constantly challenged.
Baschetti R.		Chronic fatigue syndrome, decreased exercise capacity, and adrenal insufficiency.	Arch Intern Med. 2001 Jun 25;161(12):1558-9.	
Baschetti R.		Cognitive behaviour therapy and chronic fatigue syndrome.	Br J Gen Pract. 2001 Apr;51(465):316-7. Comment on: Br J Gen Pract. 2001 Jan;51(462):19-24.	
Baschetti R.		Orthostatic hypotension and	JAMA. 2001 Mar	

		chronic fatigue syndrome.	21;285(11):1441-2; author reply 1443. Comment on: JAMA. 1996 Feb 7;275(5):359; author reply 360.	
Baschetti R.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):240; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
Bass C.		Does myalgic encephalomyelitis exist?	Lancet. 2001 Jun 9;357(9271):1889. Comment on: Lancet. 2001 Feb 17;357(9255):562.	
Bateman C.		Unscrupulous get fat on yuppie flu.	S Afr Med J. 2001 Jan;91(1):24-5.	
Bazelmans E, Bleijenberg G, Van Der Meer JW, Folgering H.	Department of Medical Psychology, University of Nijmegen, The Netherlands.	Is physical deconditioning a perpetuating factor in chronic fatigue syndrome? A controlled study on maximal exercise performance and relations with fatigue, impairment and physical activity.	Psychol Med. 2001 Jan;31(1):107-14.	BACKGROUND: Chronic fatigue syndrome (CFS) patients often complain that physical exertion produces an increase of complaints, leading to a greater need for rest and more time spent in bed. It has been suggested that this is due to a bad physical fitness and that physical deconditioning is a perpetuating factor in CFS. Until now, studies on physical deconditioning in CFS have shown inconsistent results. METHODS: Twenty CFS patients and 20 matched neighbourhood controls performed a maximal exercise test with incremental load. Heart rate, blood pressure, respiratory tidal volume, O2 saturation, O2 consumption, CO2 production, and blood-gas values of arterialized capillary blood were measured. Physical fitness was quantified as the difference between the actual and predicted ratios of maximal workload versus increase of heart rate. Fatigue, impairment and physical activity were assessed to study its relationship with physical fitness. RESULTS: There were no statistically significant differences in physical fitness between CFS patients and their controls. Nine CFS patients had a better fitness than their control. A negative relationship between physical fitness and fatigue was found in both groups. For CFS patients a negative correlation between fitness and impairment and a positive correlation between fitness and physical activity was found as well. Finally, it was found that more CFS patients than controls did not achieve a physiological limitation at maximal exercise. CONCLUSIONS: Physical deconditioning does not seem a perpetuating factor in CFS.
Bell DS, Jordan K, Robinson M.	Primary Care Pediatrics, Lyndonville, New York, USA.	Thirteen-year follow-up of children and adolescents with chronic fatigue syndrome.	Pediatrics. 2001 May;107(5):994-8.	OBJECTIVE: To describe the educational, social, and symptomatic outcome of children and adolescents with chronic fatigue syndrome 13 years after illness onset. METHODS: Between January 1984 and December 1987, 46 children and adolescents developed an illness suggestive of chronic fatigue syndrome. Follow-up questionnaires were obtained from 35 participants an average of 13 years after illness onset. Data were obtained concerning subsequent medical diagnoses, amount of school missed, presence and severity of current symptoms, and subjective assessment of degree of illness resolution. RESULTS: Of the 35 participants, 24 were female (68.6%) and 11 were male (31.4%). Average age at illness onset was 12.1 years. Eight participants (22.9%) had an acute onset of symptoms, 27 (77.1%) had a gradual onset. No participant received an alternative medical diagnosis that could have explained the symptom complex between illness onset and follow-up. Thirteen participants (37.1%) considered themselves resolved of illness at follow-up; 15 participants (42.9%) considered themselves well but not resolved; 4 (11.4%) considered themselves chronically ill; and 3 (8.6%) considered themselves more ill than during the early years of illness. Correlation with the Medical Outcomes Study Short Form Health Survey was good for current level of symptoms and degree of recovery. Eight participants (22.9%) missed >2 years of school, and 5 of these were still ill at follow-up. Amount of school missed correlated with both illness severity at follow-up and perceived social impact of the illness. CONCLUSIONS: These data demonstrate the presence of an illness consistent with the current definition of chronic fatigue syndrome. Eighty percent of children and adolescents affected had a satisfactory outcome from their fatiguing illness, although the majority of these participants had mild to moderate persisting symptoms. Twenty percent of participants remain ill with significant symptoms and activity limitation 13 years after illness onset. Chronic fatigue syndrome in children and adolescents may result in persistent somatic symptoms and disability in a minority of those affected.
Bell IR, Baldwin CM,		Concomitant	Journal of Chronic Fatigue	Background: This study compared personality, dietary, and psychophysiological characteristics of 3 groups of

Stoltz E, Walsh BT, Schwartz GER.		Environmental Chemical Intolerance Modifies the Neurobehavioral Presentation of Women with Fibromyalgia	Syndrome 2001; 9(1/2): 3	women: fibromyalgia (FM) with illness from low levels of environmental chemicals (chemical intolerance, CI), FM alone without CI, and normal controls. CI may be a marker for enhanced central nervous system response amplification (sensitization) in limbic and mesolimbic pathways, which play a role in hedonic responses to food and drugs and in pain. Method: Fibromyalgic women with (FM/CI, n = 11) and without CI (FM, n = 10) and normals (NORM, n = 10) participated in the study. Measures included psychological trait questionnaires, a food frequency questionnaire, a taste test for hedonic and sweetness ratings of different sucrose concentrations, pain self-ratings, and resting spectral electroencephalographic alpha over midline sites, averaged over four separate days. Results: FM with CI had the highest scores on the Harm Avoidance dimension of the Tridimensional Personality Questionnaire, Carbohydrate Addicts Test, Limbic Symptom sensory and behavior subscales, and SCL-90-R somatization and obsessiveness subscales. FM groups both had the highest mean pain ratings for 21 tender point sites. Groups did not differ for macronutrient intake or for sweetness and hedonic ratings for sucrose. The combined FM groups had greater EEG alpha activity towards posterior midline sites than did normals. Conclusion: The pattern of findings may reflect impaired serotonergic function and/or elevated dopaminergic receptor activation by endogenous and/or exogenous agents. The data could have implications for pharmacological and dietary interventions in different subsets of FM patients.
Bested AC, Saunders PR, Logan AC.	Environmental Health Clinic, Sunnybrook and Women's College, Health Sciences Centre, Toronto, Canada.	Chronic fatigue syndrome: neurological findings may be related to blood-brain barrier permeability.	Med Hypotheses. 2001 Aug;57(2):231-7.	Despite volumes of international research, the etiology of chronic fatigue syndrome (CFS) remains elusive. There is, however, considerable evidence that CFS is a disorder involving the central nervous system (CNS). It is our hypothesis that altered permeability of the blood-brain barrier (BBB) may contribute to ongoing signs and symptoms found in CFS. To support this hypothesis we have examined agents that can increase the blood-brain barrier permeability (BBBP) and those that may be involved in CFS. The factors which can compromise the normal BBBP in CFS include viruses, cytokines, 5-hydroxytryptamine, peroxynitrite, nitric oxide, stress, glutathione depletion, essential fatty acid deficiency, and N-methyl-D-aspartate overactivity. It is possible that breakdown of normal BBBP leads to CNS cellular dysfunction and disruptions of neuronal transmission in CFS. Abnormal changes in BBBP have been linked to a number of disorders involving the CNS; based on review of the literature we conclude that the BBB integrity in CFS warrants investigation. Copyright 2001 Harcourt Publishers Ltd.
Binder LM, Storzbach D, Campbell KA, Rohlman DS, Anger WK; Members of the Portland Environmental Hazards Research Center.	Oregon Health Sciences University, Portland, USA. Larry_Binder@email.msn.com	Neurobehavioral deficits associated with chronic fatigue syndrome in veterans with Gulf War unexplained illnesses.	J Int Neuropsychol Soc. 2001 Nov;7(7):835-9.	Gulf War unexplained illnesses (GWUI) are a heterogeneous collection of symptoms of unknown origin known to be more common among veterans of the Gulf War than among nonveterans. In the present study we focused on one of these unexplained illnesses. We tested the hypothesis that in a sample of Persian Gulf War veterans chronic fatigue syndrome (CFS) was associated with cognitive deficits on computerized cognitive testing after controlling for the effects of premorbid cognitive differences. We obtained Armed Forces Qualification Test (AFQT) data acquired around the date of induction into the military on 94 veterans of the Gulf War, 32 with CFS and 62 healthy controls. Controls performed better than participants diagnosed with CFS on the AFQT. Cognitive deficits were associated with CFS on 3 of 8 variables after the effect of premorbid AFQT scores was removed with ANCOVA.
Bourdette DN, McCauley LA, Barkhuizen A, Johnston W, Wynn M, Joos SK, Storzbach D, Shuell T, Sticker D.	Portland Veterans Affairs Medical Center, Department of Neurology, Mailcode P-3-NEURO, 3710 SW US Veteran's Hospital Road, Portland, OR 97201, USA. Dennis.Bourdette@med.va.gov	Symptom factor analysis, clinical findings, and functional status in a population-based case control study of Gulf War unexplained illness.	J Occup Environ Med. 2001 Dec;43(12):1026-40.	Few epidemiological studies have been conducted that have incorporated clinical evaluations of Gulf War veterans with unexplained health symptoms and healthy controls. We conducted a mail survey of 2022 Gulf War veterans residing in the northwest United States and clinical examinations on a subset of 443 responders who seemed to have unexplained health symptoms or were healthy. Few clinical differences were found between cases and controls. The most frequent unexplained symptoms were cognitive/psychological, but significant overlap existed with musculoskeletal and fatigue symptoms. Over half of the veterans with unexplained musculoskeletal pain met the criteria for fibromyalgia, and a significant portion of the veterans with unexplained fatigue met the criteria for chronic fatigue syndrome. Similarities were found in the clinical interpretation of unexplained illness in this population and statistical factor analysis performed by this study group and others.
Brewer JH, Berg D.		Hypercoaguable State Associated with Active Human Herpesvirus-6 (HHV-6) Viremia in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 111	Objectives: A subset of patients with Chronic Fatigue Syndrome (CFS) have been found to be hypercoaguable in small previous studies. We wanted to analyze the incidence of a hypercoaguable state and assess hereditary hypercoaguable risk factors in a group of patients with known CFS and HHV-6 viremia. Methods: Thirty patients diagnosed with CFS that had at least one prior positive blood culture for active HHV-6 by rapid culture method were studied. A hypercoaguable panel was obtained to assess activation of coagulation. Two or more positive tests were determined to represent activation of coagulation. Hereditary thrombosis risk panels were also performed which included eight different genetic tests to assess hereditary abnormalities. Results: Twenty-four of thirty (80%) patients had a hypercoaguable state, thus activation of coagulation. Twenty-five of thirty (83%) of patients had a hereditary abnormality. Conclusions: CFS patients with active HHV-6 infection (viremia) have activation of coagulation and are hypercoaguable. Hereditary thrombosis risk factors are very prevalent in these patients. These

				hereditary abnormalities increase the hypercoaguable tendencies. The hypercoaguable state associated with active HHV-6 infection may be a significant contributing factor to the symptoms seen in CFS patients.
Brunet JL, Liaudet AP, Later R, Peyramond D, Cozon GJ.	Infectious Diseases Department-Hopital de la Croix-Rousse-69317 Lyon, France.	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.	Chronic fatigue syndrome or benign myalgic encephalomyelitis has been extensively described and investigated. Although numerous immunological abnormalities have been linked with the syndrome, none have been found to be specific. This article describes the detection of delayed-type hypersensitive responses to certain common environmental antigens in almost fifty per cent of patients with this syndrome. Such hypersensitivity can be detected by the intradermal administration of antigens derived from commensal organisms like the yeast <i>Candida albicans albicans</i> , and then monitoring for a systemic reaction over the following six to forty-eight hours. This approach can be consolidated by performing lymphocyte activation tests in parallel and measuring in vitro T-cell activation by <i>Candida albicans albicans</i> antigens by three-colour flow cytometry based on CD3, CD4 and either CD69 or CD25. Another useful parameter is the kinetics of neopterin excretion in the urine over the course of the skin test. The results showed that the intensity of the DTH response correlated with the number of T-cells activated in vitro. Various factors have been implicated in the fatigue of many patients, notably lack of sleep. However, it remains difficult to establish causality in either one direction or the other. This work is in the spirit of a multifactorial approach to the group of conditions referred to as "chronic fatigue syndrome".
Buchwald D, Herrell R, Ashton S, Belcourt M, Schmalig K, Sullivan P, Neale M, Goldberg J.	Department of Medicine, University of Washington, Seattle, WA, USA. dedra@u.washington.edu	A twin study of chronic fatigue.	Psychosom Med. 2001 Nov-Dec;63(6):936-43.	OBJECTIVE: The etiology of chronic fatigue syndrome is unknown, but genetic influences may be important in its expression. Our objective was to assess the role of genetic and environmental factors in unexplained chronic fatigue. METHODS: A classic twin study was conducted using 146 female-female twin pairs, of whom at least one member reported > or =6 months of fatigue. After completing questionnaires on symptoms, zygosity, physical health, and a psychiatric interview, twins were classified using three increasingly stringent definitions: 1) chronic fatigue for > or =6 months, 2) chronic fatigue not explained by exclusionary medical conditions, and 3) idiopathic chronic fatigue not explained by medical or psychiatric exclusionary criteria of the chronic fatigue syndrome case definition. Concordance rates in monozygotic and dizygotic twins were calculated for each fatigue definition along with estimates of the relative magnitude of genetic and environmental influences on chronic fatigue. RESULTS: The concordance rate was higher in monozygotic than dizygotic twins for each definition of chronic fatigue. For idiopathic chronic fatigue, the concordance rates were 55% in monozygotic and 19% in dizygotic twins (p =.042). The estimated heritability in liability was 19% (95% confidence interval = 0-56) for chronic fatigue > or =6 months, 30% (95% confidence interval = 0-81) for chronic fatigue not explained by medical conditions, and 51% (95% confidence interval = 7-96) for idiopathic chronic fatigue. CONCLUSIONS: These results provide evidence supporting the familial aggregation of fatigue and suggest that genes may play a role in the etiology of chronic fatigue syndrome.
Buskila D, Press J.	Rheumatic Disease Unit and Department of Medicine 'B', Soroka Medical Centre and Ben-Gurion University, Beer-Sheva, 84101, Israel.	Neuroendocrine mechanisms in fibromyalgia-chronic fatigue.	Best Pract Res Clin Rheumatol. 2001 Dec;15(5):747-58.	Fibromyalgia and chronic fatigue syndrome are poorly understood disorders that share similar demographic and clinical characteristics. Because of the clinical similarities between both disorders it was suggested that they share a common pathophysiological mechanism, namely, central nervous system dysfunction. This chapter presents data demonstrating neurohormonal abnormalities, abnormal pain processing and autonomic nervous system dysfunction in fibromyalgia and chronic fatigue syndrome. The possible contribution of the central nervous system dysfunction to the development and symptomatology of these conditions is discussed. The chapter concludes by reviewing the effect of current treatments and emerging therapeutic modalities in fibromyalgia and chronic fatigue syndrome. Copyright 2001 Harcourt Publishers Ltd.
Buskila D.	Ben Gurion University of the Negev, Faculty of Health Sciences, Soroka Medical Center, Beer Sheva, Israel.	Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome.	Curr Opin Rheumatol. 2001 Mar;13(2):117-27.	The prevalence of chronic widespread pain in the general population in Israel was comparable with reports from the USA, UK, and Canada. Comorbidity with fibromyalgia (FM) resulted in somatic hyperalgesia in patients with irritable bowel syndrome. One sixth of the subjects with chronic widespread pain in the general population were also found to have a mental disorder. Mechanisms involved in referred pain, temporal summation, muscle hyperalgesia, and muscle pain at rest were attenuated by the N-methyl-D-aspartate (NMDA) antagonist, ketamine, in FM patients. Delayed corticotropin release, after interleukin-6 administration, in FM was shown to be consistent with a defect in hypothalamic corticotropin-releasing hormone neural function. The basal autonomic state of FM patients was characterized by increased sympathetic and decreased parasympathetic systems tones. The severity of functional impairment as assessed by the Medical Outcome Survey Short Form (SF-36) discriminated between patients with widespread pain alone and FM patients. Chronic fatigue syndrome (CFS) occurred in about 0.42% of a random community-based sample of 28,673 adults in Chicago, Illinois. A significant clinical overlap between CFS and FM was reported. Cytokine dysregulation was not found to be a singular or dominant factor in the pathogenesis of CFS. A favorable outcome of CFS in children was reported; two thirds recovered and resumed

				normal activities. No major therapeutic trials in FM and CFS were reported over the past year.
Butler JA, Chalder T, Wessely S.	Department of Psychological Medicine, Maudsley Hospital, London.	Causal attributions for somatic sensations in patients with chronic fatigue syndrome and their partners.	Psychol Med. 2001 Jan;31(1):97-105.	BACKGROUND: Patients with chronic fatigue syndrome (CFS) often make somatic attributions for their illness which has been associated with poor outcome. A tendency to make somatic attributions in general may be a vulnerability factor for the development of CFS. METHODS: This cross-sectional study based on self-report questionnaire data aimed to investigate the type of attributions for symptoms made by patients with CFS and to compare this to attributions made by their partners. It was hypothesized that patients with CFS would make more somatic attributions for their own symptoms than control subjects and that partners of patients with CFS would make more somatic attributions for their ill relative's symptoms but would be similar to controls regarding their own symptoms. Fifty patients with CFS were compared to 50 controls from a fracture clinic in the same hospital and 46 relatives living with the patients with CFS. A modified Symptom Interpretation Questionnaire was used to assess causal attributions. RESULTS: CFS patients were more likely to make somatic attributions for their symptoms. The relatives of patients with CFS made significantly more somatic attributions for symptoms in their ill relative. However, they were like the fracture clinic controls in terms of making predominantly normalizing attributions for their own symptoms. CONCLUSIONS: The data support modification of existing cognitive behavioural treatments for CFS to investigate whether addressing partners' attributions for patients' symptoms improves recovery in the patient. Furthermore, a tendency to make somatic attributions for symptoms may be a vulnerability factor for the development of CFS.
Caserta MT, Mock DJ, Dewhurst S.	Department of Pediatrics, University of Rochester Medical Center, Rochester, NY 14642, USA.	Human herpesvirus 6.	Clin Infect Dis. 2001 Sep 15;33(6):829-33. Epub 2001 Aug 10.	The development of techniques for the culture of lymphoid cells and the isolation of viruses that infect these cells led to the discovery of human herpesvirus (HHV) 6 in 1986. At the time, HHV-6 was the first new human herpesvirus to be discovered in roughly a quarter of a century, and its isolation marked the beginning of an era of discovery in herpesvirology, with the identification of HHV-7 and HHV-8 (Kaposi's sarcoma-associated herpesvirus) during the following decade. Like most human herpesviruses, HHV-6 is ubiquitous and capable of establishing a lifelong, latent infection of its host. HHV-6 is particularly efficient at infecting infants and young children, and primary infection with the virus is associated with roseola infantum (exanthem subitum) and, most commonly, an undifferentiated febrile illness. Viral reactivation in the immunocompromised host has been linked to a variety of diseases, including encephalitis, and HHV-6 has been tentatively associated with multiple sclerosis. This article discusses the major properties of HHV-6, its association with human disease, and the pathobiological significance of viral reactivation.
Chaudhuri A.		Patient education to encourage graded exercise in chronic fatigue syndrome. Trial has too many shortcomings.	BMJ. 2001 Jun 23;322(7301):1545-6. Comment on: BMJ. 2001 Feb 17;322(7283):387-90.	
Chaudhuri A.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):238; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
Clauw DJ.	Georgetown Chronic Pain and Fatigue Research Center, Department of Medicine, Georgetown University Medical Center, Washington, District of Columbia 20007, USA.	Potential mechanisms in chemical intolerance and related conditions.	Ann N Y Acad Sci. 2001 Mar;933:235-53.	The symptom of chemical intolerance may occur in isolation, but often occurs in conjunction with other chronic symptoms such as pain, fatigue, memory disturbances, etc. This frequent clustering of symptoms in individuals has led to the definition of several chronic multisymptom syndromes, such as multiple chemical sensitivity, fibromyalgia, chronic fatigue syndrome, and Gulf War illnesses. The aggregate research into these syndromes has suggested some unifying mechanisms that contribute to symptomatology. Multiple lines of evidence suggest that there is aberrant function of numerous efferent neural pathways, such as the autonomic nervous system and hypothalamic-pituitary axes, in subsets of individuals with these conditions. There is perhaps the greatest evidence for abnormal sensory processing in these syndromes, with a low "unpleasantness threshold" for multiple types of sensory stimuli. Psychological and behavioral factors are known to play a significant role in initiating or perpetuating symptoms in some persons with these illnesses. In the field of pain research, the interrelationship between physiologic and psychologic factors in symptom expression has been well studied. Using both established and novel methodologies, studies have suggested that psychologic factors such as hypervigilance and expectancy are playing a relatively minor role in most individuals with fibromyalgia and that clear evidence exists of physiologic amplification of sensory stimuli. These studies need to be extended to more sensory tasks and to larger

				numbers of subjects with related conditions. It is of note, though, that existing data on this spectrum of illnesses would suggest that there may be greater psychologic contributions to symptomatology if an illness is defined in part by behavior (e.g., avoidance of chemical exposures) rather than on the basis of symptoms alone.
Claypoole K, Mahurin R, Fischer ME, Goldberg J, Schmalig KB, Schoene RB, Ashton S, Buchwald D.	Departments of Psychiatry and Behavioral Sciences, University of Washington, Seattle, Washington, USA.	Cognitive compromise following exercise in monozygotic twins discordant for chronic fatigue syndrome: fact or artifact?	Appl Neuropsychol. 2001;8(1):31-40.	This study examined the effects of exhaustive exercise on cognitive functioning among 21 monozygotic twin pairs discordant for chronic fatigue syndrome (CFS). The co-twin control design adjusts for genetic and family environmental factors not generally accounted for in more traditional research designs of neuropsychological function. Participants pedaled a cycle ergometer to exhaustion; maximum oxygen output capacity (VO2max) as well as perceived exertion were recorded. Neuropsychological tests of brief attention and concentration, speed of visual motor information processing, verbal learning and recognition memory, and word and category fluency were administered with alternate forms to participants pre- and postexercise. The preexercise neuropsychological test performance of CFS twins tended to be slightly below that of the healthy twin controls on all measures. However, twins with CFS did not demonstrate differential decrements in neuropsychological functioning after exercise relative to their healthy co-twins. Because exercise does not appear to diminish cognitive function, rehabilitative treatment approaches incorporating exercise are not contraindicated in CFS.
Cleare AJ, Blair D, Chambers S, Wessely S.	Department of Psychological Medicine, Guy's King's and St. Thomas' School of Medicine and the Institute of Psychiatry, 103 Denmark Hill, London SE5 8AZ, UK. a.cleare@iop.kcl.ac.uk	Urinary free cortisol in chronic fatigue syndrome.	Am J Psychiatry. 2001 Apr;158(4):641-3.	OBJECTIVE: The authors measured 24-hour urinary free cortisol in a group of well-characterized patients with chronic fatigue syndrome. METHOD: They obtained 24-hour urine collections from 121 consecutive clinic patients with chronic fatigue syndrome and 64 comparison subjects without the syndrome. RESULTS: Urinary free cortisol was significantly lower in the subjects with chronic fatigue syndrome regardless of the presence or absence of current or past comorbid psychiatric illness. Lower levels of urinary free cortisol were not related to medication use, sleep disturbance, or disability levels. CONCLUSIONS: There is mild hypocortisolism in chronic fatigue syndrome. Whether a primary feature or secondary to other factors, hypocortisolism may be one factor contributing to the symptoms of chronic fatigue syndrome.
Cleare AJ, Miell J, Heap E, Sookdeo S, Young L, Malhi GS, O'Keane V.	Department of Psychological Medicine, Institute of Psychiatry and Guy's, King's and St Thomas' School of Medicine, London SE5 8AZ, United Kingdom. a.cleare@iop.kcl.ac.uk	Hypothalamo-pituitary-adrenal axis dysfunction in chronic fatigue syndrome, and the effects of low-dose hydrocortisone therapy.	J Clin Endocrinol Metab. 2001 Aug;86(8):3545-54.	These neuroendocrine studies were part of a series of studies testing the hypotheses that 1) there may be reduced activity of the hypothalamic-pituitary-adrenal axis in chronic fatigue syndrome and 2) low-dose augmentation with hydrocortisone therapy would improve the core symptoms. We measured ACTH and cortisol responses to human CRH, the insulin stress test, and D-fenfluramine in 37 medication-free patients with CDC-defined chronic fatigue syndrome but no comorbid psychiatric disorders and 28 healthy controls. We also measured 24-h urinary free cortisol in both groups. All patients (n = 37) had a pituitary challenge test (human CRH) and a hypothalamic challenge test [either the insulin stress test (n = 16) or D-fenfluramine (n = 21)]. Baseline cortisol concentrations were significantly raised in the chronic fatigue syndrome group for the human CRH test only. Baseline ACTH concentrations did not differ between groups for any test. ACTH responses to human CRH, the insulin stress test, and D-fenfluramine were similar for patient and control groups. Cortisol responses to the insulin stress test did not differ between groups, but there was a trend for cortisol responses both to human CRH and D-fenfluramine to be lower in the chronic fatigue syndrome group. These differences were significant when ACTH responses were controlled. Urinary free cortisol levels were lower in the chronic fatigue syndrome group compared with the healthy group. These results indicate that ACTH responses to pituitary and hypothalamic challenges are intact in chronic fatigue syndrome and do not support previous findings of reduced central responses in hypothalamic-pituitary-adrenal axis function or the hypothesis of abnormal CRH secretion in chronic fatigue syndrome. These data further suggest that the hypocortisolism found in chronic fatigue syndrome may be secondary to reduced adrenal gland output. Thirty-two patients were treated with a low-dose hydrocortisone regime in a double-blind, placebo-controlled cross-over design, with 28 days on each treatment. They underwent repeated 24-h urinary free cortisol collections, a human CRH test, and an insulin stress test after both active and placebo arms of treatment. Looking at all subjects, 24-h urinary free cortisol was higher after active compared with placebo treatments, but 0900-h cortisol levels and the ACTH and cortisol responses to human CRH and the insulin stress test did not differ. However, a differential effect was seen in those patients who responded to active treatment (defined as a reduction in fatigue score to the median population level or less). In this group, there was a significant increase in the cortisol response to human CRH, which reversed the previously observed blunted responses seen in these patients. We conclude that the improvement in fatigue seen in some patients with chronic fatigue syndrome during hydrocortisone treatment is accompanied by a reversal of the blunted cortisol responses to human CRH.
Cleare AJ, O'Keane V, Miell J.	Department of Psychological Medicine, Guy's, King's and St	Plasma leptin in chronic fatigue syndrome and a placebo-controlled study of	Clin Endocrinol (Oxf). 2001 Jul;55(1):113-9.	OBJECTIVE: Previous studies have suggested that chronic fatigue syndrome (CFS) is associated with changes in appetite and weight, and also with mild hypocortisolism. Because both of these features may be related to leptin metabolism, we undertook a study of leptin in CFS. DESIGN: (i) A comparison of morning leptin concentration in

	Thomas' School of Medicine, 103 Denmark Hill, London SE3 8AF, UK. a.cleare@iop.kcl.ac.uk	the effects of low-dose hydrocortisone on leptin secretion.		patients with CFS and controls and (ii) a randomized, placebo-controlled crossover study of the effects of hydrocortisone on leptin levels in CFS. PATIENTS: Thirty-two medication free patients with CFS but not comorbid depression or anxiety. Thirty-two age, gender, weight, body mass index and menstrual cycle matched volunteer subjects acted as controls. MEASUREMENTS: We measured basal 0900 h plasma leptin levels in patients and controls. All 32 patients were taking part in a randomized, placebo-controlled crossover trial of low dose (5 or 10 mg) hydrocortisone as a potential therapy for CFS. We measured plasma leptin after 28 days treatment with hydrocortisone and after 28 days treatment with placebo. RESULTS: At baseline, there was no significant difference in plasma leptin between patients [mean 13.8, median 7.4, interquartile range (IQR) 18.0 ng/ml] and controls (mean 10.2, median 5.5, IQR 11.3 ng/ml). Hydrocortisone treatment, for both doses combined, caused a significant increase in leptin levels compared to placebo. When the two doses were analysed separately, only 10 mg was associated with a significant effect on leptin levels. We also compared the hydrocortisone induced increase in leptin between those who were deemed treatment-responders and those deemed nonresponders. Responders showed a significantly greater hydrocortisone-induced rise in leptin than nonresponders. This association between a clinical response to hydrocortisone and a greater rise in leptin levels may indicate a greater biological effect of hydrocortisone in these subjects, perhaps due to increased glucocorticoid receptor sensitivity, which may be present in some patients with CFS. CONCLUSIONS: We conclude that, while we found no evidence of alterations in leptin levels in CFS, low dose hydrocortisone therapy caused increases in plasma leptin levels, with this biological response being more marked in those CFS subjects who showed a positive therapeutic response to hydrocortisone therapy. Increases in plasma leptin levels following low dose hydrocortisone therapy may be a marker of pretreatment physiological hypocortisolism and of response to therapy.
Cleare AJ.	Guy's, King's and St Thomas' School of Medicine, Institute of Psychiatry, Division of Psychological Medicine, London, UK. a.cleare@iop.kcl.ac.uk	Regulatory disturbance of energy.	Adv Psychosom Med. 2001;22:17-34.	
Cochran John W.		Effect of Modafinil on Fatigue Associated with Neurological Illnesses	Journal of Chronic Fatigue Syndrome 2001; 8(2): 65	Fatigue is a common symptom of a variety of neurological illnesses, such as Alzheimer's disease, chronic fatigue syndrome, multiple sclerosis, Parkinson's disease, and stroke. Fatigue severely impairs productivity, performance, social functioning, and quality of life. Modafinil (PROVIGIL®) has been shown to significantly improve fatigue associated with multiple sclerosis and depression. Here, a retrospective review of the medical charts of 25 patients treated with modafinil for fatigue associated with various neurological illnesses was conducted. Modafinil was effective for the treatment of fatigue in 21 of 25 patients (84%), and was well tolerated. Therefore, modafinil appears to be a potentially attractive candidate for the treatment of fatigue associated with neurological disorders.
Coetzer P, Lockyer I, Schorn D, Boshoff L.	Sanlam, Bellville, Republic of South Africa.	Assessing impairment and disability for syndromes presenting with chronic fatigue.	J Insur Med. 2001;33(2):170-82.	Many disability claims are based on the subjective symptom of fatigue, which can be caused by a wide spectrum of diagnoses including fibromyalgia, chronic fatigue syndrome and cardiopulmonary diseases. Chronic pain is very often a compounding problem. It is vital for every insurer to have fair and objective criteria to distinguish between invalid claims and those with merit. This review article proposes objective tools and parameters to achieve this goal.
Cohen H, Neumann L, Kotler M, Buskila D.	Anxiety and Stress Research Unit, Ministry of Health Mental Health Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel. hagitc@bgumail.bgu.ac.il	Autonomic nervous system derangement in fibromyalgia syndrome and related disorders.	Isr Med Assoc J. 2001 Oct;3(10):755-60.	Fibromyalgia syndrome is a chronic, painful musculoskeletal disorder of unknown etiology and/or pathophysiology. During the last decade many studies have suggested autonomic nervous system involvement in this syndrome, although contradictory results have been reported. This review focuses on studies of the autonomic nervous system in fibromyalgia syndrome and related disorders, such as chronic fatigue syndrome and irritable bowel syndrome on the one hand and anxiety disorder on the other, and highlights techniques of dynamic assessment of heart rate variability. It raises the potentially important prognostic implications of protracted autonomic dysfunction in patient populations with fibromyalgia and related disorders, especially for cardiovascular morbidity and mortality.
Cook DB, Lange G, DeLuca J, Natelson BH.	Department of Neurosciences, UMDNJ-New Jersey Medical School, Newark, NJ 07103, USA.	Relationship of brain MRI abnormalities and physical functional status in chronic fatigue syndrome.	Int J Neurosci. 2001 Mar;107(1-2):1-6.	Chronic Fatigue Syndrome (CFS) is an unexplained illness that is characterized by severe fatigue. Some have suggested that CFS is a "functional somatic syndrome" in which symptoms of fatigue are inappropriately attributed to a serious illness. However, brain magnetic resonance imaging (MRI) data suggest that there may be an organic abnormality associated with CFS. To understand further the significance of brain MRI abnormalities, we examined the relationship between MRI identified brain abnormalities and self-reported physical functional status in 48

				subjects with CFS who underwent brain MR imaging and completed the Medical Outcomes Study SF-36. Brain MR images were examined for the presence of abnormalities based on 5 general categories previously shown to be sensitive to differentiating CFS patients from healthy controls. There were significant negative relationships between the presence of brain abnormalities and both the physical functioning (PF) ($\rho=-.31$, $p=.03$), and physical component summary PCS ($\rho=-.32$, $p=.03$) subscales of the SF-36. CFS patients with MRI identified brain abnormalities scored significantly lower on both PF ($t(1,46) = 2.3$, $p=.026$) and the PCS ($t(1,41) = 2.4$, $p=.02$) than CFS subjects without an identified brain abnormality. When adjusted for age differences only the PF analysis remained significant. However, the effect sizes for both analyses were large indicating meaningful differences in perceived functional status between the groups. These results demonstrate that the presence of brain abnormalities in CFS are significantly related to subjective reports of physical function and that CFS subjects with MRI brain abnormalities report being more physically impaired than those patients without brain abnormalities.
Cordingley L, Wearden A, Appleby L, Fisher L.	School of Psychiatry and Behavioural Sciences, University of Manchester, Room 704, Stopford Building, Oxford Road, M13 9PT, Manchester, UK. lis.cordingley@man.ac.uk	The Family Response Questionnaire: a new scale to assess the responses of family members to people with chronic fatigue syndrome.	J Psychosom Res. 2001 Aug;51(2):417-24.	OBJECTIVE: Family responses to patients with chronic fatigue syndrome (CFS) may influence the course of the disorder and family members themselves are likely to be adversely affected. However, the beliefs and responses of relatives of CFS patients have been under-researched. The aim of this study was to produce an easy-to-administer questionnaire to assess the responses of family members to people with CFS. METHODS: Seventy-eight people, all close relatives of (physician-diagnosed) CFS sufferers, completed the first version of the Family Response Questionnaire (FRQ). RESULTS: Examination of the correlation matrix and a cluster analysis of the items support four scales rather than the original five. The four response scales were labelled: sympathetic-empathic, active engagement, rejecting-hostile, and concern with self. Measures of test-retest and internal reliability were high. Participants found the items both comprehensible and relevant to their experiences of living with people with CFS. CONCLUSION: The new version of the FRQ will be useful in further examination of the responses of CFS on individuals and their families.
Coutts R, Weatherby R, Davie A.	School of Exercise Science and Sport Management, Southern Cross University, P.O. Box 157, New South Wales 2480, Lismore, Australia.rcoutts@scu.edu.au	The use of a symptom "self-report" inventory to evaluate the acceptability and efficacy of a walking program for patients suffering with chronic fatigue syndrome.	J Psychosom Res. 2001 Aug;51(2):425-9.	OBJECTIVES: The purpose of this research was to evaluate the effectiveness of the modality of walking as a management strategy for patients suffering with chronic fatigue syndrome (CFS). METHODS: Six males and fourteen females with medically diagnosed CFS (CDC, 1994), completed a 12-week walking program. Prior to starting the program subjects underwent an incremental walking exercise test to predetermine their walking intensity. The SCL-90-R symptom "self-report" questionnaire was administered prior to, and at the completion of, the walking program. RESULTS: At the completion of the 12 weeks of walking, changes in four of the nine SCL-90-R dimensions were significant (somatisation, paranoid ideation, phobic anxiety, and psychoticism). Also significant were the changes in the combination indices, the Global Indices of Distress (GID) and the Positive Symptom Total (PST). CONCLUSION: This group of CFS subjects, by way of "self-report", indicated the possibility of an exercise-induced decrease in psychological stress. The walking intervention may have evoked positive changes in their well-being and, furthermore, provided no evidence of any exacerbation in their symptoms.
Creswell C, Chalder T.	Sub-Department of Clinical Health Psychology, University College London, Gower Street, WC1E 6BT, London, UK. c.creswell@ucl.ac.uk	Defensive coping styles in chronic fatigue syndrome.	J Psychosom Res. 2001 Oct;51(4):607-10.	OBJECTIVE: The cognitive-behavioral model of chronic fatigue syndrome (CFS) proposes that rigidly held beliefs act to defend individuals against low self-esteem. This study is the first to investigate the prevalence of a potential mechanism, the Defensive High Anxious coping style, among individuals with CFS. METHODS: The study comprised 68 participants (24 CFS; 24 healthy volunteers; 20 chronic illness volunteers). Participants completed the Bendig short form of the Taylor Manifest Anxiety Scale (B-MAS) and the Marlowe-Crowne Social Desirability Scale (MC) in order to ascertain the distribution of participants in each group within the four coping styles defined by Weinberger et al. [J. Abnorm. Psychol. 88 (1979) 369]. RESULTS: A greater number of participants in the CFS group (46%) were classified as Defensive High Anxious compared to the two comparison groups [$\chi^2(2)=8.84$, $P=.012$]. CONCLUSION: This study provides support for the existence of defensive coping mechanisms as described by the cognitive-behavioral model of CFS. Furthermore, it has been suggested that this particular coping style may impinge directly on physical well being through similar mechanisms as identified in CFS, and further research linking these areas of research is warranted.
Csef H.	Arbeitsbereich Psychosomatische Medizin und Psychotherapie, Medizinische Poliklinik, der Universität, Klinikstrasse 8, 97070 Würzburg.	[Chronic fatigue] [Article in German]	Internist (Berl). 2001 Nov;42(11):1495-502, 1504; quiz 1504-7.	

Curt GA.	National Cancer Institute, National Institutes of Health, Clinical Center, Oncology Program, Building 10, Room 12N214, 9000 Rockville Pike, Bethesda, Maryland 20892, USA.	[Fatigue syndrome caused by malignant tumor. An increasing priority in patient care] [Article in Italian]	Recenti Prog Med. 2001 Jun;92(6):408-12.	As oncologists have become more effective in alleviating pain, nausea and depression, fatigue has emerged as the most important symptom suffered by cancer patients. Indeed, the current literature suggests that fatigue is currently the most important untreated symptom in cancer medicine. In recent surveys of patients and their caregivers, fatigue is more important for the quality of life than pain, nausea or depression. Yet these same surveys confirm that oncologists underestimate the importance of cancer related fatigue. This may be partly because patients often do not fully share the full nature of their concerns. When patients do raise the issue of fatigue, the physicians' recommendations are often non specific. However, recent research has shown that fatigue is not inevitable and untreatable, but a symptom amenable to differential diagnosis and specific intervention. Like pain, fatigue is intrinsically a subjective problem where the doctor relies on the patient's reporting. Weakness, exhaustion, lethargy and asthenia are all used as functional descriptions of fatigue. While these are descriptive terms, clinical research in the measurement and alleviation of fatigue requires reproducible measurement tools. Several studies already exist and have begun to explore this important area of symptom management.
Custaud MA.	Laboratoire de physiologie de l'environnement (Pr C. Gharib) EA 645 Faculte de medecine Lyon-Grange Blanche 8, avenue Rockefeller 69373 Lyon. Claude.Gharib@univ-lyon1.fr	[Don't forget the gravity] [Article in French]	Rev Prat. 2001 Oct 15;51(16):1745-7.	
Daly E, Komaroff AL, Bloomingdale K, Wilson S, Albert MS.	Department of Psychiatry, Massachusetts General Hospital, 149 13th Street, Charlestown, MA 02129, USA. albert@psych.mgh.harvard.edu	Neuropsychological function in patients with chronic fatigue syndrome, multiple sclerosis, and depression.	Appl Neuropsychol. 2001;8(1):12-22.	Patients with chronic fatigue syndrome (CFS), multiple sclerosis (MS), and major depression were compared with controls and with each other on a neuropsychological battery that included standard neuropsychological tests and a computerized set of tasks that spanned the same areas of ability. A total of 101 participants were examined, including 29 participants with CFS, 24 with MS, 23 with major depressive disorder, and 25 healthy controls. There were significant differences among the groups in 3 out of 5 cognitive domains: memory, language, and spatial ability. Assessment of psychiatric symptoms indicated that all 3 patient groups had a higher prevalence of depression than the controls. A total measure of psychiatric symptomatology also differentiated the patients from the controls. After covarying the cognitive test scores by a measure of depression, the patient groups continued to differ from controls primarily in the area of memory. The findings support the view that the cognitive deficits found in CFS cannot be attributed solely to the presence of depressive symptomatology in the patients.
Davey NJ, Puri BK, Nowicky AV, Main J, Zaman R.	Department of Sensimotor Systems, Division of Neuroscience and Psychological Medicine, Imperial College School of Medicine, Charing Cross Hospital, Fullham Palace Road, W6 8RF, London, UK. n.davey@ic.ac.uk	Voluntary motor function in patients with chronic fatigue syndrome.	J Psychosom Res. 2001 Jan;50(1):17-20.	INTRODUCTION: The pathogenesis of chronic fatigue syndrome (CFS) remains unknown. In particular, little is known of the involvement of the motor cortex and corticospinal system. METHODS: Transcranial magnetic stimulation (TMS) was used to assess corticospinal function in terms of latency and threshold of motor-evoked potentials (MEPs) in thenar muscles. Reaction times and speed of movement were assessed using button presses in response to auditory tones. RESULTS: Patients had higher ($P < .05$) self-assessed indices of fatigue (7/10) than for pain (5/10), anxiety (4/10) or depression (3/10). Mean (+/-S.E.M.) simple reaction times (SRTs) were longer ($P < .05$) in the patients (275+/-19 ms) than in the controls (219+/-9 ms); choice reaction times (CRTs) were not significantly longer in the patients. Movement times, once a reaction task had been initiated, were longer ($P < .05$) in the patients in both SRTs (patients, 248+/-13 ms; controls, 174+/-9 ms) and CRTs (patients, 269+/-13 ms; controls, 206+/-12 ms). There was no difference ($P > .05$) in threshold or latency of MEPs in hand muscles between the patients (threshold, 54.5+/-2.2% maximum stimulator output [% MSO]; latency 22+/-0.3 ms) and controls (threshold 54.6+/-3.6% MSO; latency 22.9+/-0.5 ms). Regression analysis showed no correlation ($P > .05$) of SRTs with either threshold for MEPs or fatigue index. CONCLUSION: Corticospinal conduction times and excitability were within the normal range despite a slower performance time for motor tasks and an increased feeling of fatigue. This suggests that the feeling of fatigue and the slowness of movement seen in CFS are manifest outside the corticospinal system.
De Becker P, McGregor N, De Meirleir K.	VUB, Vakgroep Interne Geneeskunde, KRO gebouw niv.-1, Laarbeeklaan 101, 1090 Brussels, Belgium. pdbeck@minf.vub.ac.be	A definition-based analysis of symptoms in a large cohort of patients with chronic fatigue syndrome.	J Intern Med. 2001 Sep;250(3):234-40.	OBJECTIVE: The Holmes and Fukuda criteria are widely used criteria all over the world, yet a specific European study regarding chronic fatigue syndrome (CFS) patient symptomatology has not been conducted so far. This study was performed to answer the need to assess the homogeneity of a large CFS population in relationship to the Fukuda or Holmes definitions and to assess the importance of a symptom severity scale. DESIGN: Multivariate analyses were performed to assess the symptom presentation within a fatigued population and the differences between the Fukuda and Holmes definitions compared with an excluded chronic fatigued group in a large cohort of

				<p>fatigued patients. SETTING: An outpatient tertiary care setting fatigue clinic in Brussels. MAIN OUTCOME MEASURES: Prevalence and severity of symptoms and signs in a CFS population and in a chronic fatigued population. SUBJECTS AND METHODS: A total of 2073 consecutive patients with major complaints of prolonged fatigue participated in this study. Multivariate analyses were performed to assess the symptom presentation and severity and the differences between the Fukuda and Holmes definitions. RESULTS: Of the 2073 patients complaining of chronic fatigue (CF), 1578 CFS patients fulfilled the Fukuda criteria (100% of CFS group) and 951 (60.3% of the CFS group) fulfilled the Holmes criteria. Discriminant function analysis revealed that the Fukuda and Holmes definitions can be differentiated by symptom severity and prevalence. The Holmes definition was more strongly associated than the Fukuda definition with the symptoms that differentiated the CFS patients from the patients that did not comply with the CFS definitions. The inclusion of 10 additional symptoms was found to improve the sensitivity/specificity and accuracy for selection of CFS patients. CONCLUSIONS: The CFS patients fulfilling the Holmes criteria have an increased symptom prevalence and severity of many symptoms. Patients fulfilling the Fukuda criteria were less severely affected patients which leads to an increase in clinical heterogeneity. Addition of certain symptoms and removal of others would strengthen the ability to select CFS patients.</p>
De Toni T, Calvillo M.	Istituto G. Gaslini, Dipartimento di Pediatria, Centro di Adolescentologia, Universita degli Studi, Genova, Italy.	[Adolescents and the problem of a chronic disease] [Article in Italian]	Minerva Pediatr. 2001 Oct;53(5):383-9.	
De Vries M, Soetekouw PM, Van Der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Medical Centre St Radboud, Nijmegen, The Netherlands.	Natural course of symptoms in Cambodia veterans: a follow-up study.	Psychol Med. 2001 Feb;31(2):331-8.	<p>BACKGROUND: Dutch (ex-)servicemen were deployed in the 1992-3-peace operation UNTAC in Cambodia. Since their return, they have voiced concerns about the health consequences of their service and they have reported symptoms such as fatigue and cognitive problems. The natural course of symptoms in Dutch Cambodia veterans was evaluated in a prospective study. METHODS: At 18-months follow-up, a questionnaire was sent to 354 veterans who met a set case definition for symptoms in Cambodia veterans or who had sub-threshold scores. Initial measurement of fatigue severity, psychological well-being, depression, post-traumatic stress disorder, trait-anxiety, self-efficacy and causal attributions, was used to evaluate predictors for self-reported improvement and low levels of fatigue at follow-up. RESULTS: At follow-up, 19% of the respondents reported complete recovery, 20% felt much better, 57% had the same complaints and 4% had become worse compared with their initial assessment. Self-reported improvement and less severe fatigue at follow-up were predicted by less severe fatigue at initial assessment and more perceived control over symptoms. CONCLUSIONS: Self-reported improvement was reported in a considerable percentage of Cambodia veterans, whereas another substantial percentage of Cambodia veterans continued to suffer with severe levels of fatigue and related symptoms. Predictors of improvement in Cambodia veterans and patients with chronic fatigue syndrome show similarities and also seem to bear importance for Gulf War veterans.</p>
Deale A, Husain K, Chalder T, Wessely S.	Academic Department of Psychological Medicine, Guy's, King's, and St. Thomas's School of Medicine, London, UK. a.deale@iop.kcl.ac.uk	Long-term outcome of cognitive behavior therapy versus relaxation therapy for chronic fatigue syndrome: a 5-year follow-up study.	Am J Psychiatry. 2001 Dec;158(12):2038-42.	<p>OBJECTIVE: This study evaluated the long-term outcome of cognitive behavior therapy versus relaxation therapy for patients with chronic fatigue syndrome. METHOD: Sixty patients who participated in a randomized controlled trial of cognitive behavior therapy versus relaxation therapy for chronic fatigue syndrome were invited to complete self-rated measures and participate in a 5-year follow-up interview with an assessor who was blind to treatment type. RESULTS: Fifty-three patients (88%) participated in the follow-up study: 25 received cognitive behavior therapy and 28 received relaxation therapy. A total of 68% of the patients who received cognitive behavior therapy and 36% who received relaxation therapy rated themselves as "much improved" or "very much improved" at the 5-year follow-up. Significantly more patients receiving cognitive behavior therapy, in relation to those in relaxation therapy, met criteria for complete recovery, were free of relapse, and experienced symptoms that had steadily improved or were consistently mild or absent since treatment ended. Similar proportions were employed, but patients in the cognitive behavior therapy group worked significantly more mean hours per week. Few patients crossed the threshold for "normal" fatigue, despite achieving a good outcome on other measures. Cognitive behavior therapy was positively evaluated and was still used by over 80% of the patients. CONCLUSIONS: Cognitive behavior therapy for chronic fatigue syndrome can produce some lasting benefits but is not a cure. Once therapy ends, some patients have difficulty making further improvements. In the future, attention should be directed toward ensuring that gains are maintained and extended after regular treatment ends.</p>
Deale A, Wessely S.	Academic Department of	Patients' perceptions of	Soc Sci Med. 2001	This study investigated perceptions of medical care among patients with chronic fatigue syndrome (CFS) referred

	Psychological Medicine, Guy's, King's and St Thomas's School of Medicine, Kings College, University of London, UK. alicia.deale@kcl.ac.uk	medical care in chronic fatigue syndrome.	Jun;52(12):1859-64.	to a specialist clinic. Sixty-eight patients completed a questionnaire survey on their overall satisfaction with medical care received since the onset of their illness, and their views on specific aspects of care. Two-thirds of patients were dissatisfied with the quality of medical care received. Dissatisfied patients were significantly more likely to describe delay, dispute or confusion over diagnosis; to have received and rejected a psychiatric diagnosis; to perceive doctors as dismissive, skeptical or not knowledgeable about CFS and to feel that the advice given was inadequate or conflicting. Satisfied patients were significantly more likely to perceive doctors as caring, supportive and interested in their illness; to state that they did not expect their doctors to cure CFS and to perceive their GP or hospital doctor as the source of greatest help during their illness. Many patients were critical of the paucity of treatment, but this was not associated with overall satisfaction. The findings suggest that medical care was evaluated less on the ability of doctors to treat CFS, and more on their interpersonal and informational skills. Dissatisfaction with these factors is likely to impede the development of a therapeutic doctor-patient alliance, which is central to the effective management of CFS. The findings suggest a need for better communication and better education of doctors in the diagnosis and management of CFS.
Dendy C, Cooper M, Sharpe M.	Isis Education Centre, Warneford Hospital, Oxford, UK.	Interpretation of symptoms in chronic fatigue syndrome.	Behav Res Ther. 2001 Nov;39(11):1369-80.	Chronic fatigue syndrome (CFS) is an illness characterised by fatigue and other symptoms. Both psychological and biological aetiological factors have been proposed, but the disorder is of uncertain origin. The aetiology of the symptoms is therefore ambiguous. It has been suggested (a) that patients with CFS tend to interpret their symptoms as indicating physical illness and (b) they tend not to interpret these symptoms in terms of negative emotion. In order to test these hypotheses we developed a self-report questionnaire to assess the interpretation of symptoms in patients with CFS. It was administered to patients with CFS, patients with depression, patients with multiple sclerosis (MS), and normal controls. Preliminary results suggest that the measure has acceptable psychometric properties. Patients with CFS were more likely than either depressed patients or normal controls to interpret symptoms (characteristic of CFS) in terms of physical illness, but did not differ in this from the MS patients. When compared with all three other groups (including the MS patients), the patients with CFS were least likely to interpret symptoms in terms of negative emotional states. The theoretical and clinical implications of the findings are discussed.
DiClementi JD, Schmalig KB, Jones JF.	Department of Psychology, University of Colorado at Denver, Denver, CO, USA. diclemej@ipfw.edu	Information processing in chronic fatigue syndrome: a preliminary investigation of suggestibility.	J Psychosom Res. 2001 Nov;51(5):679-86.	This study examines the effects of certain types of information processing on the subjective experience of cognitive deficits in persons with chronic fatigue syndrome (CFS). Two groups of participants, persons with CFS and a group of healthy controls, were administered a symptom inventory and measures of intellectual functioning, memory, automatic processing, and suggestibility. The groups differed significantly on number and severity of reported symptoms and on measures of global suggestibility and automatic processing, but not on measures of intellectual functioning and memory. Suggestibility was related to number and severity of reported symptoms, as well as the inability to inhibit the automatic processing of information. Implications of these findings are discussed, as well as directions for future research and treatment of symptoms associated with CFS.
Dinan TG, Scott LV, Thakore J, Naesdal J, Keeling PW.	Department of Pharmacology and Therapeutics, University College Cork, The Cork Clinic, Western Road, Cork, Ireland. tdinan@indigo.ie	Impact of cortisol on buspirone stimulated prolactin release: a double-blind placebo-controlled study.	Psychoneuroendocrinology. 2001 Oct;26(7):751-6.	Buspirone is known to stimulate prolactin release. Clinical studies (e.g. in chronic fatigue syndrome) suggest that the response may be influenced by baseline cortisol levels. We conducted a double-blind placebo-controlled study to examine the relationship between the prolactin response to buspirone challenge and baseline cortisol level. Fifty healthy volunteers took part in the study. Buspirone was found to consistently elevate PRL levels above those seen following placebo administration. The PRL response as measured by area under the curve was highly correlated with the baseline cortisol level.
Dobbs BM, Dobbs AR, Kiss I.	Department of Psychology, University of Alberta, Edmonton, Canada. bdobbs@ualberta.ca	Working memory deficits associated with chronic fatigue syndrome.	J Int Neuropsychol Soc. 2001 Mar;7(3):285-93.	Cognitive impairments are among the most frequently reported and least investigated components of the chronic fatigue syndrome (CFS). As part of a multifaceted study of the CFS, the present study investigated the cognitive functioning of chronic fatigue patients. The performance of 20 CFS patients was compared to that of controls (N = 20) on 4 tests of working memory (WM). Digit Span Forward was used to assess the storage capacity of WM. Multiple aspects of central executive functioning were assessed using several standard measures: Digit Span Backward, and Trails A and Trails B. More recently developed measures of WM were used to assess control of processing under temporal demands (working memory task) and resistance to interference (a sustained attention task). Deficits were restricted to more demanding tasks, requiring resistance to interference and efficient switching between processing routines. The overall results clearly implicate deficits in the control aspects of central executive function in CFS.
Edwards R, Suresh R, Lynch S, Clarkson P.	Division of Psychiatry and Behavioural Sciences,	Illness perceptions and mood in chronic fatigue	J Psychosom Res. 2001 Feb;50(2):65-8.	BACKGROUND: Individual beliefs and cognitions may affect adjustment to chronic fatigue syndrome (CFS) and illness perceptions, in particular, have been reported to correlate with both disability and psychological adjustment

Stanley P.	University of Leeds, LS9 7TF, Leeds, UK.	syndrome.		to CFS in self-diagnosed cases. OBJECTIVES: The aim of the present study was to examine these relationships in a clinic sample of CFS patients assessed by both a physician and psychiatrist. METHOD: A sample of 173 patients referred to a multidisciplinary CFS clinic and fulfilling current operational criteria for CFS [Ann Intern Med 121 (1994) 953; J R Soc Med 84 (1991) 118.] were randomly selected from the clinic database and surveyed with the Hospital Anxiety and Depression scale, Fatigue Questionnaire and Illness Perceptions Questionnaire [J Psychosom Res 37 (1993) 147; Psychol Health 11 (1996) 431; Acta Psychiatr Scand 67 (1983) 361.]. RESULTS: A total of 126 patients responded (73% response rate). The illness perception components studied were consequences (of illness), illness identity, causes (of illness), the ability to control/cure the illness and (expected) timeline of the illness. These components accounted for 15%, 28% and 30% of the variance in levels of fatigue, depression and anxiety, respectively. Two of the illness perception components (consequences and illness identity) were stronger predictors of fatigue score than mood scores. CONCLUSIONS: These findings confirmed in a clinical sample that illness perceptions are associated with variation in both disability and psychological adjustment in CFS. Illness perceptions may have an important and long-lasting effect on adaptation to CFS, and it is necessary to have a greater understanding of their role in order to tailor effective interventions for the condition.
Ehlert U, Gaab J, Heinrichs M.	Department of Clinical Psychology, University of Zurich, Zurichbergstrasse 43, CH-8044, Zurich, Switzerland. ehlertu@klipsy.unizh.ch	Psychoneuroendocrinological contributions to the etiology of depression, posttraumatic stress disorder, and stress-related bodily disorders: the role of the hypothalamus-pituitary-adrenal axis.	Biol Psychol. 2001 Jul-Aug;57(1-3):141-52.	Following the assumption that stressors play an important part in the etiology and maintenance of psychiatric disorders, it is necessary to evaluate parameters reflecting stress-related physiological reactions. Results from these examinations may help to deepen the insight into the etiology of psychiatric disorders and to elucidate diagnostic uncertainties. One of the best-known stress-related endocrine reactions is the hormonal release of the hypothalamic-pituitary-adrenal (HPA) axis. Dysregulations of this axis are associated with several psychiatric disorders. Profound hyperactivity of the HPA-axis has been found in melancholic depression, alcoholism, and eating disorders. In contrast, posttraumatic stress disorder, stress-related bodily disorders like idiopathic pain syndromes, and chronic fatigue syndrome seem to be associated with diminished HPA activity (lowered activity of the adrenal gland). Hypotheses referring to (a) the psychophysiological meaning and (b) the development of these alterations are discussed.
Englebienne P, Herst CV, Smet K, D'Haese A, De Meirleir K.		Interactions Between RNase L Ankyrin-Like Domain and ABC Transporters as a Possible Origin for Pain, Ion Transport, CNS and Immune Disorders of Chronic Fatigue Immune Dysfunction Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 83	Low molecular weight (LMW) ribonuclease L (RNase L) forms have been identified in peripheral blood mononuclear cells (PBMC) of patients with chronic fatigue immune dysfunction syndrome (CFIDS). Data from our laboratory indicate that these LMW RNase L proteins are produced by proteolytic cleavage of the native monomeric enzyme and we have identified calpain as one of the possible proteases involved. Using human recombinant RNase L (r-hRNase L) His-tagged at the N-terminus, we show here at the one hand that both calpain and PBMC extracts from CFIDS patients cleave the protein in fragments of identical sizes containing ankyrin-like repeat sequences. At the other hand, the activity of RNase L is modulated by its interaction with a specific inhibitor (RLI), a member of the ATP binding cassette (ABC) superfamily. RLI interacts with the ankyrin domain of RNase L, which results in a blockade of the 2N,5N-oligoadenylate (2-5A)-binding site of the enzyme. We show that RLI contains a small ankyrin-interacting peptide cluster through which it interacts with the first two ?-hairpin coils of the RNase L ankyrin domain. A similarity search performed at the NCBI using RLI aminoacid sequence as the entry allowed to identify several other ABC transporter proteins sharing significant identities with RLI, including the ankyrin-interacting peptide. Taken together, these results show that upon pathological cleavage of RNase L, fragments containing the ankyrin domain are released, which could be capable of interacting with selected members of the human ABC superfamily, preventing their interaction with the normal cognate ankyrin protein and hence impairing their proper cellular function. This interaction constitutes a common physiological mechanism explaining numerous and currently unexplained symptoms experienced by patients with CFIDS, which are otherwise totally unrelated.
Estroff SE.	Department of Social Medicine, University of North Carolina at Chapel Hill, USA.	Transformations and reformulations: chronicity and identity in politics, policy, and phenomenology.	Med Anthropol. 2001;19(4):411-3. Comment on: Med Anthropol. 2001;19(4):299-317	
Ferguson E, Cassaday HJ.	School of Psychology, University of Nottingham, Nottingham, NG7 2RD, UK. eamonn.ferguson@nottingh	Theoretical accounts of Gulf War Syndrome: from environmental toxins to psychoneuroimmunology and neurodegeneration.	Behav Neurol. 2001-2002;13(3-4):133-47.	Non-specific illness includes a wide variety of symptoms: behavioural (e.g., reduced food and water intake), cognitive (e.g., memory and concentration problems) and physiological (e.g., fever). This paper reviews evidence suggesting that such symptoms can be explained more parsimoniously as a single symptom cluster than as a set of separate illnesses such as Gulf War Syndrome (GWS) and chronic fatigue syndrome (CFS). This superordinate syndrome could have its biological basis in the activity of pro-inflammatory cytokines (in particular interleukin-1:

	am.ac.uk			IL-1), that give rise to what has become known as the 'sickness response'. It is further argued that the persistence of non-specific illness in chronic conditions like GWS may be (in part) attributable to a bio-associative mechanism (Ferguson and Cassaday, 1999). In the case of GWS, physiological challenges could have produced a non-specific sickness response that became associated with smells (e.g., petrol), coincidentally experienced in the Persian Gulf. On returning to the home environment, these same smells would act as associative triggers for the maintenance of (conditioned) sickness responses. Such associative mechanisms could be mediated through the hypothalamus and limbic system via vagal nerve innervation and would provide an explanation for the persistence of a set of symptoms (e.g., fever) that should normally be short lived and self-limiting. We also present evidence that the pattern of symptoms produced by the pro-inflammatory cytokines reflects a shift in immune system functioning towards a (T-helper-1) Th1 profile. This position contrasts with other immunological accounts of GWS that suggest that the immune system demonstrates a shift to a Th2 (allergy) profile. Evidence pertaining to these two contrasting positions is reviewed.
Ferrada-Noli M.	Folkhälsovetenskap med inriktning mot epidemiologi, Hogskolan i Gavle. mferrada-noli@hms.harvard.edu	[Occupational stress, suicide and fatigue depression] [Article in Swedish]	Lakartidningen. 2001 Jun 27;98(26-27):3158-60.	
Fiedler N, Kipen HM.	UMDNJ-Robert Wood Johnson Medical School, Environmental and Occupational Health Sciences Institute, Piscataway, New Jersey 08854, USA. nfiedler@eoysi.rutgers.edu	Controlled exposures to volatile organic compounds in sensitive groups.	Ann N Y Acad Sci. 2001 Mar;933:24-37.	Sensitivities to chemicals are characterized by symptoms in multiple organ systems in response to low-level chemical exposures. This paper reviews studies of controlled exposures to odorants and to mixtures of volatile organic compounds. Sensitive subgroups include subjects who met Cullen's 1987 criteria for multiple chemical sensitivity (MCS), Gulf War veterans with chronic fatigue syndrome and chemical sensitivity (CFS/CS), and subjects with specific self-reported sensitivities to methyl tertbutyl ether (MTBE) in gasoline (MTBE-sensitive). All studies include comparison of age- and sex-matched healthy controls. Studies of olfaction did not support unusual sensitivity, defined as lower odor thresholds, among MCS subjects; however, a dose-response pattern of symptoms was observed in response to suprathreshold concentrations of phenyl ethyl alcohol. In blinded, controlled exposures to clean air, gasoline, gasoline/11% MTBE, and gasoline/15% MTBE, a threshold effect was observed with MTBE-sensitive subjects reporting significantly increased symptoms to gasoline/15% MTBE exposure. Autonomic arousal (heart and respiration rate; end-tidal CO ₂) in response to odor of chemical mixtures may mediate symptoms for subjects with generalized chemical sensitivities, but not for those whose sensitivities are confined to specific chemicals. For example, Gulf War veterans with CFS/CS experienced reduced end-tidal CO ₂ when exposed to diesel fumes, while exposure to MTBE did not produce any psychophysiological changes in MTBE-sensitive subjects. Controlled olfactory and exposure studies reveal that significant responses can be observed in chemically sensitive subjects even when de-adaptation has not occurred. However, these studies suggest that symptoms are not necessarily accompanied by changes in physiologic arousal. Subject characteristics play a critical role in outcomes.
Forton DM, Allsop JM, Main J, Foster GR, Thomas HC, Taylor-Robinson SD.		Evidence for a cerebral effect of the hepatitis C virus.	Lancet. 2001 Jul 7;358(9275):38-9.	Patients with hepatitis C virus (HCV) infection frequently complain of symptoms akin to the chronic fatigue syndrome and score worse on health-related quality of life indices than matched controls. We address the hypothesis that HCV itself affects cerebral function. Using proton magnetic-resonance spectroscopy we have shown elevations in basal ganglia and white matter choline/creatine ratios in patients with histologically-mild hepatitis C, compared with healthy volunteers and patients with hepatitis B. This elevation is unrelated to hepatic encephalopathy or a history of intravenous drug abuse, and suggests that a biological process underlies the extrahepatic symptoms in chronic HCV infection.
Francis C.		Take ME seriously.	Nurs Stand. 2001 Jan 10-16;15(17):22.	
Frankish H.		Some evidence cognitive therapy and exercise benefit chronic fatigue.	Lancet. 2001 Sep 22;358(9286):989.	
Friedberg F, Jason LA.	Department of Psychiatry and Behavioral Science, State University of New York at Stony Brook, USA. ffriedbe@ct1.nai.net	Chronic fatigue syndrome and fibromyalgia: clinical assessment and treatment.	J Clin Psychol. 2001 Apr;57(4):433-55.	Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are closely related illnesses of uncertain etiology. This article reviews the research literature on these biobehavioral conditions, with an emphasis on explanatory models, clinical evaluation of comorbid psychiatric disorders, assessment of stress factors, pharmacologic and alternative therapies, and cognitive-behavioral treatment studies. Furthermore, clinical protocols suitable for professional practice are presented based on an integration of the authors' clinical observations with published data. The article

				concludes with the recognition that mental health professionals can offer substantial help to these patients. Copyright 2001 John Wiley & Sons, Inc.
Friedman TC, Echeverry D, Poland RE.		Orthostatic hypotension and chronic fatigue syndrome.	JAMA. 2001 Mar 21;285(11):1442; author reply 1443. Comment on: JAMA. 1995 Sep 27;274(12):961-7. JAMA. 2001 Jan 3;285(1):52-9.	
Fuentes K, Hunter MA, Strauss E, Hultsch DF.	Department of Psychology, University of Victoria, Victoria, BC, Canada. kfuentes@uvic.ca	Intraindividual variability in cognitive performance in persons with chronic fatigue syndrome.	Clin Neuropsychol. 2001 May;15(2):210-27.	Studies of cognitive performance among persons with chronic fatigue syndrome (CFS) have yielded inconsistent results. We sought to contribute to findings in this area by examining intraindividual variability as well as level of performance in cognitive functioning. A battery of cognitive measures was administered to 14 CFS patients and 16 healthy individuals on 10 weekly occasions. Analyses comparing the two groups in terms of level of performance defined by latency and accuracy scores revealed that the CFS patients were slower but not less accurate than healthy persons. The CFS group showed greater intraindividual variability (as measured by intraindividual standard deviations and coefficients of variation) than the healthy group, although the results varied by task and time frame. Intraindividual variability was found to be stable across time and correlated across tasks at each testing occasion. Intraindividual variability also uniquely differentiated the groups. The present findings support the proposition that intraindividual variability is a meaningful indicator of cognitive functioning in CFS patients.
Gantz NM, Coldsmith EE.	Division of Infectious Diseases, Department of Medicine, Pinnacle Health System, Harrisburg, PA 17110, USA. ngantz@pinnaclehealth.org [corrected]	Chronic fatigue syndrome and fibromyalgia resources on the world wide web: a descriptive journey.	Clin Infect Dis. 2001 Mar 15;32(6):938-48. Epub 2001 Mar 09.	A wealth of information on chronic fatigue syndrome (CFS) and fibromyalgia is available on the World Wide Web for health care providers and patients. These illnesses have overlapping features, and their etiologies remain unknown. Multiple Web sites were reviewed, and selected sites providing useful information were identified. Sites were classified according to their content and target audience and were judged according to suggested standards of Internet publishing. Fifty-eight sites were classified into groups as follows: comprehensive and research Web sites for CFS and fibromyalgia, meetings, clinical trials, literature search services, bibliographies, journal, and CFS and fibromyalgia Web sites for the patient.
Garland EM, Robertson D.	Autonomic Dysfunction Center, Department of Medicine, Vanderbilt University, Nashville, Tennessee, USA.	Chiari I malformation as a cause of orthostatic intolerance symptoms: a media myth?	Am J Med. 2001 Nov;111(7):546-52.	There is much interest in a putative relationship between Chiari I malformation and symptoms of orthostatic intolerance. It has been reported at scientific meetings that a number of patients with chronic fatigue syndrome or fibromyalgia have Chiari I malformation, or hindbrain compression in the absence of Chiari, and that they experience improvement after decompression surgery. Many of these patients have symptoms of orthostatic intolerance. A connection between Chiari I malformation and these conditions has been discussed in newspaper articles and on national television programs. Patients have also had access to much information on this topic via the Internet. Unfortunately, the Chiari I malformation and orthostatic intolerance connection is almost entirely unsupported by peer-reviewed literature. The purpose of this article is to provide an objective review of the available information.
Garralda ME, Rangel L.		Childhood chronic fatigue syndrome.	Am J Psychiatry. 2001 Jul;158(7):1161.	
Gartner BC, Fischinger JM, Roemer K, Mak M, Fleurent B, Mueller-Lantsch N.	Department of Virology, University of Homburg/Saar, Kirrbergerstr. Haus 47, D-66421 Homburg Saar, Germany.	Evaluation of a recombinant line blot for diagnosis of Epstein-Barr Virus compared with ELISA, using immunofluorescence as reference method.	J Virol Methods. 2001 Apr;93(1-2):89-96.	A commercial line blot using recombinant antigens was compared with a commercial ELISA and 'in-house' IFA (reference test). Two panels were evaluated: Panel A was selected to distinguish between primary infections (89), past infections (20) and seronegatives (8) in immunocompetent individuals. In panel B, patients with a high number of reactivations were included: immunosuppressed patients (37), lymphoma (19), nasopharyngeal carcinoma (10), chronic fatigue syndrome (14). Blood donors (43) and cross-reactive sera (29) were added as controls. Line blot and IFA were concordant in 94% of primary infections, 100% of seronegatives and 100% of past infections, similar to ELISA. Results differed significantly with regard to reactivations. When compared with IFA, the incidence of reactivations was overestimated by the blot, 24 and 58% in blood donors and cross-reactive sera, respectively. ELISA showed a similar problems with 21 and 34% indeterminate results, respectively. The line blot is easy to carry out, has a good concordance with the reference IFA for primary infections, and is, therefore, a sufficient choice for distinguishing primary infection from seronegative and past infection. EBV reactivation assessment will require other methods such as EBV viral load.
Gilhooly PE, Ottenweller JE, Lange G, Tiersky L, Natelson BH.	Veterans Administration, New Jersey Health Care System, 385 Tremont	Chronic fatigue and sexual dysfunction in female Gulf War veterans.	J Sex Marital Ther. 2001 Oct-Dec;27(5):483-7.	Chronic fatigue (CF) is one of the most common conditions reported by Gulf War veterans. This study evaluated female sexual dysfunction (FSD) in veterans with or without complaints of CF. Subjects were screened for medical and psychiatric causes of CF. They included 22 healthy subjects and 26 with fatiguing symptoms. FSD was

	Avenue, East Orange, NJ 07018, USA. PEGMD6@aol.com			reported by 10% of controls and by 60% of the fatigued ($p < .002$) while 19% versus 81% ($p < .001$) noted decreased libido. FSD was more prevalent in fatigued veterans than in the controls. This relationship was not mediated by an Axis I diagnosis. This appears to be the first report of sexual dysfunction in CF.
Gorman D, Monigatti J, Glass B, Gronwall D, Beasley M.	University of Auckland, New Zealand. d.gorman@auckland.ac.nz	Assessment of pentachlorophenol-exposed timber workers using a test-of-poisoning model.	Int J Occup Environ Health. 2001 Jul-Sep;7(3):189-94.	Sixty-two former New Zealand timber workers who were exposed to pentachlorophenol (PCP) at work were interviewed, examined, and assessed both by laboratory investigations and psychometrically for clinical syndromes that could be related to PCP exposure. Three such syndromes were identified: an acute complex of fever, headaches, upper and lower respiratory tract and eye irritation, skin disease, and foul smelling and discolored sweat; a chronic fatigue syndrome, beginning while still at work and frequently persisting; and a delayed encephalopathy. Neither of the sustained syndromes was considered characteristic of PCP poisoning, and many confounders were identified. An exposure index and a test-of-poisoning score had a statistically insignificant correlation.
Goudsmit E.		Response to Renckens.	J Psychosom Obstet Gynaecol. 2001 Mar;22(1):61-3. Comment on: J Psychosom Obstet Gynaecol. 2000 Dec;21(4):235-9.	
Goudsmit EM.		Measuring the quality of trials of treatments for chronic fatigue syndrome.	JAMA. 2001 Dec 26;286(24):3078-9. Comment on: JAMA. 2001 Sep 19;286(11):1360-8 Erratum in: JAMA 2002 Mar 20;287(11):1401.	
Gow JW, Simpson K, Behan PO, Chaudhuri A, McKay IC, Behan WM.	Department of Neurology, University of Glasgow, Scotland, United Kingdom.	Antiviral pathway activation in patients with chronic fatigue syndrome and acute infection.	Clin Infect Dis. 2001 Dec 15;33(12):2080-1. Epub 2001 Nov 06. Comment in: Clin Infect Dis. 2002 May 15;34(10):1420-1; discussion 1421-2.	Gene expression of key enzymes in 2 antiviral pathways (ribonuclease latent [RNase L] and RNA-regulated protein kinase [PKR]) was compared in 22 patients with chronic fatigue syndrome (CFS), 10 patients with acute gastroenteritis, and 21 healthy volunteers. Pathway activation in the group of patients with infections differed significantly from that of the other 2 groups, in whom there was no evidence of upregulation. Therefore, assay of activation is unlikely to provide the basis for a diagnostic test for CFS.
Gray D, Parker-Cohen NY, White T, Clark ST, Seiner SH, Achilles J, McMahon WM.	Department of Psychiatry, University of Utah, Salt Lake City 84108, USA. Douglas.gray@hsc.utah.edu	A comparison of individual and family psychology of adolescents with chronic fatigue syndrome, rheumatoid arthritis, and mood disorders.	J Dev Behav Pediatr. 2001 Aug;22(4):234-42.	Chronic fatigue syndrome (CFS) is a controversial diagnosis with unknown cause. Adult studies indicate high rates of psychosocial dysfunction and psychiatric comorbidity. The authors compared three groups of pediatric patients selected by diagnosis—(1) CFS ($n = 15$), (2) juvenile rheumatoid arthritis ($n = 15$), and (3) mood disorders ($n = 15$)—across many psychological measures. CFS subjects had dramatic elevation of the Somatic Complaints subscale (mean T score = 75), whereas the mood disorders group had higher externalizing scores (mean T score = 68) on the Child Behavior Checklist. The CFS subjects missed significantly more school compared with the two control groups. After the onset of CFS, 13 of 15 of the CFS patients required significant educational accommodation. Only 4 of the 15 CFS patients had an Axis I psychiatric diagnosis, as determined by the Computerized Diagnostic Interview for Children. Despite a low rate of psychiatric diagnosis in the CFS sample, these data attest to their psychosocial and school dysfunction.
Grossman ER.		Does myalgic encephalomyelitis exist?	Lancet. 2001 Jun 9;357(9271):1889-90. Comment on: Lancet. 2001 Feb 17;357(9255):562.	
Grubb BP, Kanjwal MY, Kosinski DJ.	Electrophysiology Section, Division of Cardiology, Department of Medicine, The Medical College of Ohio, Toledo OH 43614-2598, USA. bgrubb@mco.edu	Review: The postural orthostatic tachycardia syndrome: current concepts in pathophysiology diagnosis and management.	J Interv Card Electrophysiol. 2001 Mar;5(1):9-16.	
Hamilos DL, Nutter D,	Washington University	Circadian rhythm of core	Clin Physiol. 2001	The pathophysiological basis for chronic fatigue syndrome (CFS) remains poorly understood. Certain symptoms of

<p>Gershtenson J, Ikle D, Hamilos SS, Redmond DP, Di Clementi JD, Schmaling KB, Jones JF.</p>	<p>School of Medicine, Division of Allergy and Immunology, Euclid Avenue, St Louis, Missouri, USA. dhamilos@im.wustl.edu</p>	<p>body temperature in subjects with chronic fatigue syndrome.</p>	<p>Mar;21(2):184-95.</p>	<p>CFS, namely fatigue, neurocognitive symptoms and sleep disturbance, are similar to those of acute jet lag and shift work syndromes thus raising the possibility that CFS might be a condition associated with disturbances in endogenous circadian rhythms. In this study, we tested this hypothesis by examining the circadian rhythm of core body temperature (CBT) in CFS and control subjects. Continuous recordings of CBT were obtained every 5 min over 48 h in a group of 10 subjects who met the Center for Disease Control (CDC) definition of CFS and 10 normal control subjects. Subjects in the two groups were age, sex and weight-matched and were known to have normal basal metabolic rates and thyroid function. CBT recordings were performed under ambulatory conditions in a clinical research centre with the use of an ingestible radio frequency transmitter pill and a belt-worn receiver-logger. CBT time series were analysed by a cosinor analysis and by a harmonic-regression-plus-correlated-noise model to estimate the mean, amplitude and phase angle of the rhythm. The goodness of fit of each model was also compared using the Akaike Information Criterion (AIC) and sigma2. Average parameters for each group were compared by Student's t-test. By cosinor analysis, the only significant difference between CFS and control groups was in the phase angle of the third harmonic (P=0.02). The optimal harmonic-regression-plus-correlated-noise models selected were ARMA(1,1): control 7, CFS 6; ARMA(2,0): control 1, CFS 4; and ARMA(2,1): control 2 subjects. The optimal fit ARMA model contained two harmonics in eight of 10 control subjects but was more variable in the CFS subjects (1 harmonic: 5 subjects; 2 harmonics: 1 subject; 3 harmonics: 4 subjects). The goodness of fit measures for the optimal ARMA model were also better in the control than the CFS group, but the differences were not statistically significant. We conclude that, measured under ambulatory conditions, the circadian rhythm of CBT in CFS is nearly indistinguishable from that of normal control subjects although there was a tendency for greater variability in the rhythm. Hence, it is unlikely that the symptoms of CFS are because of disturbance in the circadian rhythm of CBT.</p>
<p>Hamilton W..</p>	<p>Chronic fatigue syndrome</p>		<p>Br J Gen Pract. 2001 Dec;51(473):1015. Comment on: Br J Gen Pract. 2001 Jul;51(468):553-8. Br J Gen Pract. 2001 Sep;51(470):758.</p>	
<p>Hamilton WT, Hall GH, Round AP.</p>	<p>North and East Devon Health Authority, Exeter. w.hamilton@cwcom.net</p>	<p>Frequency of attendance in general practice and symptoms before development of chronic fatigue syndrome: a case-control study.</p>	<p>Br J Gen Pract. 2001 Jul;51(468):553-8. Comment in: Br J Gen Pract. 2001 Dec;51(473):1015. Br J Gen Pract. 2001 Sep;51(470):758.</p>	<p>BACKGROUND: Chronic fatigue syndrome (CFS) research has concentrated on infective, immunological, and psychological causes. Illness behaviour has received less attention, with most research studying CFS patients after diagnosis. Our previous study on the records of an insurance company showed a highly significant increase in illness reporting before development of CFS. AIM: To investigate the number and type of general practitioner (GP) consultations by patients with CFS for 15 years before they develop their condition. DESIGN OF STUDY: Case-control study in 11 general practices in Devon. SETTING: Forty-nine patients with CFS (satisfying the Centers for Disease Control criteria), 49 age, sex, and general practice matched controls, and 37 patients with multiple sclerosis (MS) were identified from the general practices' computerised databases. METHOD: The number of general practice consultations and symptoms recorded in three five-year periods (quinquennia) were counted before development of the patients' condition. RESULTS: The median number of consultations was significantly higher for CFS patients than that of matched controls in each of the quinquennia: ratios for first quinquennium = 1.88, P = 0.01; second quinquennium = 1.70, P = 0.005; last quinquennium = 2.25, P < 0.001. More CFS patients than controls attended for 13 of the 18 symptoms studied. Significant increases were found for upper respiratory tract infection (P < 0.001), lethargy (P < 0.001), and vertigo (P = 0.02). Similar results were found for CFS patients when compared with MS. CONCLUSIONS: CFS patients consulted their GP more frequently in the 15 years before development of their condition, for a wide variety of complaints. Several possibilities may explain these findings. The results support the hypothesis that behavioural factors have a role in the aetiology of CFS.</p>
<p>Hammond DC.</p>	<p>Department of Physical Medicine & Rehabilitation, University of Utah School of Medicine, Salt Lake City, UT, USA. D.C.Hammond@m.cc.utah.edu</p>	<p>Treatment of chronic fatigue with neurofeedback and self-hypnosis.</p>	<p>NeuroRehabilitation. 2001;16(4):295-300.</p>	<p>A 21 year old patient reported a relatively rapid onset of serious chronic fatigue syndrome (CFS), with her worst symptoms being cognitive impairments. Congruent with research on rapid onset CFS, she had no psychiatric history and specialized testing did not suggest that somatization was likely. Neuroimaging and EEG research has documented brain dysfunction in cases of CFS. Therefore, a quantitative EEG was done, comparing her to a normative data base. This revealed excessive left frontal theta brainwave activity in an area previously implicated in SPECT research. Therefore, a novel treatment approach was utilized consisting of a combination of EEG neurofeedback and self-hypnosis training, both of which seemed very beneficial. She experienced considerable</p>

				improvement in fatigue, vigor, and confusion as measured pre-post with the Profile of Mood States and through collaborative interviews with both parents. Most of the changes were maintained at 5, 7, and 9 month follow-up testing.
Hanson SJ, Gause W, Natelson B.	Department of Psychology, Rutgers University, Newark, New Jersey 07102, USA. jose@kreizler.rutgers.edu	Detection of immunologically significant factors for chronic fatigue syndrome using neural-network classifiers.	Clin Diagn Lab Immunol. 2001 May;8(3):658-62.	Neural-network classifiers were used to detect immunological differences in groups of chronic fatigue syndrome (CFS) patients that heretofore had not shown significant differences from controls. In the past linear methods were unable to detect differences between CFS groups and non-CFS control groups in the nonveteran population. An examination of the cluster structure for 29 immunological factors revealed a complex, nonlinear decision surface. Multilayer neural networks showed an over 16% improvement in an n-fold resampling generalization test on unseen data. A sensitivity analysis of the network found differences between groups that are consistent with the hypothesis that CFS symptoms are a consequence of immune system dysregulation. Corresponding decreases in the CD19(+) B-cell compartment and the CD34(+) hematopoietic progenitor subpopulation were also detected by the neural network, consistent with the T-cell expansion. Of significant interest was the fact that, of all the cytokines evaluated, the only one to be in the final model was interleukin-4 (IL-4). Seeing an increase in IL-4 suggests a shift to a type 2 cytokine pattern. Such a shift has been hypothesized, but until now convincing evidence to support that hypothesis has been lacking.
Hardt J, Buchwald D, Wilks D, Sharpe M, Nix WA, Egle UT.	Department of Psychosomatic Medicine and Psychotherapy, University of Mainz, Untere Zahlbacher 8, D-55101, Mainz, Germany. hardt@mail.uni-mainz.de	Health-related quality of life in patients with chronic fatigue syndrome: an international study.	J Psychosom Res. 2001 Aug;51(2):431-4.	OBJECTIVE: Chronic fatigue syndrome (CFS) has been reported worldwide. Our objectives were to determine if patients from different countries have similar profiles of impairments. METHODS: Health-related quality of life (HRQoL) was assessed in 740 CFS patients in the US, 82 in the UK, and 65 in Germany using the eight subscales of the Short-Form General Health Survey (SF-36). To examine the internal structure, factor analyses were performed. RESULTS: Overall, there was a remarkable similarity in HRQoL among all CFS patients, regardless of location. Patients scored two to three standard deviations below normal on six subscales and one standard deviation below normal on the other two subscales. Factor analysis suggested a two-factor model where the same six subscales constitute the first factor and the two others the second factor. CONCLUSION: HRQoL is poor in CFS patients from three countries. This study is a first step towards conducting further comparative cross-cultural and international studies.
Hausotter W.		[Modern illnesses from the critical viewpoint] [Article in German]	Versicherungsmedizin. 2001 Dec 1;53(4):177-81. Comment in: Versicherungsmedizin. 2002 Sep 1;54(3):149-50; discussion 150.	Psychosomatic illness as "modern diseases" are of increasing interest to the public. Environmental illnesses, for example assumed intoxication with organic solvents, multiple chemical sensitivity, sick building syndrome, chronic fatigue syndrome, fibromyalgia, the influence of amalgam or of electromagnetic waves and ozone are often causes of anxiety. There are many hypotheses about the origin of these diseases. Some scientists emphasize an organic basis; however, this is not generally accepted. Very often with good reason a psychological cause is supposed. Objective diagnostic criteria are not available, therefore these diagnoses may only be applied after sufficient exclusion of other known organic diseases. Mostly a psychological treatment is refused by the person affected, and a scientifically based somatic concept for the therapy does not exist. The medicolegal problems are important and often the reason for prolonged forensic confrontations.
Hickie IB, Bansal AS, Kirk KM, Lloyd AR, Martin NG.	School of Psychiatry, University of New South Wales, Sydney, Australia. i.hickie@unsw.edu.au	A twin study of the etiology of prolonged fatigue and immune activation.	Twin Res. 2001 Apr;4(2):94-102.	Risk factors to prolonged fatigue syndromes (PFS) are controversial. Pre-morbid and/or current psychiatric disturbance, and/or disturbed cell-mediated immunity (CMI), have been proposed as etiologic factors. Self-report measures of fatigue and psychologic distress and three in vitro measures of CMI were collected from 124 twin pairs. Crosstwin-crosstrait correlations were estimated for the complete monozygotic (MZ; 79 pairs) and dizygotic (DZ; 45 pairs) twin groups. Multivariate genetic and environmental models were fitted to explore the patterns of covariation between etiologic factors. For fatigue, the MZ correlation was more than double the DZ correlation (0.49 versus 0.16) indicating strong genetic control of familial aggregation. By contrast, for in vitro immune activation measures MZ and DZ correlations were similar (0.49-0.69 versus 0.42-0.53) indicating the etiologic role of shared environments. As small univariate associations were noted between prolonged fatigue and the in vitro immune measures ($r = -0.07$ to -0.12), multivariate models were fitted. 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. PFS that are associated with in vitro measures of immune activation are most likely to be the consequence of current environmental rather than genetic factors. Such environmental factors could include physical agents such as infection and/or psychological stress.
Hickie IB, Davenport TA,	School of Psychiatry,	Development of a simple	Med J Aust. 2001 Jul	OBJECTIVE: To develop and validate a self-report screening tool for common mental disorders. DESIGN AND

Hadzi-Pavlovic D, Koschera A, Naismith SL, Scott EM, Wilhelm KA.	University of New South Wales, Sydney. ian.hickie@beyondblue.org.au	screening tool for common mental disorders in general practice.	16;175 Suppl:S10-7. Comment in: Med J Aust. 2001 Jul 16;175 Suppl:S6-7	SETTING: Sequential development and validation studies in three cohorts of patients in general practice and one cohort of patients in a specialist psychiatry clinic. PARTICIPANTS: 1585 patients in general practice examined cross-sectionally and longitudinally; 46515 patients attending 386 general practitioners nationwide; 364 patients participating in a longitudinal study of psychiatric disorders in general practice; and 522 patients attending a specialist psychiatry clinic. MAIN OUTCOME MEASURES: Performance of the 12 items from the 34-item SPHERE questionnaire against DSM-III-R and DSM-IV diagnoses of psychiatric disorder, self-reported Brief Disability Questionnaire findings, GPs' ratings of patients' needs for psychological care and degree of risk resulting from mental disorder, and patients' and GPs' reports of reasons for presentation. RESULTS: Six somatic and six psychological questions identify two levels (and three types) of mental disorder: patients reporting both characteristic psychological and somatic symptoms (Level 1, Type 1), and patients reporting either psychological symptoms (Level 2, Type 2) or somatic symptoms (Level 2, Type 3). This classification system predicts disability ratings (Level 1, 8.2 "days out of role in the last month" and Level 2, 4.1 and 5.4 "days out of role in the last month" for Types 2 and 3, respectively), rates of lifetime psychiatric diagnoses (Level 1, 63% and Level 2, 59% and 48%, respectively), both patients' and GPs' report of reasons for presentation, and doctors' ratings of risk as a result of mental disorder. There are important and differing sociodemographic correlates for the three types of mental disorders. CONCLUSION: A classification system based on the 12 items from the 34-item SPHERE questionnaire can be used to identify common mental disorders. This system has acceptable validity and reliability, and is suited specifically for general practice settings.
Inbar O, Dlin R, Rotstein A, Whipp BJ.	Department of Life Sciences, Zinman College, Wingate Institute, Netania, Israel. inbar@macam98.ac.il	Physiological responses to incremental exercise in patients with chronic fatigue syndrome.	Med Sci Sports Exerc. 2001 Sep;33(9):1463-70.	PURPOSE: The purpose of this investigation was to characterize the physiological response profiles of patients with chronic fatigue syndrome (CFS), to an incremental exercise test, performed to the limit of tolerance. METHODS: Fifteen patients (12 women and three men) who fulfilled the case definition for chronic fatigue syndrome, and 15 healthy, sedentary, age- and sex-matched controls, performed an incremental progressive all-out treadmill test (cardiopulmonary exercise test). RESULTS: As a group, the CFS patients demonstrated significantly lower cardiovascular as well as ventilatory values at peak exercise, compared with the control group. At similar relative submaximal exercise levels (% peak VO(2)), the CFS patients portrayed response patterns (trending phenomenon) characterized, in most parameters, by similar intercepts, but either lower (VCO(2), HR, O(2)pulse), V(E), V(T), PETCO(2)) or higher (B(f), V(E)/VCO(2)) trending kinetics in the CFS compared with the control group. It was found that the primary exercise-related physiological difference between the CFS and the control group was their significantly lower heart rate at any equal relative and at maximal work level. Assuming maximal effort by all (indicated by RER, PETCO(2), and subjective exhaustion), these results could indicate either cardiac or peripheral insufficiency embedded in the pathology of CFS patients. CONCLUSION: We conclude that indexes from cardiopulmonary exercise testing may be used as objective discriminatory indicators for evaluation of patients complaining of chronic fatigue syndrome.
Jason LA, Eisele H, Taylor RR.	DePaul University, USA.	Assessing attitudes toward new names for chronic fatigue syndrome.	Eval Health Prof. 2001 Dec;24(4):424-35.	A questionnaire was distributed at the American Association of Chronic Fatigue Syndrome's biannual convention in Washington in January 2001 as well as through various Internet Web sites and listserves during early February and March of 2001. The sample consisted of 432 respondents. Most respondents (86%) indicated they wanted a name change, although more patients than scientists were in favor of this change. It was also apparent that the patients and physicians were clearly split between adopting a name such as myalgic encephalopathy versus one such as neuro-endocrine immune disorder. Also, among those respondents who selected either of these two choices for a new name, less than 30% of them supported the other name. Although the majority of respondents feel the name should be changed at this time, this survey suggests there are different stakeholders involved in the name-change process, each with strong and sometimes disparate feelings about changing the name.
Jason LA, Taylor RR, Carrico AW.	DePaul University, Department of Psychology, Chicago, IL 60614, USA. ljason@wppost.depaul.edu	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.	One proposed hypothesis regarding the etiology of chronic fatigue syndrome (CFS) is that there is a subgroup of patients in which symptom onset is precipitated by a viral infection. If this is indeed true, then one would anticipate a greater incidence of the emergence of CFS symptoms during months when viral infections occur with the greatest frequency. The current community-based epidemiology study examined the month of symptom onset for 31 patients with CFS and 44 others with idiopathic chronic fatigue (ICF). It was determined that the distribution of the month of illness onset for the CFS and ICF groups was nonrandom, with greater numbers of participants than expected reporting an onset of CFS and ICF during January.
Jason LA, Taylor RR, Kennedy CL, Harding ST, Song S, Johnson D,		Subtypes of Chronic Fatigue Syndrome: A Review of Findings	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 1	Most studies of Chronic Fatigue Syndrome (CFS) have been based on patients recruited from primary or tertiary care settings. Patients from such settings might not be typical of patients in the general population and may not accurately reflect the heterogeneity among individuals diagnosed with this condition. The current paper reviews

Chimata R.				four community-based studies that examined subtypes of individuals with CFS. Distinctions between subtype groups based on sociodemographics, illness onset and duration, stressful precipitating events, symptom frequency, and comorbidity characteristics are made with respect to outcome measures of fatigue and symptom severity, functional ability, and psychiatric comorbidity.
Jason LA, Taylor RR.		Measuring Attributions About Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 31	Three studies explored the effects of different diagnostic labels and different types of recommended treatments for Chronic Fatigue Syndrome upon attributions regarding its cause, nature, severity, contagion, prognosis, and treatment. Attributions for Chronic Fatigue Syndrome appear to change based upon the diagnostic label given for the syndrome and the type of treatment recommended. Results suggest that, in comparison to the Chronic Fatigue Syndrome label, the Myalgic Encephalopathy label prompts attributions that this syndrome is a serious condition associated with a physiologically-based etiology, a poor prognosis, and decreased potential for organ donation. Results also suggest that, compared with cognitive coping skills treatment, treatment with amplitgen appears to be associated with perceptions of chronic fatigue syndrome as an accurate diagnosis and as a severely disabling condition.
Jay SJ.		Orthostatic hypotension and chronic fatigue syndrome.	JAMA. 2001 Mar 21;285(11):1442-3. Comment on: JAMA. 2001 Jan 3;285(1):52-9.	
Johnson SK, Lange G, Tiersky L, DeLuca J, Natelson BH.		Health-Related Personality Variables in Chronic Fatigue Syndrome and Multiple Sclerosis	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 41	This study investigated personality variables in patients with Chronic Fatigue Syndrome (CFS) and Multiple Sclerosis (MS), with healthy, sedentary subjects as controls. CFS and MS groups were higher on alexithymia, characterized as difficulty in describing and differentiating emotions and marked externalization. CFS and MS groups reported a more depressive attributional style than healthy participants, reflecting beliefs that causes for good events are not diffused into other areas of life while causes for bad events will always be present. The CFS group was significantly lower on Doctors/Others locus of control indicating lack of trust in medical professionals. Results indicate that CFS and MS are similar to each other while different from the healthy group on certain personality variables that likely reflect the demoralizing effects of coping with a chronic, disabling illness marked by uncertainty.
Kaminaga T, Kunimatsu N, Chikamatsu T, Furui S.	Department of Radiology, Teikyo University School of Medicine, Tokyo, Japan. kami@med.teikyo-u.ac.jp	Validation of CBF measurement with non-invasive microsphere method (NIMS) compared with autoradiography method (ARG).	Ann Nucl Med. 2001 Feb;15(1):61-4.	The purpose of this study is to examine the correlation of measured regional cerebral blood flow (rCBF) by means of a new microsphere method (non-invasive microsphere method), to the autoradiography (ARG) method, which is an established quantification method for 123I-IMP brain SPECT. The non-invasive microsphere (NIMS) method and ARG method were simultaneously applied to 30 patients, and quantified rCBF maps were calculated with each method. A significant correlation ($r = 0.70$; $p < 0.001$) was detected between mCBF values calculated with the NIMS and ARG methods. This new method seems to reliably quantify rCBF with brain SPECT.
Karpukhin IV.		[Use of local negative pressure in combination with electric sleep or Charcot's douche for treatment of erectile dysfunctions] [Article in Russian]	Vopr Kurortol Fizioter Lech Fiz Kult. 2001 Jul-Aug;(4):32-4.	43 patients with psychogenic erectile dysfunction aged 20-43 years received therapeutic complex including local negative pressure and electric sleep or Charcot's douche. The results obtained show that this complex is effective in erectile dysfunctions secondary to stress, neurosis and chronic fatigue syndrome.
Kenny RA, Graham LA.		Chronic fatigue syndrome symptoms common in patient with vasovagal syncope.	Am J Med. 2001 Feb 15;110(3):242-3.	
Kerr JR, Barah F, Matthey DL, Laing I, Hopkins SJ, Hutchinson IV, Tyrrell DA.	Department of Microbiology, Royal Brompton Hospital, National Heart and Lung Institute, Imperial College School of Medicine, Sydney Street, London SW3 6NP, UK.	Circulating tumour necrosis factor-alpha and interferon-gamma are detectable during acute and convalescent parvovirus B19 infection and are associated with prolonged and chronic fatigue.	J Gen Virol. 2001 Dec;82(Pt 12):3011-9.	To investigate whether cytokine responses may have a bearing on the symptoms and outcome of parvovirus B19 infection, circulating cytokines were measured during acute infection (n=51), follow-up of acute infection (n=39) and in normal healthy controls (n=50). At acute B19 virus infection (serum anti-B19 IgM-positive), patients ranged in age from 4 to 54 years, with a mean age of 28.2 years. The male:female ratio was 1:4.1 and symptoms were rash (n=15), arthralgia (n=31), fatigue (n=8), lymphadenopathy (n=4), foetal hydrops (n=3), transient aplastic crisis (n=2), neutropenia (n=2), myelodysplasia (n=1), thrombocytopenia (n=1) and pancytopenia (n=1). Of these patients, 39 were contacted after a follow-up period of 2-37 months (mean of 22.5 months). In comparison with normal controls, detectable IL-6 was associated with acute B19 virus infection (26%; $P=0.0003$), but not with

	j.kerr@ic.ac.uk			follow-up (6%; P=0.16). Detection of interferon (IFN)-gamma was associated with acute B19 virus infection (67%; P<0.0001) and follow-up (67%; P<0.0001). Detection of tumour necrosis factor (TNF)-alpha was associated with acute B19 virus infection (49%; P<0.0001) and follow-up (56%; P<0.0001). IL-1beta was detected in acute infection (20%), but not at follow-up. At acute B19 virus infection, detection of serum/plasma IL-6 was associated with rheumatoid factor (P=0.038) and IFN-gamma (> or =7 pg/ml) was associated with fatigue in those patients of > or =15 years of age (P=0.022). At follow-up, fatigue was associated with IFN-gamma (> or =7 pg/ml) and/or TNF-alpha (> or =40 pg/ml) (P=0.0275). Prolonged upregulation of serum IFN-gamma and TNF-alpha appears to represent a consistent host response to symptomatic B19 virus infection.
Klimas NG, Patarca-Montero R, Maher K, Smith M, Bathe O, Fletcher MA.		Clinical and Immunologic Effects of Autologous Lymph Node Cell Transplant in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(1): 39	An open labeled, phase 1, safety and feasibility study using lymph node extraction, ex vivo lymph node cell expansion, followed by autologous cell reinfusion was evaluated as a potential immunomodulatory treatment strategy in patients with chronic fatigue syndrome (CFS). The experimental therapy utilized the cells of the lymph node, activated and grown in culture with defined media, interleukin-2 (IL-2) and anti-CD3 to activate and enhance cellular immunological functions. This procedure was designed to change the cytokine pattern of the lymph node lymphocytes to favor expression of T-helper (Th)1-type over Th2-type cytokines. The mixed population of ex vivo immune-enhanced cells were reinfused into the donor, who was carefully monitored for adverse events and possible clinical benefit. There were no adverse events. There were significant improvements in clinical status in association with a significant decrease in Th2-type cytokine production.
Kovaleva AI, Pyshnov Glu.		[Problems of chronic fatigue] [Article in Russian]	Med Tr Prom Ekol. 2001;(11):1-5.	The review covers some human pathologic conditions defined as chronic fatigue syndrome, caroshi, burnout. Concerning nonspecific manifestations, one could characterize these conditions as general overfatigue of human. The authors attempt to consider these conditions from the viewpoint of occupationally induced disorders.
Krueger GR, Koch B, Hoffmann A, Rojo J, Brandt ME, Wang G, Buja LM.	Department of Pathology & Laboratory Medicine, University of Texas-Houston Medical School, 6431 Fannin St, MSB 2.246, Houston, Texas 77030, USA. Gerhard.Krueger@uthmce du	Dynamics of chronic active herpesvirus-6 infection in patients with chronic fatigue syndrome: data acquisition for computer modeling.	In Vivo. 2001 Nov-Dec;15(6):461-5.	Ten adult patients with persistent active HHV-6 variant A infection and clinical chronic fatigue syndrome (CFS) were studied over a period of 24 months after initial clinical diagnosis. CFS was diagnosed according to IIP-revised CDC-criteria as defined by the CFS Expert Advisory Group to the German Federal Ministry of Health in 1994. Changes in HHV-6 antibody titer, viral DNA load, peripheral blood T lymphocytes and subpopulations, as well as CD4/CD8 cell ratio and cell death (apoptosis) were monitored. Data were collected for comparison with respective changes in acute HHV-6 infection and as a basis for future computer simulation studies. The results showed variable but slightly elevated numbers of HHV-6 DNA copies in the blood of patients with CFS, while PBL (peripheral blood lymphocyte) apoptosis rates were clearly increased. CD4/CD8 cell ratios varied from below 1 up to values as seen in autoimmune disorders. Contrary to acute HHV-6 infection, T lymphocytes do not exhibit the usual response to HHV-6, that is elevation of mature and immature populations suggesting a certain degree of unresponsiveness. The data suggest that persistent low-dose stimulation by HHV-6 may favor imbalanced immune response rather than overt immune deficiency. This hypothesis requires confirmation through additional functional studies.
Kuratsune H, Kondo K, Ikuta K, Yamanishi K, Watanabe Y, Kitani T.		[Chronic fatigue syndrome (CFS)] [Article in Japanese]	Nippon Naika Gakkai Zasshi. 2001 Dec 10;90(12):2431-7.	
LaManca JJ, Peckerman A, Sisto SA, DeLuca J, Cook S, Natelson BH.	Chronic Fatigue Syndrome Cooperative Research Center, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, New Jersey, USA.	Cardiovascular responses of women with chronic fatigue syndrome to stressful cognitive testing before and after strenuous exercise.	Psychosom Med. 2001 Sep-Oct;63(5):756-64.	OBJECTIVE: The purpose of this study was to compare the cardiovascular responses of patients with chronic fatigue syndrome (CFS) to healthy control subjects when performing stressful cognitive tasks before and after strenuous exercise. METHOD: Beat-by-beat blood pressure and electrocardiogram were recorded on 19 women with CFS and 20 healthy nonexercising (ie, sedentary) women while they performed cognitive tests before, immediately after, and 24 hours after incremental exercise to exhaustion. RESULTS: Diminished heart rate (p <.01) and systolic (p <.01) and diastolic (p <.01) blood pressure responses to stressful cognitive testing were seen in patients with CFS when compared with healthy, sedentary controls. This diminished stress response was seen consistently in patients with CFS across three separate cognitive testing sessions. Also, significant negative correlations between self-ratings of CFS symptom severity and cardiovascular responses were seen (r = -0.62, p <.01). CONCLUSIONS: Women with CFS have a diminished cardiovascular response to cognitive stress; however, exercise did not magnify this effect. Also, the data showed that the patients with the lowest cardiovascular reactivity had the highest ratings of CFS symptom severity, which suggests that the individual response of the patient with CFS to stress plays a role in the common complaint of symptoms worsening after stress.
Lange G, Holodny AI, DeLuca J, Lee HJ, Yan	Departments of Psychiatry and Radiology, University	Quantitative assessment of cerebral ventricular	Appl Neuropsychol. 2001;8(1):23-30.	Previous qualitative volumetric assessment of lateral ventricular enlargement in chronic fatigue syndrome (CFS) has provided evidence for subtle structural changes in the brains of some individuals with CFS. The aim of this

XH, Steffener J, Natelson BH.	of Medicine and Dentistry of New Jersey, New Jersey Medical School, 30 Bergen Street, Newark, NJ 07107, USA. langegu@umdnj.edu	volumes in chronic fatigue syndrome.		pilot study was to determine whether a more sensitive quantitative assessment of the lateral ventricular system would support the previous qualitative findings. In this study, we compared the total lateral ventricular volume, as well as the right and left hemisphere subcomponents in 28 participants with CFS and 15 controls. Ventricular volumes in the CFS group were larger than in control groups, a difference that approached statistical significance. Group differences in ventricular asymmetry were not observed. The results of this study provide further evidence of subtle pathophysiological changes in the brains of participants with CFS.
Lange G, Tiersky LA, Scharer JB, Policastro T, Fiedler N, Morgan TE, Natelson BH.	Center for Environmental Hazards Research, DVA NJ Health Care System, East Orange, NJ, USA. langegu@umdnj.edu	Cognitive functioning in Gulf War Illness.	J Clin Exp Neuropsychol. 2001 Apr;23(2):240-9.	A comprehensive neuropsychological battery was administered to 48 veterans with Gulf War Illness (GWI) characterized by severe fatigue (GV-F) and 39 healthy veterans (GV-H). Subjects were matched on intelligence and did not differ on age, gender, race, and alcohol consumption. Compared to GV-H, GV-F were significantly impaired on four tasks: three attention, concentration, information processing tasks and one measure of abstraction and conceptualization. After considering the presence of post-war Axis I psychopathology, GWI remained a significant predictor of cognitive performance on one of the attention, concentration, and information processing tasks and one abstraction and conceptualization measure. Performance on the remaining two attention, concentration, and information processing tasks was only significantly predicted by Axis I psychopathology with post-war onset. The results suggest that Gulf War Illness is associated with some aspects of cognitive dysfunction in Gulf Veterans, over and above the contribution of psychopathology.
Lassenen KM.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):239; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
Lerner AM, Zervos M, Chang CH, Beqaj S, Goldstein J, O'Neill W, Dworkin H, Fitzgerald T, Deeter RG.		A small, randomized, placebo-controlled trial of the use of antiviral therapy for patients with chronic fatigue syndrome.	Clin Infect Dis. 2001 Jun 1;32(11):1657-8. Comment on: Clin Infect Dis. 1999 Sep;29(3):526-7.	
Levin AM.		Chronic Fatigue Syndrome: The Yeast Concept	Journal of Chronic Fatigue Syndrome 2001; 8(2): 71	Many theories abound as to the cause of CFS, but none have been proven conclusively. Because of the prevalence of the condition in many different countries throughout the world, it is becoming increasingly necessary to find a common link in the causative mechanism. The cause must be present at an international level. The overgrowth of bowel yeast and its infiltration through the bowel wall into the blood stream would appear to be the starting point in the development of CFS. This invasion of yeast can occur for different reasons. Therapeutic interventions based on the years of hypothesis are suggested.
Levin J, Steele L.		On the epidemiology of 'mysterious' phenomena.	Altern Ther Health Med. 2001 Jan;7(1):64-6.	In the field of epidemiology, research topics are favored or dismissed depending on whether respective variables under investigation are believed to exist according to current scientific theories. Unconventional independent variables or exposures, such as religiousness and spirituality, and controversial dependent variables or outcomes, such as chronic fatigue syndrome, may be considered unacceptable topics for researchers because they do not fit comfortably into the consensus clinical perspectives of mainstream medical scientists or physicians. Disapproval of research in these and other taboo areas is generally masked by claims that such studies are "pseudoscientific," despite hundreds or thousands of peer-reviewed publications on these topics. In reality, seemingly "mysterious" variables are equally as amenable to epidemiologic research as any other exposure or disease. Similarly, alternative therapies are able to be investigated using existing methods, despite claims to the contrary. Such research is vital for scientific understanding to be expanded into new areas of inquiry.
Levine PH, Klimas N, Armitage R, Fredericks R, Stewart J, Torch W, Schwartz S, Suhadolnik R, Reichenbach NL, Rhodes L.		Nevada Chronic Fatigue Syndrome Consensus Conference	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 53	
Levine S, Eastman H, Ablashi DV.		Prevalence of IgM and IgG Antibody to HHV-6 and HHV-8 and Results of	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 31	Human herpes virus-6 is a beta herpes virus that was first described in 1986 and which occurs in the form of at least two variants, A and B. Healthy donors in the general population are carriers for mainly the B variant, in whom 90% harbor the DNA of this type in their peripheral blood mononuclear cells (PBMNC). A higher prevalence of

		Plasma PCR to HHV-6 and HHV-7 in a Group of CFS Patients and Healthy Donors		<p>this virus has been detected by testing of plasma and PBMNCs by IFA, ELISA and by the nested PCR technique, in addition to direct culture for HHV-6 in certain groups of immunosuppressed patients such as those with multiple sclerosis and HIV. It has also been isolated to a greater degree using these techniques from patients who meet the case definition for the chronic fatigue syndrome (CFS). We determined IgG and IgM antibody titers to HHV-6; IgG to HHV-8 and performed PCR testing for HHV-6 on the plasma of 46 patients with CFS and on 7 healthy donors (HD). We also performed PCR testing for HHV-7 on 15 CFS patients and on 4 HD(s). We found a higher prevalence of IgM antibody in CFS patients 23/36 (50%) versus 2/7 (28.5%) of HD. The prevalence of IgG antibody to HHV-8 was zero among both CFS patients and HD. Three out of forty six (6.5%) of CFS patients demonstrated a positive plasma by PCR to HHV-6 compared to zero out of 7 HD(s). Finally, four out of fifteen (26.7%) CFS patients and zero out of four HD (s) demonstrated a positive plasma PCR to HHV-7. Our results were influenced by the presence of various subpopulations of CFS patients among our study group, in addition to our reliance on the results of single specimens as opposed to a series of multiple samples over time in individual subjects, and by methodological variability (decreasing our yield because of diminished viral shedding in cell-free samples or increasing it compared to other research groups who failed to co-culture the PBMNCs with indicator cells, e.g., PHA-stimulated human cord blood cells or human fibroblasts for short-term culture [15 day]). Nevertheless, it is clear that the study of plasma and perhaps other tissue samples, such as cerebral spinal fluid and gastric mucosa from patients with CFS in better defined subgroups, as well as defined population of HDs using a variety of methodological techniques will increase our knowledge about the role of HHV-6 in this complex disorder.</p>
Levine S.		Prevalence in the Cerebrospinal Fluid of the Following Infectious Agents in a Cohort of 12 CFS Subjects: Human Herpes Virus-6 and 8; Chlamydia Species; Mycoplasma Species; EBV; CMV; and Coxsackievirus	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 41	<p>Over the last decade a wide variety of infectious agents has been associated with the chronic fatigue syndrome (CFS) as potential etiologies for this disorder by researchers from all over the world. Many of these agents are neurotropic and have been linked previously to other diseases involving the central nervous system (CNS). Human herpes virus-6 (HHV-6), especially the B variant, has been found in autopsy specimens of patients who suffered from multiple sclerosis. Because patients with CFS manifest a wide range of symptoms involving the CNS as shown by abnormalities on brain MRIs, SPECT scans of the brain and results of tilt table testing we sought to determine the prevalence of HHV-6, HHV-8, Epstein-Barr virus (EBV), cytomegalovirus (CMV), Mycoplasma species, Chlamydia species, and Coxsackie virus in the spinal fluid of a group of 12 patients with CFS. Although we intended to search mainly for evidence of actively replicating HHV-6, a virus that has been associated by several researchers with this disorder, we found evidence of HHV-8, Chlamydia species, CMV and Coxsackie virus in 6/12 samples. Attempts were made to correlate the clinical presentations of each of these patients, especially the neurological exams and results of objective testing of the CNS, with the particular infectious agent isolated. It was also surprising to obtain such a relatively high yield of infectious agents on cell free specimens of spinal fluid that had not been centrifuged. Future research in spinal fluid analysis, in addition to testing tissue samples by polymerase chain reaction (PCR) and other direct viral isolation techniques will be important in characterizing subpopulations of CFS patients, especially those with involvement of the CNS.</p>
Lewis DH, Mayberg HS, Fischer ME, Goldberg J, Ashton S, Graham MM, Buchwald D.	Departments of Radiology, University of Washington, Seattle, USA.	Monozygotic twins discordant for chronic fatigue syndrome: regional cerebral blood flow SPECT.	Radiology. 2001 Jun;219(3):766-73.	<p>PURPOSE: To evaluate the relationship between regional cerebral blood flow (rCBF) and chronic fatigue syndrome (CFS) in monozygotic twins discordant for CFS. MATERIALS AND METHODS: The authors conducted a co-twin control study of 22 monozygotic twins in which one twin met criteria for CFS and the other was healthy. Twins underwent a structured psychiatric interview and resting technetium 99m-hexamethyl-propyleneamine oxime single photon emission computed tomography of the brain. They also rated their mental status before the procedure. Scans were interpreted independently by two physicians blinded to illness status and then at a blinded consensus reading. Imaging fusion software with automated three-dimensional matching of rCBF images was used to coregister and quantify results. Outcomes were the number and distribution of abnormalities at both reader consensus and automated quantification. Mean rCBF levels were compared by using random effects regression models to account for the effects of twin matching and potential confounding factors. RESULTS: The twins with and those without CFS were similar in mean number of visually detected abnormalities and in mean differences quantified by using image registration software. These results were unaltered with adjustments for fitness level, depression, and mood before imaging. CONCLUSION: The study results did not provide evidence of a distinctive pattern of resting rCBF abnormalities associated with CFS. The described method highlights the importance of selecting well-matched control subjects.</p>
Lipschitz EL		Chronic fatigue syndrome and posttraumatic stress	JAMA. 2001 Aug 22-29;286(8):916-7. Comment	

		disorder.	on: JAMA. 2001 May 23-30;285(20):2557-9.	
Logan AC, Wong C.	CFS/FM Integrative Care Centre, Toronto, ON, Canada. alanloganND@excite.com	Chronic fatigue syndrome: oxidative stress and dietary modifications.	Altern Med Rev. 2001 Oct;6(5):450-9.	Chronic fatigue syndrome (CFS) is an illness characterized by persistent and relapsing fatigue, often accompanied by numerous symptoms involving various body systems. The etiology of CFS remains unclear; however, a number of recent studies have shown oxidative stress may be involved in its pathogenesis. The role of oxidative stress in CFS is an important area for current and future research as it suggests the use of antioxidants in the management of CFS. Specifically, the dietary supplements glutathione, N-acetylcysteine, alpha-lipoic acid, oligomeric proanthocyanidins, Ginkgo biloba, and Vaccinium myrtillus (bilberry) may be beneficial. In addition, research on food intolerance is discussed, since food intolerance may be involved in CFS symptom presentation and in oxidation via cytokine induction. Finally, recent evidence suggests celiac disease can present with neurological symptoms in the absence of gastrointestinal symptoms; therefore, celiac disease should be included in the differential diagnosis of CFS.
Logan AC.		Nutritional strategies for treating chronic fatigue syndrome.	Altern Med Rev. 2001 Feb;6(1):4-6. Comment on: Altern Med Rev. 2000 Apr;5(2):93-108.	
Manuel y Keenoy B, Moorkens G, Vertommen J, De Leeuw I.	University Hospital, University of Antwerp, Belgium. begona@uia.ua.ac.be	Antioxidant status and lipoprotein peroxidation in chronic fatigue syndrome.	Life Sci. 2001 Mar 16;68(17):2037-49.	The aetiology and pathogenesis of the Chronic Fatigue Syndrome (CFS) are still largely unresolved. Accompanying metabolic disorders such as selective n-6 fatty acid depletion suggest that oxidative stress and more specifically lipid peroxidation might play a role in its pathogenesis. In order to investigate this hypothesis, oxidant-antioxidant status and its impact on lipoprotein peroxidation in vitro was examined in 61 patients with unexplained fatigue lasting more than 1 month. They were subdivided into 2 groups: group CFS+ (33 subjects) fulfilled the 1988 Center of Disease Control criteria for CFS and group CFS- did not but was similar as regards age, sex distribution and clinical characteristics. Antioxidant status was similar in the 2 groups except for lower serum transferrin in the CFS+ (mean (95 % CI) 2.41 (2.28-2.54) versus 2.73 (2.54-2.92) g/L in the CFS-, p = 0.009) and higher lipoprotein peroxidation in vitro: 6630 (5949-7312) versus 5581 (4852-6310) nmol MDA/mg LDL and VLDL cholesterol x minutes, p = 0.035). CFS intensified the influence of LDL cholesterol (p = 0.012) and of transferrin (p = 0.045) on peroxidation in vitro, suggesting additional pro-oxidant effects. These results indicate that patients with CFS have increased susceptibility of LDL and VLDL to copper-induced peroxidation and that this is related both to their lower levels of serum transferrin and to other unidentified pro-oxidising effects of CFS.
Maquet D, Croisier JL, Crielaard JM.	Medecine de l'appareil locomoteur, CHU Sart Tilman, 4000 Liege, Belgique, France. d.maquet@belgacom.net	[What happens to the fibromyalgia syndrome?] [Article in French]	Ann Readapt Med Phys. 2001 Jul;44(6):316-25.	OBJECTIVE: To realize a clarification about fibromyalgia, attempting to consider diagnostic criteria, prevalence, pathophysiology and therapeutic approach. METHOD: A systematic literature search was conducted to select articles about fibromyalgia and connected diseases. The database are Premedline, Medline and Medlineplus. RESULTS: Fifty-eight articles about fibromyalgia and twelve articles about connected diseases were selected to realize this review of literature. DISCUSSION: Fibromyalgia constitutes a syndrome characterized by widespread musculo-skeletal pain, present above the waist and below the waist and in the axial skeleton. Widespread pain must have been present for at least three months. "Spasmophilie", chronic fatigue syndrome and myofascial syndrome represent diseases connected with fibromyalgia: differential diagnosis must be established. Researches related to fibromyalgia suggest a reduction of muscular performances associated with histological and biochemical anomalies. Patients are characterized by shorter and nonrestorative sleep. Psychological, neuroendocrine and central alterations appear often associated with fibromyalgia. The reduction of pressure tolerance and pain thresholds may be linked to the alterations of neuroendocrine substances. Literature recommend a multidisciplinary therapeutic approach in management of fibromyalgia. CONCLUSION: The pathophysiologic mechanisms in fibromyalgia appear multiple and interdependent. With the aim to optimizing treatment, investigations are necessary to determine biochemical repercussions of various therapeutic approaches.
Martinez-Lavin M.	Rheumatology Department, Instituto Nacional de Cardiologia Ignacio Chavez, Juan Badiano 1., 14080 Mexico, D.F. Mexico. mmlavin@infosel.net.mx	Overlap of fibromyalgia with other medical conditions.	Curr Pain Headache Rep. 2001 Aug;5(4):347-50.	Fibromyalgia is a multisystem illness. One of its defining features, generalized pain, may also be present in other rheumatic entities. The diagnosis of fibromyalgia is not easy by any means, it requires a profound knowledge of internal medicine. This article discusses the different rheumatic and nonrheumatic diseases that overlap or are prone to be confused with fibromyalgia. It emphasizes the key points in the differential diagnosis.
Masuda A, Nakayama T,	First Department of Internal	Cognitive behavioral	Intern Med. 2001	Cognitive behavioral therapy temporarily alleviated symptoms of a chronic fatigue syndrome patient but the

Yamanaka T, Hatsutanmaru K, Tei C.	Medicine, Kagoshima University.	therapy and fasting therapy for a patient with chronic fatigue syndrome.	Nov;40(11):1158-61.	anxiety about rehabilitation into work became stronger and his symptoms worsened. This patient was successfully rehabilitated by fasting therapy. Natural killer cell activity and serum acylcarnitine levels recovered after fasting therapy. Though fasting therapy transiently increased physical and mental subjective symptoms, the patient gained self-confidence by overcoming difficulties after fasting therapy. A combination of cognitive behavioral therapy and fasting therapy is promising as a treatment for chronic fatigue syndrome.
Michiels V, Cluydts R. Department of Psychology, Free University of Brussels, Belgium.		Neuropsychological functioning in chronic fatigue syndrome: a review.	Acta Psychiatr Scand. 2001 Feb;103(2):84-93.	OBJECTIVE: In this paper we review critically the current status of neurocognitive studies in patients with chronic fatigue syndrome (CFS). METHOD: CFS literature was monitored as part of a large research project which involved several neuropsychological and psychopathological studies. The literature survey was the result of several consecutive searches on Medline and PsycInfo databases. RESULTS: The neurocognitive studies are reviewed in terms of scientifically accepted aspects of attention and memory. In addition, we review possible explanations for cognitive dysfunction in CFS. This is preceded with a discussion of the methodological limitations that are considered to explain inconsistencies across neuropsychological studies in CFS. CONCLUSION: The current research shows that slowed processing speed, impaired working memory and poor learning of information are the most prominent features of cognitive dysfunctioning in patients with CFS. Furthermore, to this date no specific pattern of cerebral abnormalities has been found that uniquely characterizes CFS patients. There is no overwhelming evidence that fatigue is related to cognitive performance in CFS, and researchers agree that their performance on neuropsychological tasks is unlikely to be accounted solely by the severity of the depression and anxiety.
Miike T.	Department of Child Development, Kumamoto University School of Medicine.	[Chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2001 Dec;59 Suppl 8:414-21.	
Miller CS.	Department of Family and Community Medicine, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas 78229-3900, USA. millercs@uthscsa.edu	Toxicant-induced loss of tolerance.	Addiction. 2001 Jan;96(1):115-37.	Drug addiction and multiple chemical intolerance (abduction) appear to be polar opposites--the former characterized by craving and dependency, the latter by aversion. However, when the two are viewed in juxtaposition similarities emerge, revealing a common underlying dynamic, one which appears to be a new paradigm of disease. TILT, or toxicant-induced loss of tolerance, bridges the gap between addiction and abduction and has the potential to explain a variety of illnesses, including certain cases of asthma, migraine headaches and depression, as well as chronic fatigue syndrome, fibromyalgia and "Gulf War syndrome". This paper argues that both addiction and chemical intolerance involve a fundamental breakdown in innate tolerance, resulting in an amplification of various biological effects, particularly withdrawal symptoms. While addicts seek further exposures so as to avoid unpleasant withdrawal symptoms, chemically intolerant individuals shun their problem exposures, but for the same reason--to avoid unpleasant withdrawal symptoms. These observations raise critical questions: do addictive drugs and environmental pollutants initiate an identical disease process? Once this process begins, can both addictants and pollutants trigger symptoms and cravings? TILT opens a new window between the fields of addiction and environmental medicine, one that has the potential to transform neighboring realms of medicine, psychology, psychiatry and toxicology.
Morrison RE, Keating HJ 3rd.	Department of Medicine, Division of General Internal Medicine, University of Tennessee at Memphis, Memphis, Tennessee, USA.	Fatigue in primary care.	Obstet Gynecol Clin North Am. 2001 Jun;28(2):225-40, v-vi.	Fatigue is a common problem in primary care that may represent a reaction to life problems or be a component of a disease state. A careful history, physical examination, and a few directed laboratory tests can usually allow the physician to differentiate between fatigue caused by depression, situational stress, or physical causes such as postviral or drug-induced fatigue, endocrine disorders, sleep disorders, infectious diseases, autoimmune disorders, or neurologic disease. Uncommonly, patients may have otherwise unexplained fatigue lasting 6 months or more that fulfills the criteria of chronic fatigue syndrome. A range of diagnostic skills coupled with a therapeutic physician-patient relationship will usually be successful in treating women with symptoms of fatigue.
Moss-Morris R, Petrie KJ.	Health Psychology Research Group, Faculty of Medical and Health Science, The University of Auckland, New Zealand.	Discriminating between chronic fatigue syndrome and depression: a cognitive analysis.	Psychol Med. 2001 Apr;31(3):469-79.	BACKGROUND: Chronic fatigue syndrome (CFS) and depression share a number of common symptoms and the majority of CFS patients meet lifetime criteria for depression. While cognitive factors seem key to the maintenance of CFS and depression, little is known about how the cognitive characteristics differ in the two conditions. METHODS: Fifty-three CFS patients were compared with 20 depressed patients and 38 healthy controls on perceptions of their health, illness attributions, self-esteem, cognitive distortions of general and somatic events, symptoms of distress and coping. A 6 month follow-up was also conducted to determine the stability of these factors and to investigate whether CFS-related cognitions predict ongoing disability and fatigue in this disorder. RESULTS: Between-group analyses confirmed that the depressed group was distinguished by low self-esteem, the propensity to make cognitive distortions across all situations, and to attribute their illness to psychological factors.

				In contrast, the CFS patients were characterized by low ratings of their current health status, a strong illness identity, external attributions for their illness, and distortions in thinking that were specific to somatic experiences. They were also more likely than depressed patients to cope with their illness by limiting stress and activity levels. These CFS-related cognitions and behaviours were associated with disability and fatigue 6 months later. CONCLUSIONS: CFS and depression can be distinguished by unique cognitive styles characteristic of each condition. The documented cognitive profile of the CFS patients provides support for the current cognitive behavioural models of the illness.
Mouterde O.		Myalgic encephalomyelitis in children.	Lancet. 2001 Feb 17;357(9255):562. Comment in: Lancet. 2001 Jun 9;357(9271):1889.	
Mueller D.	Division of Neurosurgery, University of Missouri Hospital and Clinics, USA. muellerdm@health.missouri.edu	Brainstem conundrum: the Chiari I malformation.	J Am Acad Nurse Pract. 2001 Apr;13(4):154-9.	PURPOSE: To describe the Chiari I Malformation in relation to the anatomy of the brain and spinal cord, the common manifestations of the condition, diagnostic considerations, and management for the primary care provider. DATA SOURCES: Extensive review of the world-wide scientific literature on the condition, supplemented with actual case studies. CONCLUSIONS: The adult Chiari I Malformation is an insidious congenital brainstem anomaly that consists of caudal displacement of the cerebellar tonsils, brainstem and fourth ventricle into the upper cervical space, resulting in overcrowding of the posterior fossa. IMPLICATIONS FOR PRACTICE: Due to the vague, and often ambiguous presenting symptoms of Chiari I Malformation, many patients are misdiagnosed with conditions such as multiple sclerosis, fibromyalgia, chronic fatigue syndrome, or psychiatric disorders. Patients frequently experience symptoms months to years prior to accurate diagnosis and often incur irreversible neurologic deficits.
Mullington JM, Hinze-Selch D, Pollmacher T.	Department of Neurology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts 02215, USA. jmulling@caregroup.harvard.edu	Mediators of inflammation and their interaction with sleep: relevance for chronic fatigue syndrome and related conditions.	Ann N Y Acad Sci. 2001 Mar;933:201-10.	In humans, activation of the primary host defense system leads to increased or decreased NREM sleep quality, depending on the degree of early immune activation. Modest elevations of certain inflammatory cytokines are found during experimental sleep loss in humans and, in addition, relatively small elevations of cytokines are seen following commencement of pharmacological treatments with clozapine, a CNS active antipsychotic agent, known to have immunomodulatory properties. Cytokines such as TNF-alpha, its soluble receptors, and IL-6, present in the periphery and the CNS, comprise a link between peripheral immune stimulation and CNS-mediated behaviors and experiences such as sleep, sleepiness, and fatigue. The debilitating fatigue experienced in chronic fatigue syndrome and related diseases may also be related to altered cytokine profiles.
Murdoch JC.	Chronic fatigue syndrome.		Br J Gen Pract. 2001 Sep;51(470):758. Comment on: Br J Gen Pract. 2001 Jul;51(468):553-8.	
Naschitz JE, Rozenbaum M, Rosner I, Sabo E, Priselac RM, Shaviv N, Ahdoot A, Ahdoot M, Gaitini L, Eldar S, Yeshurun D.	Departments of Internal Medicine A, Rheumatology, Anesthesiology, and Surgery, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.	Cardiovascular response to upright tilt in fibromyalgia differs from that in chronic fatigue syndrome.	J Rheumatol. 2001 Jun;28(6):1356-60.	OBJECTIVE: To compare the cardiovascular response during postural challenge of patients with fibromyalgia (FM) to those with chronic fatigue syndrome (CFS). METHODS: Age and sex matched patients were studied, 38 with FM, 30 with CFS, and 37 healthy subjects. Blood pressure (BP) and heart rate (HR) were recorded during 10 min of recumbence and 30 min of head-up tilt. Differences between successive BP values and the last recumbent BP, their average, and standard deviation (SD) were calculated. Time curves of BP differences were analyzed by computer and their outline ratios (OR) and fractal dimensions (FD) were measured. HR differences were determined similarly. Based on the latter measurements, each subject's discriminant score (DS) was computed. RESULTS: For patients and controls average DS values were: FM: -3.68 (SD 2.7), CFS: 3.72 (SD 5.02), and healthy controls: -4.62 (SD 2.24). DS values differed significantly between FM and CFS ($p < 0.0001$). Subgroups of FM patients with and without fatigue had comparable DS values. CONCLUSION: The DS confers numerical expression to the cardiovascular response during postural challenge. DS values in FM were significantly different from DS in CFS, suggesting that homeostatic responses in FM and CFS are dissimilar. This observation challenges the hypothesis that FM and CFS share a common derangement of the stress-response system.
Naschitz JE, Sabo E, Naschitz S, Shaviv N, Rosner I, Rozenbaum M, Gaitini L, Ahdoot A, Ahdoot M, Priselac RM, Eldar S, Zukerman E.	Department of Internal Medicine A, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology,	Hemodynamic instability in chronic fatigue syndrome: indices and diagnostic significance.	Semin Arthritis Rheum. 2001 Dec;31(3):199-208.	OBJECTIVES: To evaluate the cardiovascular response to postural challenge in patients with chronic fatigue syndrome (CFS) and to determine whether the degree of instability of the cardiovascular response may aid in diagnosing CFS. METHODS: Patients with CFS ($n = 25$) and their age- and gender-matched healthy controls ($n = 37$), patients with fibromyalgia ($n = 30$), generalized anxiety disorder ($n = 15$), and essential hypertension ($n = 20$) were evaluated with the aid of a standardized tilt test. The blood pressure (BP) and heart rate (HR) were recorded during 10 minutes of recumbence and 30 minutes of head-up tilt. We designated BP changes as the differences

Yeshurun D.	Haifa, Israel.			between successive BP values and the last recumbent BP. The average and standard deviation (SD) were calculated. Time curves of BP differences were loaded into a computerized image analyzer, and their outline ratios and fractal dimensions were measured. HR changes were determined similarly. The average and SD of the parameters were calculated, and intergroup comparisons were performed. RESULTS: On multivariate analysis, the independent predictors of CFS patients versus healthy controls were the fractal dimension of absolute values of the systolic BP changes (SYST-FD.abs), the standard deviation of the current values of the systolic BP changes (SYST-SD.cur), and the standard deviation of the current values of the heart rate changes (HR-SD.cur). The following equation was deduced to calculate the hemodynamic instability score (HIS) in the individual patient: $HIS = 64.3303 + (SYST-FD.abs \times -68.0135) + (SYST-SD.cur \times 111.3726) + (HR-SD.cur \times 60.4164)$. The best cutoff differentiating CFS from the healthy controls was -0.98. HIS values >-0.98 were associated with CFS (sensitivity 97%, specificity 97%). The HIS differed significantly between CFS and other groups ($P < .0001$) except for generalized anxiety disorder. Group averages (SD) of HIS were CFS = +3.72 (5.02), healthy = -4.62 (2.26), fibromyalgia = -3.27 (2.63), hypertension = -5.53 (2.24), and generalized anxiety disorder = +1.08 (5.2). CONCLUSION: The HIS adds objective criteria confirming the diagnosis of CFS. Copyright 2001 by W.B. Saunders Company
Natelson BH.	Fatigue Research Center, New Jersey Medical School, 88 Ross St, East Orange, NJ 07018. bhn@njneuromed.org	Chronic fatigue syndrome.	JAMA. 2001 May 23- 30;285(20):2557-9. Comment in: JAMA. 2001 Aug 22-29;286(8):916-7.	
Nelson JJ, Natelson BH, Peckerman A, Pollet C, Lange G, Tiersky L, Servatius RJ, Policastro T, Fiedler N, Ottenweller JE.	Center for Environmental Hazards Research, Department of Veterans Affairs Medical Center, East Orange, NJ 07018, USA.	Medical follow-up of Persian Gulf War Veterans with severe medically unexplained fatigue: a preliminary study.	Mil Med. 2001 Dec;166(12):1107-9.	An important question for researchers interested in long-term consequences of military service is the health outcome of symptomatic Persian Gulf War Veterans. From an original group of 76 Gulf War Veterans who received the diagnosis of severe fatiguing illness, we attempted to get 58 veterans to return to our center for a second evaluation. Thirteen returned. Two had recovered by the time of revisit, but the rest remained ill; however, only one was so ill as to be unable to work. The data suggest that the medical consequences of serving in the Persian Gulf are not transient. The difficulty in getting veterans to return to our center suggests potential problems in the proposed nation-wide longitudinal health outcome study of Persian Gulf War Veterans.
Nesher G, Margalit R, Ashkenazi YJ.	Department of Rheumatology Service, Hebrew University Medical School, Jerusalem, Israel. nesher@inter.net.il	Anti-nuclear envelope antibodies: Clinical associations.	Semin Arthritis Rheum. 2001 Apr;30(5):313-20.	OBJECTIVES: Characterization of the clinical associations and clinical implications of antibodies reacting with antigens of the nuclear envelope. METHODS: Description of an illustrative case and a MEDLINE search-assisted literature review of relevant cases. RESULTS: With indirect immunofluorescence, autoantibodies directed against various antigens of the nuclear envelope stain the nucleus in a ring-like (rim) pattern. Autoantibodies against 5 antigenic components of the nuclear envelope have been described: anti-gp210, p62, lamina, lamina-associated polypeptides, and lamin B receptor. Antibodies to antigens of the nuclear pore complex, such as gp210 and p62, are highly specific ($> 95\%$) for primary biliary cirrhosis and may aid in the serologic diagnosis of this condition, especially in cases in which antimitochondrial antibodies are not detectable. In contrast, antilamin antibodies are not disease-specific but seem to be associated with lupus anticoagulant or anticardiolipin antibodies, antiphospholipid syndrome, thrombocytopenia, autoimmune liver diseases, and arthralgia. High-titered antilamin antibodies help to define a subset of lupus patients with antiphospholipid antibodies who are at a lower risk of developing thrombotic events. In addition, preliminary data suggest that the presence of antilamin antibodies may be helpful in the diagnosis of chronic fatigue syndrome. CONCLUSIONS: Each of the antibodies reacting with nuclear membrane antigens has its own spectrum of disease associations. RELEVANCE: Determination of anti-nuclear envelope antibody pattern by indirect immunofluorescence, with subsequent determination of the specific antibody, carries important diagnostic and prognostic implications in various autoimmune conditions.
Nishikai M, Tomomatsu S, Hankins RW, Takagi S, Miyachi K, Kosaka S, Akiya K.	National Tokyo Medical Center, Tokyo, Japan.	Autoantibodies to a 68/48 kDa protein in chronic fatigue syndrome and primary fibromyalgia: a possible marker for hypersomnia and cognitive disorders.	Rheumatology (Oxford). 2001 Jul;40(7):806-10.	OBJECTIVE: To identify antinuclear antibodies (ANA) specific for chronic fatigue syndrome (CFS), and in related conditions such as fibromyalgia (FM) or psychiatric disorders. METHODS: One hundred and fourteen CFS patients and 125 primary and secondary FM patients were selected based on criteria advocated by the Centers for Disease Control and Prevention and by the American College of Rheumatology, respectively. As controls, healthy subjects and patients with either various psychiatric disorders or diffuse connective tissue diseases were included. Autoantibodies were examined by immunoblot utilizing HeLa cell extracts as the antigen. RESULTS: Autoantibodies to a 68/48 kDa protein were present in 13.2 and 15.6% of patients with CFS and primary FM, respectively. In addition, autoantibodies to a 45 kDa protein were found in 37.1 and 21.6% of the patients with secondary FM and psychiatric disorders, respectively. Meanwhile, these two autoantibodies were not found at all in

				connective tissue disease patients without FM, nor in healthy subjects ($P<0.05$). As a group, the anti-68/48 kDa-positive CFS patients presented more frequently with hypersomnia ($P<0.005$), short-term amnesia ($P<0.07$) or difficulty in concentration ($P<0.05$) than those CFS patients without the antibodies. CONCLUSIONS: The presence of the anti-68/48 kDa protein antibodies in a portion of both CFS and primary FM patients suggests the existence of a common immunological background. These antibodies may find utility as possible markers for a clinicoserological subset of CFS/FM patients with hypersomnia and cognitive complaints.
Nonaka I.	National Center of Neurology and Psychiatry.	[Complex III (ubiquinone-cytochrome c reductase) deficiency] [Article in Japanese]	Ryoikibetsu Shokogun Shirizu. 2001;(36):135-6.	
Nye F..		Infectious mononucleosis: not always what it seems	Hosp Med. 2001 Jul;62(7):388-9. Comment in: Hosp Med. 2002 Jan;63(1):54.	
Okuyama T, Tanaka K, Akechi T, Kugaya A, Okamura H, Nishiwaki Y, Hosaka T, Uchitomi Y.	Psycho-Oncology Division, National Cancer Center Research Institute East, Kashiwa, Japan.	Fatigue in ambulatory patients with advanced lung cancer: prevalence, correlated factors, and screening.	J Pain Symptom Manage. 2001 Jul;22(1):554-64.	Although it has been indicated that patients with lung cancer experience higher level of fatigue than patients with other cancers, few published studies have focused on the characteristics of this fatigue and how it interferes with daily activities. The purpose of this study was to clarify fatigue prevalence and the factors correlated with fatigue, and to develop a screening method for fatigue in patients with advanced lung cancer. One hundred fifty-seven patients completed two fatigue scales (Cancer Fatigue Scale [CFS], and Fatigue Numerical Scale [FNS]) plus other measures, along with a self-administered questionnaire asking whether fatigue had interfered with any of 7 areas of daily activities. Fifty-nine percent of patients had experienced clinical fatigue, which was defined as fatigue that interfered with any daily activities. Logistic regression analysis demonstrated that symptoms of dyspnea on walking, appetite loss, and depression were significant correlated factors. Both CFS and FNS were found to have sufficient sensitivity and specificity for use as a screening tool. The results indicated that fatigue is a frequent and important symptom, which is associated with both physical and psychological distress in this population. The CFS and FNS were confirmed to have sufficient screening ability.
Otteweller JE, Sisto SA, McCarty RC, Natelson BH.	Department of Neurosciences, New Jersey Medical School, University of Medicine and Dentistry of New Jersey, Newark, USA. jeo@nbunj.jvnc.net	Hormonal responses to exercise in chronic fatigue syndrome.	Neuropsychobiology. 2001 Jan;43(1):34-41.	Chronic fatigue syndrome (CFS) is a debilitating disease characterized by severe, unexplained fatigue and postexertional exacerbation of symptoms. We examined basal endocrine function in a group of CFS patients and a carefully matched group of sedentary controls. The subjects then completed a graded, maximal exercise test on a treadmill, and additional blood samples were drawn 4 min and a day after the end of exercise. There were no differences in basal hormone levels before exercise. Plasma adrenocorticotropin, epinephrine, prolactin and thyrotropin responses 4 min after exercise were lower in the CFS group, but the growth hormone response may have been exaggerated, and the plasma norepinephrine response was similar to that in controls. The next day, there were no differences in hormone levels between the groups, which suggests that long-term changes in endocrine function are unlikely to be a cause of the prolonged fatigue that occurs in CFS patients after a bout of exertion. Copyright 2001 S. Karger AG, Basel
Overstreet DH, Djuric V.	Department of Psychiatry and Center for Alcohol Studies, University of North Carolina at Chapel Hill, 27599-7178, USA. dhover@med.unc.edu	A genetic rat model of cholinergic hypersensitivity: implications for chemical intolerance, chronic fatigue, and asthma.	Ann N Y Acad Sci. 2001 Mar;933:92-102.	The fact that only some individuals exposed to environmental chemicals develop chemical intolerance raises the possibility that genetic factors could be contributing factors. The present communication summarizes evidence from a genetic animal model of cholinergic supersensitivity that suggests that an abnormal cholinergic system could be one predisposing genetic factor. The Flinders Sensitive Line (FSL) rats were established by selective breeding for increased responses to an organophosphate. It was subsequently found that these FSL rats were also more sensitive to direct-acting muscarinic agonists and had elevated muscarinic receptors compared to the selectively bred parallel group, the Flinders Resistant Line (FRL) rats, or randomly bred control rats. Increased sensitivity to cholinergic agents has also been observed in several human populations, including individuals suffering from chemical intolerance. Indeed, the FSL rats exhibit certain behavioral characteristics such as abnormal sleep, activity, and appetite that are similar to those reported in these human populations. In addition, the FSL rats have been reported to exhibit increased sensitivity to a variety of other chemical agents. Peripheral tissues, such as intestinal and airway smooth muscle, appear to be more sensitive to both cholinergic agonists and an antigen, ovalbumin. Hypothermia, a centrally mediated response, is more pronounced in the FSL rats after nicotine and alcohol, as well as agents that are selective for the dopaminergic and serotonergic systems. In some cases, the increased sensitivity has been detected in the absence of any changes in the receptors with which the drugs interact (dopamine receptors), while receptor changes have been seen in other cases (nicotine receptors). Therefore, there

				may be multiple mechanisms underlying the multiple chemical sensitivity-chemical intolerance of the FSL rats. An elucidation of these mechanisms may provide useful clues to those involved in chemical intolerance in humans.
Pall ML, Satterle JD.	School of Molecular Biosciences, Washington State University, Pullman 99164-4660, USA. martin_pall@wsu.edu	Elevated nitric oxide/peroxynitrite mechanism for the common etiology of multiple chemical sensitivity, chronic fatigue syndrome, and posttraumatic stress disorder.	Ann N Y Acad Sci. 2001 Mar;933:323-9.	Various types of evidence implicate nitric oxide and an oxidant, possibly peroxynitrite, in MCS and chemical intolerance (CI). The positive feedback loops proposed earlier for CFS may explain the chronic nature of MCS (CI) as well as several of its other reported properties. These observations raise the possibility that this proposed elevated nitric oxide/peroxynitrite mechanism may be the mechanism of a new disease paradigm, answering the question raised by Miller earlier: "Are we on the threshold of a new theory of disease?"
Pall ML.		Cobalamin Used in Chronic Fatigue Syndrome Therapy Is a Nitric Oxide Scavenger	Journal of Chronic Fatigue Syndrome 2001; 8(2): 39	Cobalamin (vitamin B12) in the form of hydroxocobalamin or cyanocobalamin injections has been widely used to treat chronic fatigue syndrome (CFS). Hydroxocobalamin is a nitric oxide scavenger and is proposed here to act as such a scavenger in CFS treatment. Its possible efficacy in CFS treatment, if further substantiated, may provide confirmation of a prediction of the elevated nitric oxide/peroxynitrite theory of CFS etiology. This interpretation of the possible role of cobalamin in CFS treatment suggests a useful perspective for confirming and optimizing this treatment.
Pall ML.	School of Molecular Biosciences and Program in Medical Sciences, Washington State University, Pullman, 99164-4660, USA. pall@mail.wsu.edu	Common etiology of posttraumatic stress disorder, fibromyalgia, chronic fatigue syndrome and multiple chemical sensitivity via elevated nitric oxide/peroxynitrite.	Med Hypotheses. 2001 Aug;57(2):139-45.	Three types of overlap occur among the disease states chronic fatigue syndrome (CFS), fibromyalgia (FM), multiple chemical sensitivity (MCS) and posttraumatic stress disorder (PTSD). They share common symptoms. Many patients meet the criteria for diagnosis for two or more of these disorders and each disorder appears to be often induced by a relatively short-term stress which is followed by a chronic pathology, suggesting that the stress may act by inducing a self-perpetuating vicious cycle. Such a vicious cycle mechanism has been proposed to explain the etiology of CFS and MCS, based on elevated levels of nitric oxide and its potent oxidant product, peroxynitrite. Six positive feedback loops were proposed to act such that when peroxynitrite levels are elevated, they may remain elevated. The biochemistry involved is not highly tissue-specific, so that variation in symptoms may be explained by a variation in nitric oxide/peroxynitrite tissue distribution. The evidence for the same biochemical mechanism in the etiology of PTSD and FM is discussed here, and while less extensive than in the case of CFS and MCS, it is nevertheless suggestive. Evidence supporting the role of elevated nitric oxide/peroxynitrite in these four disease states is summarized, including induction of nitric oxide by common apparent inducers of these disease states, markers of elevated nitric oxide/peroxynitrite in patients and evidence for an inductive role of elevated nitric oxide in animal models. This theory appears to be the first to provide a mechanistic explanation for the multiple overlaps of these disease states and it also explains the origin of many of their common symptoms and similarity to both Gulf War syndrome and chronic sequelae of carbon monoxide toxicity. This theory suggests multiple studies that should be performed to further test this proposed mechanism. If this mechanism proves central to the etiology of these four conditions, it may also be involved in other conditions of currently obscure etiology and criteria are suggested for identifying such conditions. Copyright 2001 Harcourt Publishers Ltd.
Papp KK, Erokwu B, Decker M, Strohl KP.	Louis B. Stokes Cleveland V.A. Medical Center and Case Western Reserve University School of Medicine, Cleveland, Ohio, USA. kkp4@po.cwru.edu	Medical student competence in eliciting a history for "chronic fatigue".	Sleep Breath. 2001 Sep;5(3):123-9.	PURPOSE: We report an observational study of medical students' abilities in taking a complex history for which sleep disorders is one of several possible conditions. METHODS: Students are observed taking a focused history from a simulated patient whose chief complaint is "I am tired. I cannot get anything done." Nine groups of students (n = 360) completing the internal medicine core-clerkship were evaluated by one of three examiners. Students received full, partial, or no credit for each item on a uniform behavioral checklist, which included prompts for common medical and psychiatric disorders associated with chronic fatigue. RESULTS: Observed means were lowest for items pertaining to sleep behaviors and head trauma. Fewer than half of the students inquired about whether or not the person had difficulty falling asleep at night, family history of sleep apnea, and frequency and length of naps. In contrast, the majority of students inquired about heart disease, metabolic disorders, the use of illicit drugs, alcohol consumption, and the taking of medications. Examiners accounted for a significant source of variance in scores; yet the station discriminated among top and bottom students as measured by the Objective Structured Clinical Examination (OSCE) overall. No statistically significant differences were observed on the basis of clerkship site, primary care versus traditional-track students, time of year, or gender. CONCLUSION: A majority of students do not adequately cover issues relevant to sleep in contrast to other associated disorders when taking a focused history for chronic fatigue.
Parker AJ, Wessely S,	Department of	The neuroendocrinology of	Psychol Med. 2001	BACKGROUND: Disturbance of the HPA axis may be important in the pathophysiology of chronic fatigue

Cleare AJ.	Psychological Medicine, Guy's, King's and St Thomas' School of Medicine and the Institute of Psychiatry, London.	chronic fatigue syndrome and fibromyalgia.	Nov;31(8):1331-45.	syndrome (CFS) and fibromyalgia. Symptoms may be due to: (1) low circulating cortisol; (2) disturbance of central neurotransmitters; or (3) disturbance of the relationship between cortisol and central neurotransmitter function. Accumulating evidence of the complex relationship between cortisol and 5-HT function, make some form of hypothesis (3) most likely. We review the methodology and results of studies of the HPA and other neuroendocrine axes in CFS. METHOD: Medline, Embase and Psychlit were searched using the Cochrane Collaboration strategy. A search was also performed on the King's College CFS database, which includes over 3000 relevant references, and a citation analysis was run on the key paper (Demitrack et al. 1991). RESULTS: One-third of the studies reporting baseline cortisol found it to be significantly low, usually in one-third of patients. Methodological differences may account for some of the varying results. More consistent is the finding of reduced HPA function, and enhanced 5-HT function on neuroendocrine challenge tests. The opioid system, and arginine vasopressin (AVP) may also be abnormal, though the growth hormone (GH) axis appears to be intact, in CFS. CONCLUSIONS: The significance of these changes, remains unclear. We have little understanding of how neuroendocrine changes relate to the experience of symptoms, and it is unclear whether these changes are primary, or secondary to behavioural changes in sleep or exercise. Longitudinal studies of populations at risk for CFS will help to resolve these issues.
Patarca R.	Department of Medicine, University of Miami School of Medicine, Florida 33101, USA. rpatarca@pol.net	Cytokines and chronic fatigue syndrome.	Ann N Y Acad Sci. 2001 Mar;933:185-200.	Chronic fatigue syndrome (CFS) patients show evidence of immune activation, as demonstrated by increased numbers of activated T lymphocytes, including cytotoxic T cells, as well as elevated levels of circulating cytokines. Nevertheless, immune cell function of CFS patients is poor, with low natural killer cell cytotoxicity (NKCC), poor lymphocyte response to mitogens in culture, and frequent immunoglobulin deficiencies, most often IgG1 and IgG3. Immune dysfunction in CFS, with predominance of so-called T-helper type 2 and proinflammatory cytokines, can be episodic and associated with either cause or effect of the physiological and psychological function derangement and/or activation of latent viruses or other pathogens. The interplay of these factors can account for the perpetuation of disease with remission/exacerbation cycles. A T-helper type 2 predominance has been seen among Gulf War syndrome patients and this feature may also be present in other related disorders, such as multiple chemical sensitivity. Therapeutic intervention aimed at induction of a more favorable cytokine expression pattern and immune status appears promising.
Patarca-Montero R, Antoni M, Fletcher MA, Klimas NG.	E. M. Papper Laboratory of Clinical Immunology, Center for Behavioral Medicine Research, Miami Veterans Administration Medical Center, University of Miami School of Medicine, P.O. Box 016960, Miami, FL 33101, USA.	Cytokine and other immunologic markers in chronic fatigue syndrome and their relation to neuropsychological factors.	Appl Neuropsychol. 2001;8(1):51-64.	The literature is reviewed and data are presented that relate to a model we have developed to account for the perpetuation of the perplexing disorder currently termed chronic fatigue syndrome (CFS). In patients with CFS there is chronic lymphocyte overactivation with cytokine abnormalities that include perturbations in plasma levels of proinflammatory cytokines and decrease in the ratio of Type 1 to Type 2 cytokines produced by lymphocytes in vitro following mitogen stimulation. The initiation of the syndrome is frequently sudden and often follows an acute viral illness. Our model for the subsequent chronicity of this disorder holds that the interaction of psychological factors (distress associated with either CFS-related symptoms or other stressful life events) and the immunologic dysfunction contribute to (a) CFS-related physical symptoms (e.g., perception of fatigue and cognitive difficulties, fever, muscle and joint pain) and increases in illness burden and (b) impaired immune surveillance associated with cytotoxic lymphocytes with resulting activation of latent herpes viruses.
Patarca-Montero R, Klimas NG, Fletcher MA.		Immunotherapy of Chronic Fatigue Syndrome: Therapeutic Interventions Aimed at Modulating the Th1/Th2 Cytokine Expression Balance	Journal of Chronic Fatigue Syndrome 2001; 8(1): 3	Based on the postulates of viral and autoimmune etiologies of CFS, several interventions have been designed and tested by different research groups around the world, including the United States, Sweden, United Kingdom, Italy, and Japan. This review addresses those interventions aimed at altering the balance of certain cytokines, the mediators of immune responses. Patients with CFS who show evidence of activation of the immune system have poor immune cell function and a predominance of what is called a T-helper (Th)2-type cytokine response when their lymphocytes are activated. A Th2-type response, which is characterized by production of cytokines such as interleukin (IL)-4, -5, and -10, favors the function of B lymphocytes, the cellular factories of immunoglobulins. A predominance of a Th2-type response is therefore consistent with pathologies, such as autoimmunity and atopy, which are based on inappropriate production of immunoglobulins. Many of the CFS therapies discussed decrease the Th2-type predominance seen at baseline in CFS patients, thereby allowing a greater predominance of a Th1-type response, which favors the function of macrophages and natural killer cells. The function of the latter cells, which have the natural ability of directly destroying invading microbes and cancer cells, is defective in untreated CFS patients. Typical Th1-type cytokines include IL-2 and interferon-gamma, and some of the therapies induce their production. The interventions discussed in this review cover a wide spectrum of therapeutic tools ranging from lymph node cell immunotherapy, herbal products, and small molecules to vaccines. Despite the controversies on the etiology of CFS, immunotherapy research is useful and necessary.

Patarca-Montero R.		Fibromyalgia: Literature in Review (1999-2000)	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 63	Definition of Fibromyalgia, Disability and Functional Status Assessments, Endocrinology, Epidemiology, Immunology, Microbiology, Neurology, Pathophysiology, Pediatrics, Psychiatry, Psychology, Related Disorders and Complications, Treatment.
Patarca-Montero R.		Fibromyalgia	Journal of Chronic Fatigue Syndrome 2001; 9(3/4): 21 - 161	Although much has been learned over the last decade about fibromyalgia, much remains to be learned about its causes, nosology, treatment, and overlap with a variety of rheumatic and nonrheumatic conditions. Advances in rheumatology, cardiovascular medicine, endocrinology, epidemiology, immunology, infectious diseases, neurology, psychiatry, and psychology have served as the basis for the formulation of new lines of research and novel therapeutic interventions. The purpose of this review is to summarize the knowledge gained and published mainly within the last decade.
Pauk J, Buchwald D, Corey L.		Letter to the editor: human herpesvirus 6 serologic responses.	J Clin Virol. 2001 Apr;21(1):103-4.	
Paul LM, Wood L, Maclaren W.	Department of Physiotherapy, Podiatry and Radiography, Glasgow Caledonian University, City Campus, Cowcaddens Road, Scotland G4 OBA, Glasgow, UK. l.paul@gcal.ac.uk	The effect of exercise on gait and balance in patients with chronic fatigue syndrome.	Gait Posture. 2001 Jul;14(1):19-27.	This study investigated anecdotal reports of gait and balance abnormalities in subjects with Chronic Fatigue Syndrome (CFS) by examining the effects of a light exercise test on postural sway and various gait parameters. Tests were performed on 11 CFS patients and 11 age- and sex-matched sedentary controls. Results demonstrated that postural sway was not significantly different in both groups before or after the exercise test. There were, however, significant differences in gait parameters between the two groups confirming anecdotal evidence, but these differences were not exacerbated by the exercise test. Heart rate responses demonstrated that both groups were exercising at similar loads, although this was perceived to be higher by the CFS group.
Peachey E.	Salisbury District Hospital.	Myalgic encephalomyelitis. Myth, mystery or misunderstood?	Pract Midwife. 2001 Apr;4(4):29-31.	
Petri H, Graffelman AW, Knuistingh Neven A, Springer MP, Mearin L, Von Blomberg BM, Visser JT.		Coeliac disease and chronic fatigue syndrome.	Int J Clin Pract. 2001 Jan-Feb;55(1):71.	
Petrie KJ, Sivertsen B, Hysing M, Broadbent E, Moss-Morris R, Eriksen HR, Ursin H.	Health Psychology Research Group, Faculty of Medicine and Health Sciences, The University of Auckland, Auckland, New Zealand. kj.petrie@auckland.ac.nz	Thoroughly modern worries: the relationship of worries about modernity to reported symptoms, health and medical care utilization.	J Psychosom Res. 2001 Jul;51(1):395-401.	OBJECTIVE: There is now greater public concern about how features of modern life pose threats to personal health. In two studies, we investigated the relationship between individuals' worries about modernity affecting health to symptom reports, perceptions of health and health care utilization. METHODS: In the first study, 526 University students completed a questionnaire measuring modern health worries (MHW), symptom reports and health perceptions. A second study utilized an existing national survey database of 7869 New Zealanders. Part of the survey examined people's concerns of modernity affecting their health in the past 12 months, as well as the use of conventional medical and alternative health care. RESULTS: We found concerns about modernity affecting health were made up of four major components: environmental pollution, toxic interventions, tainted food and radiation. MHW were significantly associated with somatic complaints and ratings of the importance of health to the individual. We also found individuals with high levels of MHW had a higher rate of food intolerance and chronic fatigue syndrome (CFS). In the second study, we found MHW to be associated with medical care utilization, particularly of alternative health practitioners. CONCLUSIONS: The results of these studies suggest concerns about modernity do cause changes in the way individuals interpret somatic information and may play a role in undermining perceptions of health. The area of MHW is worthy of study and may hold importance for understanding aspects of functional disorders.
Powell P, Bentall RP, Nye FJ, Edwards RH.	Regional Infectious Diseases Unit, University Hospital Aintree, Liverpool L9 7AL.	Randomised controlled trial of patient education to encourage graded exercise in chronic fatigue syndrome.	BMJ. 2001 Feb 17;322(7283):387-90. Comment in: ACP Journal Club 2001 Sep-Oct;135(2):46. BMJ. 2001 Jun 23;322(7301):1545-6.	OBJECTIVE: To assess the efficacy of an educational intervention explaining symptoms to encourage graded exercise in patients with chronic fatigue syndrome. DESIGN: Randomised controlled trial. SETTING: Chronic fatigue clinic and infectious diseases outpatient clinic. SUBJECTS: 148 consecutively referred patients fulfilling Oxford criteria for chronic fatigue syndrome. INTERVENTIONS: Patients randomised to the control group received standardised medical care. Patients randomised to intervention received two individual treatment sessions and two telephone follow up calls, supported by a comprehensive educational pack, describing the role of disrupted physiological regulation in fatigue symptoms and encouraging home based graded exercise. The minimum intervention group had no further treatment, but the telephone intervention group received an additional seven

				follow up calls and the maximum intervention group an additional seven face to face sessions over four months. MAIN OUTCOME MEASURE: A score of ≥ 25 or an increase of ≥ 10 on the SF-36 physical functioning subscale (range 10 to 30) 12 months after randomisation. RESULTS: 21 patients dropped out, mainly from the intervention groups. Intention to treat analysis showed 79 (69%) of patients in the intervention groups achieved a satisfactory outcome in physical functioning compared with two (6%) of controls, who received standardised medical care ($P < 0.0001$). Similar improvements were observed in fatigue, sleep, disability, and mood. No significant differences were found between the three intervention groups. CONCLUSIONS: Treatment incorporating evidence based physiological explanations for symptoms was effective in encouraging self managed graded exercise. This resulted in substantial improvement compared with standardised medical care.
Prins JB, Bleijenberg G, Bazelmans E, Elving LD, de Boo TM, Severens JL, van der Wilt GJ, Spinhoven P, van der Meer JW.	Department of Medical Psychology, University Medical Centre, Nijmegen, The Netherlands. j.prins@cksmips.azn.nl	Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial.	Lancet. 2001 Mar 17;357(9259):841-7.	BACKGROUND: Cognitive behaviour therapy (CBT) seems a promising treatment for chronic fatigue syndrome (CFS), but the applicability of this treatment outside specialised settings has been questioned. We compared CBT with guided support groups and the natural course in a randomised trial at three centres. METHODS: Of 476 patients diagnosed with CFS, 278 were eligible and willing to take part. 93 were randomly assigned CBT (administered by 13 therapists recently trained in this technique for CFS), 94 were assigned the support-group approach, and 91 the control natural course. Multidimensional assessments were done at baseline, 8 months, and 14 months. The primary outcome variables were fatigue severity (on the checklist individual strength) and functional impairment (on the sickness impact profile) at 8 and 14 months. Data were analysed by intention to treat. FINDINGS: 241 patients had complete data (83 CBT, 80 support groups, 78 natural course) at 8 months. At 14 months CBT was significantly more effective than both control conditions for fatigue severity (CBT vs support groups 5.8 [2.2-9.4]; CBT vs natural course 5.6 [2.1-9.0]) and for functional impairment (CBT vs support groups 263 [38-488]; CBT vs natural course 222 [3-441]). Support groups were not more effective for CFS patients than the natural course. Among the CBT group, clinically significant improvement was seen in fatigue severity for 20 of 58 (35%), in Karnofsky performance status for 28 of 57 (49%), and self-rated improvement for 29 of 58 (50%). Prognostic factors for outcome after CBT were a higher sense of control predicting more improvement, and a passive activity pattern and focusing on bodily symptoms predicting less improvement. INTERPRETATION: CBT was more effective than guided support groups and the natural course in a multicentre trial with many therapists. Our study showed a lower proportion of patients with improvement than CBT trials with a few highly skilled therapists.
Proctor SP, Heaton KJ, White RF, Wolfe J.	Boston Environmental Hazards Center (116B-4), 150 South Huntington Avenue, Boston, MA 02130-4893, USA. sproctor@bu.edu	Chemical sensitivity and chronic fatigue in Gulf War veterans: a brief report.	J Occup Environ Med. 2001 Mar;43(3):259-64.	The foci of this brief report are to (1) describe the prevalence of chemical sensitivity (CS) and chronic fatigue (CF) symptomatology and of presumptive multiple CS and CF syndrome diagnoses, and (2) explore the potential overlap between one purported case definition (i.e., chronic multi-symptom illness) and these unexplained symptom syndromes in a well-characterized group of Gulf War veterans. The number of subjects with CS and CF symptomatology and presumptive multiple CS and CF syndrome diagnoses was higher in the Gulf War-deployed group compared with a group deployed to Germany during the Gulf War. However, the percent differences were not significant when comparing the presumptive diagnoses of multiple CS and CF syndrome. The characteristic differences between the groups and the overlap with chronic multi-symptom illness are also discussed.
Racciatti D, Guagnano MT, Vecchiet J, De Remigis PL, Pizzigallo E, Della Vecchia R, Di Sciascio T, Merlitti D, Sensi S.	Clinic of Infectious Diseases, University of Chieti, Chieti, Italy.	Chronic fatigue syndrome: circadian rhythm and hypothalamic-pituitary-adrenal (HPA) axis impairment.	Int J Immunopathol Pharmacol. 2001 Jan-Apr;14(1):11-15.	Chronic Fatigue Syndrome (CFS) is a clinical condition characterized by a persistent or relapsing debilitating fatigue at rest, lasting more than 6 months, and made worse by exercise. At the present moment, there are three potential etiopathogenic factors: immunologic, viral and neuroendocrine. The purpose of our study was to evaluate possible alterations of the hypothalamic-pituitary-adrenal (HPA) axis in our CFS patients by studying the circadian rhythms of prolactin (PRL), thyrotropic hormone (TSH), adrenocorticotrophic hormone (ACTH), and cortisol (CS). A total of 36 patients were enrolled according to the Centers for Disease Control and Prevention case-definition criteria. Twenty healthy subjects were included as controls. Blood samples were taken every 4 hours during a single 24-hour period. We performed a fluorometric enzyme immunoassay with serum PRL, cortisol and TSH, and an immunoradiometric assay with plasma ACTH. The circadian rhythms of PRL, TSH, ACTH and CS were statistically significant in both CFS and control groups. At 24:00 and 04:00 hrs the CFS patients showed lower ACTH levels than healthy subjects ($p < 0.003$; 0.001); the PRL levels were higher at 04.00 h in CFS patients than in healthy subjects.
Racciatti D, Vecchiet J, Ceccomancini A, Ricci F, Pizzigallo E.	Department of Infectious Diseases, G. D'Annunzio University, Chieti Scalo, Italy. racciattd@unich.it	Chronic fatigue syndrome following a toxic exposure.	Sci Total Environ. 2001 Apr 10;270(1-3):27-31.	Chronic fatigue syndrome (CFS) is a clinical entity characterized by severe fatigue lasting more than 6 months and other well-defined symptoms. Even though in most CFS cases the etiology is still unknown, sometimes the mode of presentation of the illness implicates the exposure to chemical and/or food toxins as precipitating factors: ciguatera poisoning, sick building syndrome, Gulf War syndrome, exposure to organochlorine pesticides, etc. In

				the National Reference Center for CFS Study at the Department of Infectious Diseases of 'G. D'Annunzio' University (Chieti) we examined five patients (three females and two males, mean age: 37.5 years) 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. These patients were compared and contrasted with two sex- and age-matched subgroups of CFS patients without any history of exposure to toxins: the first subgroup consisted of patients with CFS onset following an EBV infection (post-infectious CFS), and the second of patients with a concurrent diagnosis of major depression. All subjects were investigated by clinical examination, neurophysiological and immunologic studies, and neuroendocrine tests. 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+). These findings may help in understanding the pathogenetic mechanisms involved in CFS.
Redelmeier DA, Tu JV, Schull MJ, Ferris LE, Hux JE.	Department of Medicine, University of Toronto, Toronto, Ont. dar@ices.on.ca	Problems for clinical judgement: 2. Obtaining a reliable past medical history.	CMAJ. 2001 Mar 20;164(6):809-13.	Ordinary human reasoning may lead patients to provide an unreliable history of past experiences because of errors in comprehension, recall, evaluation and expression. Comprehension of a question may change depending on the definition of periods of time and prior questions. Recall fails through the loss of relevant information, the fabrication of misinformation and distracting cues. Evaluations may be mistaken because of the "halo effect" and a reluctance to change personal beliefs. Expression is influenced by social culture and the environment. These errors can also occur when patients report a history of present illness, but they tend to be more prominent with experiences that are more remote. An awareness of these specific human fallibilities might help clinicians avoid some errors when eliciting a patient's past medical history.
Regland, Zachrisson O, Stejskal V, Gottfries C-G.		Nickel Allergy Is Found in a Majority of Women with Chronic Fatigue Syndrome and Muscle Pain-And May Be Triggered by Cigarette Smoke and Dietary Nickel Intake	Journal of Chronic Fatigue Syndrome 2001; 8(1): 57	Two hundred and four women with chronic fatigue and muscle pain, with no signs of autoimmune disorder, received immune stimulation injections with a Staphylococcus vaccine at monthly intervals over 6 months. Good response was defined as a decrease by at least 50% of the total score on an observer's rating scale. Nickel allergy was evaluated as probable if the patient had a positive history of skin hypersensitivity from cutaneous exposure to metal objects. The patient's smoking habits were recorded. Fifty-two percent of the patients had a positive history of nickel contact dermatitis. There were significantly more good responders among the non-allergic non-smokers (39%) than among the allergic smokers (6%). We also present case reports on nickel-allergic patients who apparently improved after cessation of cigarette smoking and reducing their dietary nickel intake. Our observations indicate that exposure to nickel, by dietary intake or inhalation of cigarette smoke, may trigger systemic nickel allergy and contribute to syndromes of chronic fatigue and muscle pain.
Reid S, Hotopf M, Hull L, Ismail K, Unwin C, Wessely S.	Academic Department of Psychiatry, Guy's King's and St. Thomas' School of Medicine and Institute of Psychiatry, London, United Kingdom.	Multiple chemical sensitivity and chronic fatigue syndrome in British Gulf War veterans.	Am J Epidemiol. 2001 Mar 15;153(6):604-9.	The objective of this study was to measure the prevalence of multiple chemical sensitivity (MCS) and chronic fatigue syndrome (CFS) in British Gulf War veterans and to investigate their association with reported exposures and psychologic morbidity. In 1997--1998, the authors undertook a cross-sectional survey of three cohorts of British military personnel comprising Gulf veterans (n = 3,531), those who had served in Bosnia (n = 2,050), and those serving during the Gulf War but not deployed there (Era cohort, n = 2,614). MCS and CFS were defined according to operational criteria. The prevalence of MCS in the Gulf, Bosnia, and Era cohorts was 1.3%, 0.3%, and 0.2%, respectively. For CFS, the prevalence was 2.1% (Gulf cohort), 0.7% (Bosnia cohort), and 1.8% (Era cohort). In Gulf veterans, MCS was strongly associated with exposure to pesticides (adjusted odds ratio = 12.3, 95% confidence interval: 5.1, 30.0). Both syndromes were associated with high levels of psychologic morbidity. These findings suggest that CFS and MCS account for some of the medically unexplained illnesses reported by veterans after deployment to the Gulf. MCS was particularly associated with Gulf deployment and self-reported exposure to pesticides, findings that merit further exploration given the controversial status of this diagnosis and the potential for recall bias in a questionnaire survey.
Reinhart WH, Fleisch F.	Departement Innere Medizin, Kantonsspital Chur. walter.reinhart@ksc.gr.ch	[Fatigue] [Article in German	Schweiz Rundsch Med Prax. 2001 Nov 15;90(46):2015-8.	Fatigue is one of the most frequent symptoms in medicine. A detailed history must include sleeping habits, other diseases, drugs, and concomitant symptoms. A physical examination is necessary, followed by laboratory tests and imaging techniques, which must be used in a cost-effective manner. When underlying diseases are excluded, a chronic fatigue syndrome may be present. Its pathogenesis is largely unknown. Established treatment options in chronic fatigue syndrome are graded exercise, antidepressants in case of depression and anxiety, and cognitive behaviour treatment. The large number of other treatments including diets have no proven value. Fatigue remains a diagnostic and therapeutic challenge to the physician.
Repka-Ramirez MS, Naranch K, Park YJ, Velarde A, Clauw D.	Department of Medicine, Georgetown University, Washington, DC 20007-	IgE levels are the same in chronic fatigue syndrome (CFS) and control subjects	Ann Allergy Asthma Immunol. 2001 Sep;87(3):218-21.	BACKGROUND: Chronic fatigue syndrome (CFS) has an uncertain pathogenesis. Allergies have been suggested as one cause. OBJECTIVE: The aim of this study was to compare serum immunoglobulin (Ig)E in CFS and control subjects to determine whether IgE levels were elevated in CFS. This would be suggestive of increased atopy in

Baraniuk JN.	2197, USA.	when stratified by allergy skin test results and rhinitis types.		CFS. METHODS: IgE was measured by quantitative ELISA (sandwich) immunoassay in 95 CFS and 109 non-CFS control subjects. Subjects were classified by positive or negative allergy skin tests (AST) and rhinitis questionnaires (rhinitis score, RhSc) into four rhinitis types: nonallergic rhinitis (NAR with positive RhSc and negative AST); allergic rhinitis (AR with positive AST and RhSc); atopic/no rhinitis (AST positive/RhSc negative); and nonatopic/no rhinitis (both AST and RhSc negative) subjects. RESULTS: IgE was not significantly different between control (128 +/- 18 IU/mL, mean +/- SEM) and CFS (133 +/- 43 IU/mL) groups, or between control and CFS groups classified into the four rhinitis types. IgE was significantly higher in subjects with positive AST whether or not they had positive RhSc or CFS symptoms. CONCLUSIONS: Elevated IgE and positive AST indicate allergen sensitization, but are not necessarily indicators of symptomatic allergic diseases. There was no association between IgE levels and CFS, indicating that atopy was probably not more prevalent in CFS. Therefore, TH2-lymphocyte and IgE-mast cell mechanisms are unlikely causes of CFS.
Richardson J.		Viral Isolation from Brain in Myalgic Encephalomyelitis	Journal of Chronic Fatigue Syndrome 2001; 9(3/4): 15 - 19	
Ridsdale L, Godfrey E, Chalder T, Seed P, King M, Wallace P, Wessely S; Fatigue Trialists' Group.	Department of General Practice, Guy's, King's and St Thomas's School of Medicine, King's College, 5 Lambeth Walk, London SE11 6SP. L.Ridsdale@iop.kcl.ac.uk	Chronic fatigue in general practice: is counselling as good as cognitive behaviour therapy? A UK randomised trial.	Br J Gen Pract. 2001 Jan;51(462):19-24. Comment in: Br J Gen Pract. 2001 Apr;51(465):316-7. Br J Gen Pract. 2001 Apr;51(465):317-8.	BACKGROUND: Fatigue is a common symptom for which patients consult their doctors in primary care. With usual medical management the majority of patients report that their symptoms persist and become chronic. There is little evidence for the effectiveness of any fatigue management in primary care. AIM: To compare the effectiveness of cognitive behaviour therapy (CBT) with counselling for patients with chronic fatigue and to describe satisfaction with care. DESIGN OF STUDY: Randomised trial with parallel group design. SETTING: Ten general practices located in London and the South Thames region of the United Kingdom recruited patients to the trial between 1996 and 1998. Patients came from a wide range of socioeconomic backgrounds and lived in urban, suburban, and rural areas. METHOD: Data were collected before randomisation, after treatment, and six months later. Patients were offered six sessions of up to one hour each of either CBT or counselling. Outcomes include: self-report of fatigue symptoms six months later, anxiety and depression, symptom attributions, social adjustment and patients' satisfaction with care. RESULTS: One hundred and sixty patients with chronic fatigue entered the trial, 45 (28%) met research criteria for chronic fatigue syndrome; 129 completed follow-up. All patients met Chalder et al's standard criteria for fatigue. Mean fatigue scores were 23 on entry (at baseline) and 15 at six months' follow-up. Sixty-one (47%) patients no longer met standard criteria for fatigue after six months. There was no significant difference in effect between the two therapies on fatigue (1.04 [95% CI = -1.7 to 3.7]), anxiety and depression or social adjustment outcomes for all patients and for the subgroup with chronic fatigue syndrome. Use of antidepressants and consultations with the doctor decreased after therapy but there were no differences between groups. CONCLUSION: Counselling and CBT were equivalent in effect for patients with chronic fatigue in primary care. The choice between therapies can therefore depend on other considerations, such as cost and accessibility.
Robertson-Ritchie H.		Toward a new definition of chronic fatigue syndrome.	West J Med. 2001 Apr;174(4):241.	
Robinson GL, McGregor NR, Roberts TK, Dunstan RH, Butt H.	Special Education Centre, University of Newcastle, Callaghan, New South Wales, Australia.	A biochemical analysis of people with chronic fatigue who have Irlen Syndrome: speculation concerning immune system dysfunction.	Percept Mot Skills. 2001 Oct;93(2):486-504.	This study investigated the biological basis of visual processing disabilities in adults with Chronic Fatigue Syndrome. The study involved 61 adults with symptoms of Chronic Fatigue Syndrome who were screened for visual processing problems (Irlen Syndrome) and divided into two groups according to the severity of symptoms of Irlen Syndrome. Significant variations were identified in blood lipids and urine amino and organic acids of the two groups, which may be indicative of activation of the immune system due to some infective agent. It was suggested that metabolic profiling may help the development of more valid diagnostic categories and allow more investigation of immune system dysfunction as a possible causal factor in a range of learning and behaviour disorders.
Roelens S, Herst CV, D'Haese A, De Smet K, Frémont M, De Meirleir K, Englebienne P.		G-Actin Cleavage Parallels 2-5A-Dependent RNase L Cleavage in Peripheral Blood Mononuclear Cells- Relevance to a Possible Serum-Based Screening Test for Dysregulations in the 2-5A Pathway	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 63	A dysregulation in the 2N,5N-oligoadenylate (2-5A)-dependent RNase L antiviral pathway has been detected in peripheral blood mononuclear cells (PBMC) of chronic fatigue syndrome (CFS) patients, which is characterized by an unregulated RNase L activity and the presence of a low molecular weight (LMW) 2-5A-binding protein (37-kDa 2-5A-BP). This study was undertaken to test the possibility that the 37-kDa 2-5A-BP of CFS is produced by proteolytic cleavage of the 80-kDa monomeric enzyme. Incubation of the 80-kDa human recombinant RNase L (r-hRNase L) with PBMC extracts either positive or negative for the presence of 37-kDa 2-5A-BP, respectively, demonstrates that the LMW protein is produced by the former, not the latter, and that the size of the fragment generated from the recombinant protein matches the 37-kDa size of the fragment observed in the original PBMC.

				Digestion of r-hRNase L with calpain generated the same 37-kDa 2-5A-BP observed in PBMC extracts, and calpain immunoprecipitation from PBMC extracts reduced their proteolytic activity, an observation that suggests that calpain may be involved in the cleavage. We further examined G-actin, a known calpain substrate, for possible cleavage in PBMC. Actin fragments were observed of which the presence correlated with the presence of 37-kDa 2-5-BP. Since G-actin is cleared by serum transport, we further screened serum samples for the presence of LMW forms. A single LMW actin fragment could be detected in serum, the presence of which correlated significantly with the presence of both G-actin and RNase L fragments in PBMC. This latter observation offers the opportunity to screen large populations of patients for dysregulations in the RNase L pathway by a serum-based assay.
Rosenqvist P.	Psykiatriska kliniken, Kalmar, per.rosenqvist@ltblekinge.se	[Stress-related fatigue--some therapeutic experiences] [Article in Swedish]	Lakartidningen. 2001 Nov 28;98(48):5549-50, 5553.	
Ross S, Fantie B, Straus SF, Grafman J.	Department of Psychology, American University, Washington, DC, USA.	Divided attention deficits in patients with chronic fatigue syndrome.	Appl Neuropsychol. 2001;8(1):4-11.	Chronic fatigue syndrome (CFS) patients and controls were compared on a variety of mood state, personality, and neuropsychological measures, including memory, word finding, and attentional tasks that required participants to focus, sustain, or divide their attention, or to perform a combination of these functions. CFS patients demonstrated a selective deficit on 3 measures of divided attention. Their performance on the other neuropsychological tests of intelligence, fluency, and memory was no different than that of normal controls despite their reports of generally diminished cognitive capacity. There was an inverse relation between CFS patient fatigue severity and performance on 1 of the divided attention measures. Given these findings, it is probable that CFS patients will report more cognitive difficulties in real-life situations that cause them to divide their effort or rapidly reallocate cognitive resources between 2 response channels (vision and audition).
Rowe PC, Calkins H, DeBusk K, McKenzie R, Anand R, Sharma G, Cuccherini BA, Soto N, Hohman P, Snader S, Lucas KE, Wolff M, Straus SE.	Departments of Pediatrics and Medicine, Johns Hopkins Hospital, 600 N Wolfe St, Baltimore, MD 21287, USA.	Fludrocortisone acetate to treat neurally mediated hypotension in chronic fatigue syndrome: a randomized controlled trial.	JAMA. 2001 Jan 3;285(1):52-9. Comment in: JAMA. 2001 Mar 21;285(11):1441-2; discussion 1443. JAMA. 2001 Mar 21;285(11):1442-3. JAMA. 2001 Mar 21;285(11):1442; discussion 1443.	CONTEXT: Patients with chronic fatigue syndrome (CFS) are more likely than healthy persons to develop neurally mediated hypotension (NMH) in response to prolonged orthostatic stress. OBJECTIVE: To examine the efficacy of fludrocortisone acetate as monotherapy for adults with both CFS and NMH. DESIGN: Randomized, double-blind, placebo-controlled trial conducted between March 1996 and February 1999. SETTING: Two tertiary referral centers in the United States. PATIENTS: One hundred individuals aged 18 to 50 years who satisfied Centers for Disease Control and Prevention criteria for CFS and had NMH provoked during a 2-stage tilt-table test. Eighty-three subjects had adequate outcome data to assess efficacy. INTERVENTION: Subjects were randomly assigned to receive fludrocortisone acetate, titrated to 0.1 mg/d (n = 50) or matching placebo (n = 50) for 9 weeks, followed by 2 weeks of observation after discontinuation of therapy. MAIN OUTCOME MEASURE: Proportion of subjects in each group with at least a 15-point improvement on a 100-point global wellness scale. RESULTS: Baseline demographic and illness characteristics between the groups were similar; CFS had been present for at least 3 years in 71%. Using an intention-to-treat analysis, 7 subjects (14%) treated with fludrocortisone experienced at least a 15-point improvement in their wellness scores compared with 5 (10%) among placebo recipients (P = .76). No differences were observed in several other symptom scores or in the proportion with normal follow-up tilt test results at the end of the treatment period. CONCLUSIONS: In our study of adults with CFS, fludrocortisone as monotherapy for NMH was no more efficacious than placebo for amelioration of symptoms. Failure to identify symptomatic improvement with fludrocortisone does not disprove the hypothesis that NMH could be contributing to some of the symptoms of CFS. Further studies are needed to determine whether other medications or combination therapy are more effective in treating orthostatic intolerance in patients with CFS.
Ruchko VM, Makhelai LI, Borisevich SV, Makhelai AA.		[Chronic fatigue and immune dysfunction syndrome] [Article in Russian]	Vopr Virusol. 2001 May-Jun;46(3):46-8.	
Sachs L.	Department of Communication Studies, Linköping University, Sweden. lisbeth.sachs@swipnet.se	From a lived body to a medicalized body: diagnostic transformation and chronic fatigue syndrome.	Med Anthropol. 2001;19(4):299-317. Comment in: Med Anthropol. 2001;19(4):411-3.	This paper addresses the diagnostic dilemma posed by chronic illness that offers no demonstrable evidence of serious physical disorders or pathology. Is a diagnosis such as chronic fatigue syndrome (CFS) disabling because it encourages people to identify with it? Does it become a self-fulfilling prophecy? In providing people with a name, and thus allowing them to confirm the legitimacy of their suffering, a diagnosis of CFS may help them to relate to their world and, hence, facilitate their recovery. One of the most relevant questions pertaining to a diagnosis of CFS concerns how people deal with suffering when it does not come with a biomedically established pathology. I draw upon material provided by 21 men and women diagnosed with CFS. My analysis concerns the ambivalence involved in the diagnostic process and its implications for the relationship between self-identity and chronicity.

Sakaino H.	Department of Oral Surgery, Kurume University School of Medicine, Kurume 830-0011, Japan.	The biochemical study of intermaxillary fixation (IMF) stress in oral surgery inpatients.	Kurume Med J. 2001;48(1):71-7.	Although intermaxillary fixation (IMF) is performed to treat the patients with maxillary fracture, this procedure is very stressful to the patients. IMF has been reported to increase noradrenaline (NA) release in the brain and elevate plasma corticosterone contents in the rat. These changes were significantly attenuated by diazepam, an anxiolytic of the benzodiazepine family. These results suggest that IMF could greatly affect the pituitary-adrenal system as a stress. In the present study, in order to examine the influence of IMF on the human body function, we measured levels of 17-hydrocorticosteroids (17-OHCS) and 17-ketosteroid (17-KS), which are metabolites of the adrenocortical hormone cortisol, in the urine of inpatients undergoing IMF. The subjects were requested to fill out a questionnaire on irritableness caused by IMF. In these patients, urinary 17-OHCS levels were significantly increased after IMF and well correlated to the results of the questionnaire. The finding suggested that urinary 17-OHCS levels reflect stress related to IMF, and that such stress mainly causes an irritated feeling. Natural killer cell activity (NK activity), which is considered to be related to stress, was measured in these patients. The relationship between 17-OHCS levels and NK activity was examined in reference to the results of the questionnaire. Questionnaire showed that most patients noted insomnia and an irritated feeling during IMF. To examine the influence of anxiolytic agents on stress related to IMF, an anxiolytic agent, ethyl loflazepate, was administered during IMF, and urinary 17-OHCS levels were measured. There was no correlation between 17-OHCS levels and NK activity in the patients. Furthermore, no correlation was observed between visual analogue scale (VSA) and NK activity. Increases in 17-OHCS levels in the group treated with ethyl loflazepate, an anxiolytic of the benzodiazepine family, were significantly lower than in the untreated group. This suggests that ethyl loflazepate reduced stress responses to IMF. It has been reported that NK activity is reduced inpatients with depression or chronic fatigue syndrome. However, NK activity may not be affected by mechanical stress such as IMF. The finding that an anxiolytic agent, ethyl loflazepate, inhibited stress responses to IMF further suggests that anxiolytic drugs are very useful for treatment of irritated feeling of the patients undergoing IMF.
Schacterle RS, Conti Fabrizio, Magrini L, Komaroff AL, Valesini G.		Increased Eosinophil Protein X Levels in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 21	Chronic fatigue syndrome is a condition of unknown etiology characterized by severe fatigue and accompanied by symptoms including cognitive difficulties, myalgias, and headaches. Studies of this illness have found chronic activation of the immune system, including one reporting elevated levels of eosinophil cationic protein, considered an eosinophil activation marker. The aim of this study was to measure serum levels of eosinophil protein X, a cationic protein not measured previously in this illness. Measurements are reported on serum samples from 29 patients meeting the Centers for Disease Control and Prevention criteria for chronic fatigue syndrome, and 30 healthy controls of similar age and gender. The median serum eosinophil protein X level in patients was higher than controls: 37.9 vs. 25.3 µg/L (p = 0.037). Forty-eight percent of patients versus 23% of controls had levels above the normal range. The marked increase in serum levels of eosinophil protein X in chronic fatigue syndrome patients could reflect eosinophil activation in this illness.
Selvaratnam P.	Monash University, Melbourne.	Post-operative exercise improves pain, disability and spinal function following microdiscectomy.	Aust J Physiother. 2001;47(3):218.	
Servaes P, van der Werf S, Prins J, Verhagen S, Bleijenberg G.	Dutch Fatigue Research Group, Department of Medical Psychology (118), University Hospital Nijmegen, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands. P.Servaes@cksmpps.azn.nl	Fatigue in disease-free cancer patients compared with fatigue in patients with chronic fatigue syndrome.	Support Care Cancer. 2001 Jan;9(1):11-7.	The goal of our work was to assess fatigue in disease-free cancer patients with help of a validated fatigue questionnaire. Furthermore, we wished to analyse the relationship between severe fatigue and former treatment modalities, problems of concentration and motivation, physical activity, functional impairment, depression and anxiety and finally, to compare severely fatigued disease-free cancer patients and patients with Chronic Fatigue Syndrome (CFS). The participants were 85 adult cancer patients and 16 patients with CFS. The cancer patients were all disease-free and had been off treatment for a minimum of 6 months. They were asked to participate in this study by their physician when they came to the hospital for control visits. Patients who were willing to participate completed four questionnaires. The Checklist Individual Strength was used to measure fatigue. In addition, the Beck Depression Inventory, the Spielberger Trait Anxiety Inventory and the Nottingham Health Profile were used. Results indicate that 19% of the disease-free cancer patients were severely fatigued. Their fatigue experience is comparable to that of patients with CFS. Severe fatigue is associated with problems of concentration and motivation, reduced physical activity, emotional health problems and pain. Furthermore, a relation was found between fatigue and depression and anxiety. No relation was found between fatigue and type of cancer, former treatment modalities, duration of treatment and time since treatment ended. In conclusion, for one fifth of a group of disease-free cancer patients fatigue is a severe problem long after treatment. In addition to fatigue, these patients experience several psychological and physical problems.

Sharma A, Oyebode F, Kendall MJ, Jones DA.	Department of Medicine, Queen Elizabeth Hospital, Birmingham, Edgbaston, Birmingham B15 2TH, UK. a.sharma.1@bham.ac.uk	Recovery from chronic fatigue syndrome associated with changes in neuroendocrine function.	J R Soc Med. 2001 Jan;94(1):26-7.	
Shepherd RJ.	Defence & Civil Institute of Environmental Medicine, and Faculty of Physical Education & Health, University of Toronto, Ontario, Canada. royjshep@mountain-inter.net	Chronic fatigue syndrome: an update.	Sports Med. 2001;31(3):167-94.	The chronic fatigue syndrome is characterised by a fatigue that is disproportionate to the intensity of effort that is undertaken, has persisted for 6 months or longer, and has no obvious cause. Unless there has been a long period of patient- or physician-imposed inactivity, objective data may show little reduction in muscle strength or peak aerobic power, but the affected individual avoids heavy activity. The study of aetiology and treatment has been hampered by the low disease prevalence (probably <0.1% of the general population), and (until recently) by a lack of clear and standardised diagnostic criteria. It is unclear how far the aetiology is similar for athletes and nonathletes. It appears that in top competitors, overtraining and/or a negative energy balance can be precipitating factors. A wide variety of other possible causes and/or precipitating factors have been cited in the general population, including psychological stress, disorders of personality and affect, dysfunction of the hypothalamic-pituitary-adrenal axis, hormonal imbalance, nutritional deficits, immune suppression or activation and chronic infection. However, none of these factors have been observed consistently. The prognosis is poor; often disability and impairment of athletic performance are prolonged. Prevention of overtraining by careful monitoring seems the most effective approach in athletes. In those where the condition is established, treatment should aim at breaking the vicious cycle of effort avoidance, deterioration in physical condition and an increase in fatigue through a combination of encouragement and a progressive exercise programme.
Shepherd C.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):239; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
Shetzline SE, Suhadolnik RJ.	Department of Biochemistry and the Fels Institute for Cancer Research and Molecular Biology, Temple University School of Medicine, Philadelphia, Pennsylvania 19140, USA.	Characterization of a 2',5'-oligoadenylate (2-5A)-dependent 37-kDa RNase L: azido photoaffinity labeling and 2-5A-dependent activation.	J Biol Chem. 2001 Jun 29;276(26):23707-11. Epub 2001 Apr 25. Erratum in: J Biol Chem 2001 Aug 24;276(34):32392.	Upregulation of key components of the 2',5'-oligoadenylate (2-5A) synthetase/RNase L pathway has been identified in extracts of peripheral blood mononuclear cells from individuals with chronic fatigue [corrected] syndrome, including the presence of a low molecular weight form of RNase L. In this study, analysis of 2',5'-oligoadenylate (2-5A) binding and activation of the 80- and 37-kDa forms of RNase L has been completed utilizing photolabeling/immunoprecipitation and affinity assays, respectively. Saturation of photolabeling of the 80- and the 37-kDa RNase L with the 2-5A azido photoprobe, [(32)P]pApAp(8-azidoA), was achieved. Half-maximal photoinsertion of [(32)P]pApAp(8-azidoA) occurred at 3.7 x 10(-8) m for the 80-kDa RNase L and at 6.3 x 10(-8) m for the 37-kDa RNase L. Competition experiments using 100-fold excess unlabeled 2-5A photoaffinity probe, pApAp(8-azidoA), and authentic 2-5A (p(3)A(3)) resulted in complete protection against photolabeling, demonstrating that [(32)P]pApAp(8-azidoA) binds specifically to the 2-5A-binding site of the 80- and 37-kDa RNase L. The rate of RNA hydrolysis by the 37-kDa RNase L was three times faster than the 80-kDa RNase L. The data obtained from these 2-5A binding and 2-5A-dependent activation studies demonstrate the utility of [(32)P]pApAp(8-azidoA) for the detection of the 37-kDa RNase L in peripheral blood mononuclear cell extracts.
Sirois DA, Natelson B.	Department of Oral Medicine, New York University College of Dentistry, New York, USA.	Clinicopathological findings consistent with primary Sjogren's syndrome in a subset of patients diagnosed with chronic fatigue syndrome: preliminary observations.	J Rheumatol. 2001 Jan;28(1):126-31.	OBJECTIVE: Some patients diagnosed with chronic fatigue syndrome (CFS) have symptoms commonly observed in Sjogren's syndrome (SS), particularly xerophthalmia and xerostomia, leading to speculation that some patients with CFS might have primary SS or that the 2 disorders share common pathophysiological features. We investigated the prevalence of symptoms of mucosal dryness, salivary gland pathology, lacrimal hyposalivation, and autoantibodies (antinuclear antibody, SSA/SSB) among patients diagnosed with CFS. METHODS: Twenty-five subjects with CFS and 18 healthy control subjects were interviewed and examined, had a Schirmer test and fluorescein tear dilution, and underwent minor salivary gland (MSG) biopsy. Antibody to nuclear antigen as well as anti-La (SSA) and anti-Ro (SSB) antibody were available for subjects with CFS. Pathologists unaware of the subject group assignment examined labial salivary gland biopsy specimens and calculated a standard MSG score for each specimen. RESULTS: Mucosal dryness was reported by 13/25 (52%) subjects with CFS, of which 8 (32%) also had MSG score, low Schirmer test value, and symptoms consistent with primary SS (p = 0.05). No control subject met diagnostic criteria for primary SS. MSG focus scores < or = 1 were common among both groups (CFS 14/25; controls 15/18). MSG results without pathological alteration were rare, seen in only one control and no CFS patients. Low Schirmer values were found in 10/25 (40%) CFS patients and 1/18 (6%) control (p = 0.01).

				CONCLUSION: A subset of patients with CFS may have primary SS.
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.	
Snell CR, Stevens SR, VanNess JM.		Chronic Fatigue Syndrome, Ampligen, and Quality of Life: A Phenomenological Perspective	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 117	The purpose of this investigation was to identify significant quality-of-life issues for two women previously diagnosed with chronic fatigue syndrome (CFS), and their families. Both women were participants in a cost-recovery, clinical trial of the antiviral and immunomodulatory drug, Ampligen. A qualitative, case study approach was adopted to access information not normally available from clinical trials. Specifically, semi-structured, in-depth interviews were conducted with the CFS patients, and their spouses, to discover if these families perceived any changes in their patterns of daily living contingent with participation in the Ampligen trial. Patient diaries were also analyzed for the purpose of triangulation. Content analysis of the interview transcripts and diary entries revealed a number of significant quality of life improvements for the women and their families, for which they perceived the drug therapy responsible. After an initial acclimation period, and with the exception of the day when the drug was administered, both women reported a reduction in pain, increased energy levels, and improved cognitive functioning. They each cited numerous cases to illustrate their improvement.
Soderberg S, Evengard B.	Huddinge University Hospital, M42, SE-141 86 Huddinge, Sweden. stina.soderberg@hs.sll.se	Short-term group therapy for patients with chronic fatigue syndrome.	Psychother Psychosom. 2001 Mar-Apr;70(2):108-11.	BACKGROUND: This study presents experiences of focused short-term group therapy for patients with chronic fatigue syndrome (CFS). METHODS: Fourteen women diagnosed as CFS patients were randomly placed into two groups. The control group received group therapy 5 months after the first group. The project consisted of 10 group sessions of 1.5 h per week. Sense of coherence (SOC) was used for measuring coping resources, and self-rating scales of quality of life and of fatigue were compared before and after group therapy. RESULTS: The most valuable aspect was the sharing of experiences. More than half of the patients also felt that the sessions had improved psychological well-being through adjustment of ambitions and improved coping with symptoms. CONCLUSION: The study encourages further research. If group therapy is chosen as treatment for these patients, a longer period is recommended. A possible alternative is individualized short-term therapy adapted to each patient's needs, problems and circumstances. Copyright 2001 S. Karger AG, Basel
Speight N, Franklin A.		Does myalgic encephalomyelitis exist?	Lancet. 2001 Jun 9;357(9271):1890. Comment on: Lancet. 2001 Feb 17;357(9255):562.	
Spence VA, Abbot NC.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):239-40; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
St Clair Gibson A, Lambert ML, Noakes TD.	The Medical Research Council, Department of Human Biology, University of Cape Town, South Africa. agibson@sports.uct.ac.za	Neural control of force output during maximal and submaximal exercise.	Sports Med. 2001;31(9):637-50.	A common belief in exercise physiology is that fatigue during exercise is caused by changes in skeletal muscle metabolism. This 'peripheral' fatigue results either from substrate depletion during submaximal exercise or metabolite accumulation during maximal exercise in the exercising muscles. However, if substrate depletion alone caused fatigue, intracellular ATP levels would decrease and lead to rigor and cellular death. Alternatively, metabolite accumulation would prevent any increase in exercise intensity near the end of exercise. At present, neither of these effects has been shown to occur, which suggests that fatigue may be controlled by changes in efferent neural command, generally described as 'central' fatigue. In this review, we examine neural efferent command mechanisms involved in fatigue, including the concepts of muscle wisdom during short term maximal activity, and muscle unit rotation and teleoanticipation during submaximal endurance activity. We propose that neural strategies exist to maintain muscle reserve, and inhibit exercise activity before any irreparable damage to muscles and organs occurs. The finding that symptoms of fatigue occur in the nonexercising state in individuals with chronic fatigue syndrome indicates that fatigue is probably not a physiological entity, but rather a sensory manifestation of these neural regulatory mechanisms.
Staub F, Bogousslavsky J.		[Is there such a thing as brain fatigue?] [Article in French]	Rev Neurol (Paris). 2001 Mar;157(3):259-62.	

Stein E.		Chronic Fatigue Syndrome: Overcoming the Attitudinal Impasse	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 53	Context: Patients with Chronic Fatigue Syndrome and their physicians are often in conflict about the etiology and treatment of CFS. Objectives: 1. Survey the literature regarding physician's attitudes towards CFS; 2. Examine the contributing factors to physician's attitude towards the disorder; and 3. Suggest solutions. Data Sources: The relevant medical and psychological literature (years 1988- 2000) was searched using the search term "Chronic Fatigue Syndrome." This was supplemented with papers from the bibliographies of the retrieved papers, additional related literature, and clinical experience. Data Synthesis: Forty-six to ninety percent of GPs accept CFS as a discrete clinical entity and 30-82% are willing to make the diagnosis in qualifying patients. Conclusions: CFS is a heterogeneous, multifactorial host response disorder that is inadequately described by the biomedical model. Despite substantial evidence of multisystemic physical abnormality in CFS, the lack of pathognomic tests and the female gender predominance cause some physicians to continue to treat CFS as a psychosocial disorder. This leads to conflict between patients and physicians. CFS challenges physicians to think beyond current disease models, to tolerate diagnostic and therapeutic uncertainty, and to work collaboratively with patients rather than taking the role of expert.
Stein MT, First LR, Friedman SB.	University of California, San Diego, USA.	Twelve-year-old girl with chronic fatigue, school absence, and fluctuating somatic symptoms.	J Dev Behav Pediatr. 2001 Apr;22(2 Suppl):S151-6.	
Stevens DL.	Department of Medicine, New York University School of Medicine, Gouverneur Hospital, 227 Madison St, New York, NY 10024, USA. dls3@nyu.edu	Chronic fatigue.	West J Med. 2001 Nov;175(5):315-9.	
Stewart JM.		Orthostatic Intolerance: A Review with Application to the Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(2): 45	The symptoms of the chronic fatigue syndrome closely match those of chronic orthostatic intolerance and research suggests that orthostatic intolerance plays a role in the symptomatology of CFS. Recent investigations support the hypothesis that findings in CFS patients result at least in part from impaired blood pressure and heart rate regulation. Orthostatic intolerance has been implicated. Effective and specific treatment for chronic orthostatic intolerance can only be developed when a specific etiology or etiologies are discovered.
Streeten DH.	Department of Medicine, SUNY Upstate Medical University, Syracuse, New York 13210, USA.	Role of impaired lower-limb venous innervation in the pathogenesis of the chronic fatigue syndrome.	Am J Med Sci. 2001 Mar;321(3):163-7.	BACKGROUND: In patients with acute orthostatic hypotension, there is excessive pooling of blood in the legs, which may result from the strikingly subnormal compliance that is demonstrable in the pedal veins during norepinephrine infusion. The common occurrence of delayed orthostatic hypotension and/or tachycardia in the chronic fatigue syndrome (CFS) led to the present studies of foot vein compliance in CFS patients with a linear variable differential transformer. METHODS: Seven patients with CFS were compared with 7 age- and gender matched healthy control subjects in their blood pressure, heart-rate, and plasma norepinephrine responses to prolonged standing and in measurements of their foot vein contractile responses to intravenous norepinephrine infusions with the linear variable differential transformer. RESULTS: Excessive, delayed (usually after 10 min) orthostatic reductions in systolic and diastolic blood pressure ($P < 0.01$) and inconsistently excessive increases in heart rate were found in the CFS patients, in whom venous compliance in response to infused norepinephrine was significantly reduced ($P < 0.05$). CONCLUSIONS: In these patients with CFS, delayed orthostatic hypotension was clearly demonstrable, and, as in previously reported patients with orthostatic hypotension of acute onset, this was associated with reduced pedal vein compliance during norepinephrine infusion, implying impaired sympathetic innervation of foot veins. The rapid symptomatic improvement demonstrated in previous studies of CFS patients during correction of orthostatic venous pooling by inflation of military antishock trousers (MAST) to 35 mm Hg may suggest that excessive lower body venous pooling, perhaps by reducing cerebral perfusion, is involved in the orthostatic component of fatigue in these patients.
Strickland PS, Levine PH., Peterson DL, O'Brien K, Fears T.		Neuromyasthenia and Chronic Fatigue Syndrome (CFS) in Northern Nevada/California: A Ten-Year Follow-Up of an Outbreak	Journal of Chronic Fatigue Syndrome 2001; 9(3/4): 3 - 14	In 1984-87, an outbreak of debilitating fatigue was reported by two physicians in the private practice of internal medicine in Incline Village, Nevada. Follow-up questionnaires were sent in 1995 to the 259 patients in this outbreak. The results were analyzed to determine how many patients met the latest Centers for Disease Control and Prevention (CDC) case definition for Chronic Fatigue Syndrome (CFS), Idiopathic Chronic Fatigue (ICF), or Prolonged Fatigue (PF). Data were analyzed separately for those living in the Lake Tahoe area and those referred from other locales. Of those returning questionnaires (123/259), 41% met the CDC case definition for CFS, 56% met the criteria for inclusion in the subgroup ICF, and 3% experienced PF. In the populationbased Lake Tahoe

				group, symptomatic women were more likely to have CFS than ICF whereas symptomatic men were likely to fit ICF criteria. Also in this group, full recovery was reported more often among Lake Tahoe participants classified as having ICF (43%) than participants classified as having CFS (15%).
Tarello W.	Veterinary Surgeon, Castiglione del Lago, Perugia, Italy.	Chronic fatigue syndrome in horses: diagnosis and treatment of 4 cases.	Comp Immunol Microbiol Infect Dis. 2001 Jan;24(1):57-70.	A report from England has suggested that Chronic Fatigue Syndrome exists in equines and constitutes an emerging veterinary problem. Preliminary epidemiological studies seem to confirm the zoonotic implications of CFS. An arsenical drug, sodium thiacetarsamide, was administered to four horses with a diagnosis of Chronic Fatigue Syndrome (CFS), already treated unsuccessfully with different medications. The CFS-like lethargy, with accompanying symptoms and signs, of the four animals obtained a complete remission after intravenous treatment with this drug at low dosage (0.1 mg/kg/day). No adverse side effects were ever noticed. This clinical response was associated with recovery from anaemia and decrease of muscular enzyme values in two of the four horses. In all patients, micrococci-like bacteria found before treatment adhering to the outer surface of many red blood cells, disappeared at post-treatment controls. Considerations are made on the possible action of an arsenical drug, used in isolation, in the treatment of CFS.
Tarello W.	tarello@iol.it	Chronic Fatigue Syndrome (CFS) in 15 dogs and cats with specific biochemical and microbiological anomalies.	Comp Immunol Microbiol Infect Dis. 2001 Jul;24(3):165-85.	A great deal of controversy and speculation surrounds the etiology of Chronic Fatigue Syndrome (CFS) in human patients and the existence of a similar illness in animals. To evaluate the association with a presumptive staphylococcal infection and bacteremia, seven dogs and eight cats diagnosed with CFS (two meeting the CDC working case definition) were submitted to rapid blood cultures and fresh blood smears investigations. Nine out of 15 blood cultures proved Staph-positive and four isolates were specified as <i>S. xilosus</i> (3) and <i>S. intermedius</i> (1). The presence of micrococci-like organisms in the blood was of common observation among these subjects, in association with fatigue/pain-related symptoms and biochemical abnormalities suggestive of a myopathy. Following treatment with a low dosage arsenical drug (thiacetarsamide sodium, Caparsolate, i.v., 0.1 ml/kg/day) all patients experienced complete remission. Micrococci disappeared from the blood at post-treatment controls made 10-30 days later. The outcomes were compared with those of five healthy controls and five 'sick with other illness' patients showing significant difference.
Tarello W.	wtarello@supereva.it	Chronic fatigue syndrome (CFS) associated with Staphylococcus spp. bacteremia, responsive to potassium arsenite 0.5% in a veterinary surgeon and his coworking wife, handling with CFS animal cases.	Comp Immunol Microbiol Infect Dis. 2001 Oct;24(4):233-46.	Chronic fatigue syndrome (CFS) in human patients remain a controversial and perplexing condition with emerging zoonotic aspects. Recent advances in human medicine seem to indicate a bacterial etiology and the condition has already been described in horses, dogs, cats and birds of prey in association with micrococci-like organisms in the blood. To evaluate the possibility of a chronic bacteremia, a veterinary surgeon (the author) and his coworking wife, both diagnosed with CFS and meeting the CDC working case definition, were submitted to rapid blood cultures and fresh blood smears investigations. Blood cultures proved Staph-positive and micrococci-like organisms in the blood were repeatedly observed in the 3-year period preceding the arsenical therapy, during which several medicaments, including antibiotics, proved unsuccessful. Following treatment with a low dosage arsenical drug (potassium arsenite 0.5%, im., 1 ml/12 h, for 10 days) both patients experienced complete remission. At the post-treatment control made 1 month later, micrococci had disappeared from the blood, and the CD4/CD8 ratio was raising.
Taylor RR, Jason LA.	Department of Occupational Therapy, University of Illinois at Chicago, 60612, USA.	Sexual abuse, physical abuse, chronic fatigue, and chronic fatigue syndrome: a community-based study.	J Nerv Ment Dis. 2001 Oct;189(10):709-15.	Using a randomly selected community-based sample, this investigation examined whether histories of childhood sexual, physical, and death threat abuse predicted adulthood outcomes of specific medical and psychiatric conditions involving chronic fatigue. This study also tested prior suggestions that most individuals with chronic fatigue syndrome report a past history of interpersonal abuse. Multinomial logistic regression was used to examine the relationship between abuse history and chronic fatigue group outcomes while controlling for the effects of sociodemographics. 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. A closer examination of individuals in the chronic fatigue syndrome group revealed that significantly fewer individuals with CFS reported abuse as compared with those who did not. The implications of these findings are discussed.
Teitelbaum JE, Bird B, Greenfield RM, Weiss A, Muenz L, Gould L.		Effective Treatment of Chronic Fatigue Syndrome and Fibromyalgia—A Randomized, Double-Blind, Placebo-Controlled, Intent- To-Treat Study	Journal of Chronic Fatigue Syndrome 2001; 8(2): 3	Background: Hypothalamic dysfunction has been suggested in fibromyalgia (FMS) and chronic fatigue syndrome (CFS). This dysfunction may result in disordered sleep, subclinical hormonal deficiencies, and immunologic changes. Our previously published open trial showed that patients usually improve by using a protocol which treats all the above processes simultaneously. The current study examines this protocol using a randomized, double-blind design with an intent-to-treat analysis. Methods: Seventy-two FMS patients (38 active:34 placebo; 69 also met CFS criteria) received all active or all placebo therapies as a unified intervention. Patients were treated, as indicated by

				symptoms and/or lab testing, for: (1) subclinical thyroid, gonadal, and/or adrenal insufficiency, (2) disordered sleep, (3) suspected neurally mediated hypotension (NMH), (4) opportunistic infections, and (5) suspected nutritional deficiencies. Results: At the final visit, 16 active patients were "much better," 14 "better," 2 "same," 0 "worse," and 1 "much worse" vs. 3, 9, 11, 6, and 4 in the placebo group ($p < .0001$, Cochran-Mantel-Haenszel trend test). Significant improvement in the FMS Impact Questionnaire (FIQ) scores (decreasing from 54.8 to 33.2 vs. 51.4 to 47.7) and Analog scores (improving from 176.1 to 310.3 vs. 177.1 to 211.9) (both with $p < .0001$ by random effects regression), and Tender Point Index (TPI) (31.7 to 15.5 vs. 35.0 to 32.3, $p < .0001$ by baseline adjusted linear model) were seen. Long term follow-up (mean 1.9 years) of the active group showed continuing and increasing improvement over time, despite patients being able to discontinue most treatments. Conclusions: Significantly greater benefits were seen in the active group than in the placebo group for all primary outcomes. An integrated treatment approach appears effective in the treatment of FMS/CFS.
Tiersky LA, DeLuca J, Hill N, Dhar SK, Johnson SK, Lange G, Rappolt G, Natelson BH.	School of Psychology, Fairleigh Dickinson University, 1000 River Road, Mail Stop T-WH1-01, Teaneck, NJ 07666, USA.	Longitudinal assessment of neuropsychological functioning, psychiatric status, functional disability and employment status in chronic fatigue syndrome.	Appl Neuropsychol. 2001;8(1):41-50.	The longitudinal course of subjective and objective neuropsychological functioning, psychological functioning, disability level, and employment status in chronic fatigue syndrome (CFS) was examined. The relations among several key outcomes at follow-up, as well as the baseline characteristics that predict change (e.g., improvement), were also evaluated. The study sample consisted of 35 individuals who met the 1988 and 1994 CFS case definition criteria of the Centers for Disease Control (CDC) at intake. Participants were evaluated a mean of 41.9 (SEM = 1.7) months following their initial visit (range = 24-63 months). Results indicated that objective and subjective attention abilities, mood, level of fatigue, and disability improve over time in individuals with CFS. Moreover, improvements in these areas were found to be interrelated at follow-up. Finally, psychiatric status, age, and between-test duration were significant predictors of outcome. Overall, the prognosis for CFS appears to be poor, as the majority of participants remained functionally impaired over time and were unemployed at follow-up, despite the noted improvements.
Ting JY, Brown AF.	Department of Emergency Medicine, Princess Alexandra Hospital, Brisbane, Queensland, Australia.	Ciguatera poisoning: a global issue with common management problems.	Eur J Emerg Med. 2001 Dec;8(4):295-300.	Ciguatera poisoning, a toxinological syndrome comprising an enigmatic mixture of gastrointestinal, neurocutaneous and constitutional symptoms, is a common food-borne illness related to contaminated fish consumption. As many as 50000 cases worldwide are reported annually, and the condition is endemic in tropical and subtropical regions of the Pacific Basin, Indian Ocean and Caribbean. Isolated outbreaks occur sporadically but with increasing frequency in temperate areas such as Europe and North America. Increase in travel between temperate countries and endemic areas and importation of susceptible fish has led to its encroachment into regions of the world where ciguatera has previously been rarely encountered. In the developed world, ciguatera poses a public health threat due to delayed or missed diagnosis. Ciguatera is frequently encountered in Australia. Sporadic cases are often misdiagnosed or not medically attended to, leading to persistent or recurrent debilitating symptoms lasting months to years. Without treatment, distinctive neurologic symptoms persist, occasionally being mistaken for multiple sclerosis. Constitutional symptoms may be misdiagnosed as chronic fatigue syndrome. A common source outbreak is easier to recognize and therefore notify to public health organizations. We present a case series of four adult tourists who developed ciguatera poisoning after consuming contaminated fish in Vanuatu. All responded well to intravenous mannitol. This is in contrast to a fifth patient who developed symptoms suggestive of ciguatoxicity in the same week as the index cases but actually had staphylococcal endocarditis with bacteraemia. In addition to a lack of response to mannitol, clinical and laboratory indices of sepsis were present in this patient. Apart from ciguatera, acute gastroenteritis followed by neurological symptoms may be due to paralytic or neurotoxic shellfish poisoning, scombroid and pufferfish toxicity, botulism, enterovirus 71, toxidromes and bacteraemia. Clinical aspects of ciguatera toxicity, its pathophysiology, diagnostic difficulties and epidemiology are discussed.
Tomita K, Sakurada S, Minami S.	Department of Chemistry, College of Engineering, Kanto Gakuin University, 4834 Mutsuura, Kanazawa-ku, Yokohama 236-8501, Japan. tomitak@kanto-gakuin.ac.jp	Enzymatic determination of acetylcarnitine for diagnostic applications.	J Pharm Biomed Anal. 2001 Mar;24(5-6):1147-50.	An enzymatic method was proposed for determination of acetylcarnitine (AcCar), even when carnitine (Car), non-acetylated form, co-exists. The method is consisted of four enzymatic reactions: First, AcCar is hydrolysed by acylcarnitine hydrolase to yield acetate; followed by the other three reactions coupled with three enzymes, respectively, acetate kinase, pyruvate kinase and lactate dehydrogenase; finally, the acetate formation causes a decrease in NADH. The amount of AcCar is then evaluated as the change in absorbance at 340 nm. The reagent composition of the reaction mixture was determined, and the characteristics of the method were investigated. The dilution test showed a good linearity over a wide range. The precision and accuracy tests produced satisfactory results. The co-existence of Car gave no effect on the measurement. The present method was found to be used easily, simply and rapidly for the selective determination of AcCar.
Tomoda, Jhodoi T, Miike		Chronic Fatigue Syndrome	Journal of Chronic Fatigue	Chronic fatigue syndrome occurring in previously healthy children and adolescents is one of the most vexing

T.		and Abnormal Biological Rhythms in School Children	Syndrome 2001; 8(2): 29	problems encountered by pediatric practitioners. To investigate the biological rhythms in the pediatric patients with CFS, we examined sleep pattern, and the circadian rhythm of core body temperature (CBT), and plasma cortisol in 41 patients, aged between 10 and 19 years, who did not have any physical or psychiatric disorders, but had non-specific complaints, and were suspected to have a circadian rhythm disturbance. They were diagnosed as having CFS on the basis of published criteria. Circadian variation of CBT in the CFS patients did not present a clear rhythm, and appearance time of their lowest CBT was significantly delayed compared to healthy subjects. Amplitude of circadian CBT changes, fitted to a cosinor curve by the least square method, was significantly smaller in the patients than in healthy subjects. Moreover, circadian rhythm of plasma cortisol in the patients appeared to be quite different, compared to healthy subjects. These findings suggest that their clinical psychosomatic symptoms (e.g., fatigue and sleep disturbance) might be closely related to the desynchronization of their biorhythms, particularly the circadian rhythm of body temperature and cortisol rhythm.
Tomonaga K, Kobayashi T, Ikuta K.	Department of Virology, Research Institute for Microbial Diseases, Osaka University.	[The neuropathogenesis of Borna disease virus infection] [Article in Japanese]	Nippon Rinsho. 2001 Aug;59(8):1605-13.	Borna disease virus(BDV) is a noncytolytic, neurotropic RNA virus that causes a disease of the central nervous system(CNS) in several vertebrate species, including horses, sheep, cats and ostriches. Epidemiological studies using peripheral blood or brain samples revealed that BDV can infect humans and that it may be related with certain neuropsychiatric disorders. The unique genetic and biological properties of BDV indicate that BDV develops a persistent infection in the CNS. Furthermore, a line of recent evidences suggests that BDV infection causes direct effects on brain functions in the absence of immunopathology-related brain damage. In this review, we discuss about recent data regarding neuropathogenesis of BDV infections in animals and humans.
Torpy DJ, Bachmann AW, Grice JE, Fitzgerald SP, Phillips PJ, Whitworth JA, Jackson RV.	Department of Medicine, University of Queensland, Greenslopes Private Hospital, Brisbane, Queensland 4120, Australia.	Familial corticosteroid-binding globulin deficiency due to a novel null mutation: association with fatigue and relative hypotension.	J Clin Endocrinol Metab. 2001 Aug;86(8):3692-700.	Corticosteroid-binding globulin is a 383-amino acid glycoprotein that serves a hormone transport role and may have functions related to the stress response and inflammation. We describe a 39-member Italian-Australian family with a novel complete loss of function (null) mutation of the corticosteroid-binding globulin gene. A second, previously described, mutation (Lyon) segregated independently in the same kindred. The novel exon 2 mutation led to a premature termination codon corresponding to residue -12 of the procorticosteroid-binding globulin molecule (c.121G-->A). Among 32 family members there were 3 null homozygotes, 19 null heterozygotes, 2 compound heterozygotes, 3 Lyon heterozygotes, and 5 individuals without corticosteroid-binding globulin mutations. Plasma immunoreactive corticosteroid-binding globulin was undetectable in null homozygotes, and mean corticosteroid-binding globulin levels were reduced by approximately 50% at 18.7 +/- 1.3 microg/ml (reference range, 30-52 microg/ml) in null heterozygotes. Morning total plasma cortisol levels were less than 1.8 microg/dl in homozygotes and were positively correlated to the plasma corticosteroid-binding globulin level in heterozygotes. Homozygotes and heterozygote null mutation subjects had a high prevalence of hypotension and fatigue. Among 19 adults with the null mutation, the systolic blood pressure z-score was 12.1 +/- 3.5; 11 of 19 subjects (54%) had a systolic blood pressure below the third percentile. The mean diastolic blood pressure z-score was 18.1 +/- 3.4; 8 of 19 subjects (42%) had a diastolic blood pressure z-score below 10. Idiopathic chronic fatigue was present in 12 of 14 adult null heterozygote subjects (86%) and in 2 of 3 null homozygotes. Five cases met the Centers for Disease Control criteria for chronic fatigue syndrome. Fatigue questionnaires revealed scores of 25.1 +/- 2.5 in 18 adults with the mutation vs. 4.2 +/- 1.5 in 23 healthy controls (P < 0.0001). Compound heterozygosity for both mutations resulted in plasma cortisol levels comparable to those in null homozygotes. Abnormal corticosteroid-binding globulin concentrations or binding affinity may lead to the misdiagnosis of isolated ACTH deficiency. The mechanism of the association between fatigue and relative hypotension is not established by these studies. As idiopathic fatigue disorders are associated with relatively low plasma cortisol, abnormalities of corticosteroid-binding globulin may be pathogenic.
Underhill JA, Mahalingam M, Peakman M, Wessely S.	Institute of Liver Studies, Department of Immunology, and Department of Psychological Medicine, Guy's, King's & St Thomas' School of Medicine, London, UK.	Lack of association between HLA genotype and chronic fatigue syndrome.	Eur J Immunogenet. 2001 Jun;28(3):425-8.	Although the aetiology of chronic fatigue syndrome is controversial, evidence that infective agents including viruses may have a role in the development of the condition has led to studies seeking an association with the immunomodulatory HLA genes. In the present study, we sought to extend previous work using a well-characterized patient group and modern HLA genotyping techniques. Fifty-eight patients were phenotyped for HLA A and B by microcytotoxicity and genotyped for HLA DRB, DQB and DPB by PCR oligoprobing, and the frequencies of antigens so assigned were compared with those from a control group of 134. No significant differences in HLA frequencies were found between patient and control groups. Thus, this study does not confirm previous findings of an HLA association with chronic fatigue syndrome, suggesting that neither presentation of viral antigen by HLA class I nor antigen processing genes in the HLA region is a major contributory factor in the development of the disease.
Underwood M, Eldridge		Chronic fatigue in general	Br J Gen Pract. 2001	

S.		practice.	Apr;51(465):317-8. Comment on: Br J Gen Pract. 2001 Jan;51(462):19-24.	
Ursin H, Eriksen HR.	Department of Biological and Medical Psychology, University of Bergen, Norway.	Sensitization, subjective health complaints, and sustained arousal.	Ann N Y Acad Sci. 2001 Mar;933:119-29.	The purpose of this presentation is to discuss the possibility that sensitization is a psychobiological mechanism underlying not only multiple chemical sensitivity (MCS), but a much more general cluster of illness, referred to as "subjective health complaints". Sustained arousal, or sustained "stress" responses, may be an important factor for the development of these conditions. Patients with subjective complaints without objective changes are sometimes referred to as having "fashionable diagnoses" or "unexplained symptoms". They may be given diagnoses like MCS, epidemic fatigue, chronic fatigue syndrome, burnout, stress, a variety of intoxications, environmental illness, radiation, multiple chemical hypersensitivity, food intolerance, functional dyspepsia, irritable bowel, myalgic encephalitis, postviral syndrome, yuppie flu, fibromyalgia, or vital exhaustion. One issue is whether this is one general condition or separate entities. Another issue is whether sensitization may be the psychobiological mechanism for most or all of these conditions. Finally, is it likely that sustained arousal may facilitate the development of sensitization in some or many neural circuits? In this review, the main emphasis will be on musculoskeletal pain. This is the most frequent and most expensive condition for sickness compensation and disability. The comorbidity of other complaints, however, will also be taken into account.
Valentine AD, Meyers CA.	Department of Neuro-Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, USA.	Cognitive and mood disturbance as causes and symptoms of fatigue in cancer patients.	Cancer. 2001 Sep 15;92(6 Suppl):1694-8.	Fatigue, cognitive dysfunction, and depression are very common in cancer patients. A relationship among the three entities is recognized but poorly understood. Factors that contribute to this poor understanding are the subjective nature of the symptoms, multiple potential causes, and a lack of reliable assessment tools. An understanding of fatigue in cancer patients may benefit from studies of chronic fatigue syndrome (CFS) and other nonmalignant diseases indicating that cognitive impairment varies with physical and mental fatigue, and that symptoms of depression experienced by patients with physical illnesses and primary mood disorders are qualitatively different. The multidimensional nature of fatigue suggests that interventions should be patient-specific. They could be related to lifestyle or involve the use of specific behavioral or pharmacologic therapies. As is the case with depression and cognitive disorders, targeted interventions against cancer-related fatigue will benefit from a better understanding of its potential biologic causes. Consideration of cognitive dysfunction and depression complicates the understanding of cancer-related fatigue; however, it provides opportunities to assist patients who must deal with this serious problem. Copyright 2001 American Cancer Society.
Van Houdenhove B, Neerincx E, Lysens R, Vertommen H, Van Houdenhove L, Onghena P, Westhovens R, D'Hooghe MB.	Department of Psychosomatic Rehabilitation, Katholieke Universiteit Leuven, Belgium. dewijn.VanHoudenhove@uz.kuleuven.ac.be	Victimization in chronic fatigue syndrome and fibromyalgia in tertiary care: a controlled study on prevalence and characteristics.	Psychosomatics. 2001 Jan-Feb;42(1):21-8.	The authors studied the prevalence and characteristics of different forms of victimization in 95 patients suffering from chronic fatigue syndrome (CFS) or fibromyalgia (FM) compared with a chronic disease group, including rheumatoid arthritis (RA) and multiple sclerosis (MS) patients, and a matched healthy control group. The authors assessed prevalence rates, nature of victimization (emotional, physical, sexual), life period of occurrence, emotional impact, and relationship with the perpetrator by a self-report questionnaire on burdening experiences. CFS and FM patients showed significantly higher prevalences of emotional neglect and abuse and of physical abuse, with a considerable subgroup experiencing lifelong victimization. The family of origin and the partner were the most frequent perpetrators. With the exception of sexual abuse, victimization was more severely experienced by the CFS/FM group. No differences were found between healthy control subjects or RA/MS patients, and between CFS and FM patients. These findings support etiological hypotheses suggesting a pivotal role for chronic stress in CFS and FM and may have important therapeutic implications.
Van Houdenhove B, Neerincx E, Onghena P, Lysens R, Vertommen H.	Faculty of Medicine, K.U. Leuven, Leuven, Belgium. boudewijn.vanhoudenhove@uz.kuleuven.ac.be	Premorbid "overactive" lifestyle in chronic fatigue syndrome and fibromyalgia. An etiological factor or proof of good citizenship?	J Psychosom Res. 2001 Oct;51(4):571-6.	OBJECTIVE: In a former study, we have shown that patients suffering from chronic fatigue syndrome (CFS) or chronic pain, when questioned about their premorbid lifestyle, reported a high level of "action-proneness" as compared to control groups. The aim of the present study was to control for the patients' possible idealisation of their previous attitude towards action. METHODS: A validated Dutch self-report questionnaire measuring "action-proneness" (the HAB) was completed by 62 randomly selected tertiary care CFS and fibromyalgia (FM) patients, as well as by their significant others (SOs). RESULTS: HAB scores of the patients and those of the SOs were very similar and significantly higher than the norm values. Whether or not the SO showed sympathy for the patient's illness did not influence the results to a great extent. SOs with a negative attitude towards the illness even characterized the patients as more "action-prone." CONCLUSIONS: These results provide further support for the hypothesis that a high level of "action-proneness" may play a predisposing, initiating and/or perpetuating role in CFS and FM.
van Houdenhove B.		Does myalgic	Lancet. 2001 Jun	

		encephalomyelitis exist?	9;357(9271):1889. Comment on: Lancet. 2001 Feb 17;357(9255):562.	
van Middendorp H, Geenen R, Kuis W, Heijnen CJ, Sinnema G.	Department of Pediatric Psychology, University Medical Center Utrecht, Wilhelmina Children's Hospital, The Netherlands.	Psychological adjustment of adolescent girls with chronic fatigue syndrome.	Pediatrics. 2001 Mar;107(3):E35.	OBJECTIVE: To examine psychosocial problems and adaptation of adolescent girls with chronic fatigue syndrome (CFS). METHODOLOGY: Thirty-six adolescent girls with CFS (mean age: 15.2 years; mean syndrome duration: 19.7 months) who fulfilled the criteria of the Centers for Disease Control and Prevention were examined by interviews regarding premorbid problems and by questionnaires regarding psychosocial functioning and distress, psychological attitudes, and coping resources. Data were compared with normative data. RESULTS: Of the adolescents, 86.1% reported 1 or more premorbid problems (58.3% physical, 38.9% psychological, and 52.8% familial). Normal adjustment was reported for psychosocial self-esteem, social abilities, and attentional abilities. High adjustment to adult social standards of behavior was found, but low perceived competence in specific adolescent domains, such as athletic ability, romance, and participation in recreational activities. The girls reported predominantly internalizing problems. Normal achievement motivation, no debilitating fear of failure, and high internal locus of control were observed. Palliative reaction patterns and optimism were predominantly used as coping strategies. CONCLUSIONS: The large number of premorbid problems suggests a possible contributing factor to the onset of the syndrome, although there were no reference data of healthy adolescents. In distinct domains of psychosocial adjustment, the adolescent girls with CFS showed strengths such as adequate self-esteem and scholastic and social abilities, and weaknesses such as low competence in adolescent-specific tasks and internalizing distress, which may partly be explained by syndrome-specific somatic complaints. The use of optimistic and palliative reaction patterns as coping strategies in this patient group indicates that the patients with CFS seem to retain an active and positive outlook on life, which may result in a rather adequate psychological adaptation to the syndrome, but also in maintenance of the syndrome by exceeding the physical limits brought about by the CFS. Our results on adjustment and coping strategies may be helpful to implement (individual) rehabilitation programs.
van Rensburg SJ, Potocnik FC, Kiss T, Hugo F, van Zijl P, Mansvelt E, Carstens ME, Theodorou P, Hurly PR, Emsley RA, Taljaard JJ.	Department of Chemical Pathology, University of Stellenbosch Medical School, Tygerberg Hospital, Tygerberg, South Africa. sjvr@gerga.sun.ac.za	Serum concentrations of some metals and steroids in patients with chronic fatigue syndrome with reference to neurological and cognitive abnormalities.	Brain Res Bull. 2001 May 15;55(2):319-25.	Chronic fatigue syndrome is defined by the Atlanta Centers for Disease Control (Atlanta, GA, USA) as debilitating fatigue lasting for longer than 6 months. Symptoms include disturbances of cognition. Certain factors have in the past been shown to influence cognition, including metals such as aluminum, iron, and zinc; and steroids such as dehydroepiandrosterone. In the present study, concentrations of these factors were determined in the serum and plasma of patients and their age- and gender-matched healthy controls (10 women and 5 men in each group). In addition, copper, dehydroepiandrosterone sulphate, cortisol, cholesterol, hemoglobin, ferritin and transferrin concentrations, as well as transferrin genetic subtypes were determined in both groups. The results indicate that patients had significantly increased serum aluminum and decreased iron compared to controls. In the females, serum iron and dehydroepiandrosterone sulphate were significantly decreased and correlated. Total cholesterol was significantly increased, and significantly negatively correlated with dehydroepiandrosterone sulphate. There were no differences in zinc, copper, cortisol, hemoglobin, transferrin and ferritin concentrations, or in transferrin genetic subtypes.
VanNess JM, Snell CR, Fredrickson DM, Strayer DR, Stevens SR.		Assessment of Functional Impairment by Cardiopulmonary Exercise Testing in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 103	Functional impairment in a population of patients with chronic fatigue syndrome (CFS) was determined by exercise testing. The criteria established by Weber and Janicki were employed because impairment levels are based on maximal oxygen consumption. Oxygen consumption was obtained by cardiopulmonary exercise testing and was used to classify subjects according to the severity of impairment. All the subjects in this study met the CDC case definition for CFS. All patients underwent at least two maximal graded exercise tests in which expired air was collected for assessment of VO2max. Data are included for eighty-seven CFS patients, the highest VO2 was used for determining impairment. Although all patients met the CDC case definition for CFS, only 35 (40%) would be classified as having greater than "Mild" functional impairment. The highest VO2 of any of the patients in this study was 29.5 ml/kg/min, very close to what normative data predicts to be the average maximal value for the entire group. Without a sedentary control group it is unclear if the low VO2 in this population is due to the pathology of CFS or results from the inactivity that accompanies the disease. However, use of maximal VO2 during exercise can clearly discriminate between levels of functional impairment and may be efficacious for diagnosis of CFS. Additionally, in cases where cardiopulmonary analysis is unavailable, exercise duration on a standardized test may also be employed.
Vassallo CM, Feldman E, Peto T, Castell L,	University Department of Psychiatry, Warneford	Decreased tryptophan availability but normal	Psychol Med. 2001 May;31(4):585-91.	BACKGROUND: Chronic fatigue syndrome (CFS) has been associated with increased prolactin (PRL) responses to the serotonin (5-HT) releasing agent fenfluramine. It is not known whether this abnormality is due to increased

Sharpley AL, Cowen PJ.	Hospital, Oxford.	post-synaptic 5-HT _{2c} receptor sensitivity in chronic fatigue syndrome.		5-HT release or heightened sensitivity of post-synaptic 5-HT receptors. METHODS: We measured the increase in plasma PRL produced by the directly acting 5-HT receptor agonist, m-chlorophenylpiperazine (mCPP), in patients with CFS and healthy controls. We also compared the ability of mCPP to lower slow wave sleep (SWS) in the sleep polysomnogram of both subject groups. Finally, we measured plasma amino-acid levels to determine whether tryptophan availability differed between CFS subjects and controls. RESULTS: mCPP elevated plasma PRL equivalently in patients with CFS and controls. Similarly, the decrease in SWS produced by mCPP did not differ between the two subject groups. Plasma-free tryptophan was significantly decreased in CFS. CONCLUSIONS: The sensitivity of post-synaptic 5-HT _{2c} receptors is not increased in patients with CFS. This suggests that the increased PRL response to fenfluramine in CFS is due to elevated activity of pre-synaptic 5-HT neurones. This change is unlikely to be due to increased peripheral availability of tryptophan.
Vermeulen RC, Scholte HR, Bezemer PD.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):238; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
Visser J, Graffelman W, Blauw B, Haspels I, Lentjes E, de Kloet ER, Nagelkerken L.	Division of Immunological and Infectious Diseases, TNO Prevention and Health, P.O. Box 2215, 2301 CE, Leiden, The Netherlands.	LPS-induced IL-10 production in whole blood cultures from chronic fatigue syndrome patients is increased but supersensitive to inhibition by dexamethasone.	J Neuroimmunol. 2001 Oct 1;119(2):343-9.	Several causes have been held responsible for the chronic fatigue syndrome (CFS), including an altered hypothalamus-pituitary-adrenal gland (HPA)-axis activity, viral infections and a reduced Th1 activity. Therefore, it was investigated whether the regulation of IL-10 is different in CFS. LPS-induced cytokine secretion in whole blood cultures showed a significant increase in IL-10 and a trend towards a decrease in IL-12 as compared with healthy controls. In patients and controls, IL-12 secretion was equally sensitive to suppression by dexamethasone, whereas IL-10 secretion appeared more sensitive in CFS-patients. In controls, IL-10 and IL-12 secretion were inversely correlated with free serum cortisol ($r=-0.492$, $p<0.02$ and $r=-0.434$, $p<0.05$, respectively). In CFS, such an inverse correlation was found for IL-12 ($r=-0.611$, $p<0.02$) but not for IL-10 ($r=-0.341$, ns). These data are suggestive for a disturbed glucocorticoid regulation of IL-10 in CFS.
Visser J, Lentjes E, Haspels I, Graffelman W, Blauw B, de Kloet R, Nagelkerken L.	Division of Immunological and Infectious Diseases, TNO Prevention and Health, Leiden, The Netherlands.	Increased sensitivity to glucocorticoids in peripheral blood mononuclear cells of chronic fatigue syndrome patients, without evidence for altered density or affinity of glucocorticoid receptors.	J Investig Med. 2001 Mar;49(2):195-204.	BACKGROUND: In this study we tested the hypothesis that the increased sensitivity to glucocorticoids in chronic fatigue syndrome (CFS)-patients can be attributed to an altered functioning of their glucocorticoid receptors (GR). METHODS: For this purpose, affinity and distribution of the GR were studied in purified, peripheral blood mononuclear cells (PBMC) of 10 CFS patients and 14 controls along with the responsiveness of these cells to glucocorticoids in vitro. RESULTS: Affinity (K _d) and number of GR was not different in PBMC of CFS patients when compared with the controls (K _d , 12.9 +/- 8.9 nmol vs 18.8 +/- 16.2 nmol and GR number, 4,839 +/- 2,824/cell vs 4,906 +/- 1,646/cell). Moreover, RT-PCR revealed no differences in GR messenger RNA expression. Nevertheless, PBMC from CFS patients showed an increased sensitivity to glucocorticoids in vitro. In CFS patients 0.01 micromol dexamethasone suppressed PBMC proliferation by 37%, whereas the controls were only suppressed by 17% ($P < 0.01$). Addition of phorbol 12-myristate 13-acetate to the cultures rendered the cells resistant to dexamethasone with regard to proliferation and IL-10 and IFN-gamma production, but not to IL-2 and TNF-alpha production in both patients and controls. No difference between patients and controls was observed in this respect CONCLUSIONS: In conclusion, PBMC of CFS patients display an increased sensitivity to glucocorticoids, which cannot be explained by number or affinity of the GR but should rather be attributed to molecular processes beyond the actual binding of the ligand to the GR.
Vives-Bauza C, Gamez J, Roig M, Briones P, Cervera C, Solano A, Montoya J, Andreu AL.	Research Centre for Biochemistry and Molecular Biology, Universitary Hospital Vall d'Hebron, Barcelona, Spain.	Exercise intolerance resulting from a muscle-restricted mutation in the mitochondrial tRNA(Leu (CUN)) gene.	Ann Med. 2001 Oct;33(7):493-6.	BACKGROUND: Some patients presenting with isolated lifelong exercise intolerance and ragged-red fibres, harbour skeletal-muscle restricted mutations in their mitochondrial DNA. AIM: To identify the molecular defect in a patient presenting with lifelong exercise intolerance, ragged-red fibres and deficiencies of complexes III and IV in skeletal muscle. METHODS: The muscle biopsy was studied for activities of the respiratory chain, histochemical stains, and sequencing the tRNA genes of mitochondrial DNA. RESULTS: The patient had a heteroplasmic mutation in the tRNA(Leu (CUN)) gene of mitochondrial DNA (G12334A). Clinical and morphological data as well as restriction fragment length polymorphism (RFLP) and single-fibre polymerase chain reaction (PCR) analyses strongly indicate that this molecular defect is the primary cause of the myopathy. CONCLUSION: Mutations in any mitochondrial gene should be considered in the differential diagnosis of patients with lifelong exercise intolerance, even when the neurological examination is normal.
Walsh CM, Zainal NZ, Middleton SJ, Paykel ES.	University Department of Psychiatry, Addenbrooke's Hospital, Cambridge, UK.	A family history study of chronic fatigue syndrome.	Psychiatr Genet. 2001 Sep;11(3):123-8.	Chronic fatigue syndrome (CFS) is characterized by unexplained, disabling fatigue and is associated with high rates of comorbid depression. While the aetiology is unknown, findings from recent twin surveys suggest that genetic factors may be relevant to prolonged fatigue states (> 1 month). To date, however, there has been no

				exploration of the role of familial/genetic factors in operationally defined CFS. The aims of the present study were: (i) to examine whether CFS is familial by comparing the rates of CFS in the first-degree relatives of CFS cases and medical control subjects; and (ii) to determine whether the high rate of comorbid depression in CFS is reflected in a greater familial loading for affective disorder. Twenty-five CFS cases and 36 medical control subjects were assessed for fatigue symptoms based on the Centre for Disease Control (CDC) criteria for CFS, and for lifetime psychiatric symptoms using the Schedule for Schizophrenia and Affective Disorders-Lifetime Version. Informant family history was obtained regarding first-degree relatives using the CDC criteria and the Family History Research Diagnostic Criteria. In addition, informant history was supplemented by sending a questionnaire to first-degree relatives. There were significantly higher rates of CFS in the relatives of CFS cases compared with the relatives of control subjects. The rate of depression in the CFS cases was similar to previous studies but did not appear to reflect a greater familial loading for depression when compared with control subjects. However, these analyses were complicated by higher than expected rates of depression in the control group. These findings suggest that familial factors are important in the aetiology of chronic fatigue syndrome.
Wessely S.	Guy's, King's, and St Thomas's School of Medicine and Institute of Psychiatry, London, United Kingdom. s.wessely@iop.kcl.ac.uk	Chronic fatigue: symptom and syndrome.	Ann Intern Med. 2001 May 1;134(9 Pt 2):838-43.	Chronic fatigue is common, is difficult to measure, can be associated with considerable morbidity, and is rarely a subject of controversy. The chronic fatigue syndrome also presents problems in definition and measurement, is associated with even more morbidity than chronic fatigue itself, and is often controversial. Particularly unclear is the way in which chronic fatigue and the chronic fatigue syndrome relate to each other: Is one the severe form of the other, or are they qualitatively and quantitatively different? We know that many things can cause chronic fatigue, and this is probably true for the chronic fatigue syndrome, too. We can anticipate that discrete causes of the chronic fatigue syndrome will be found in the future, even if these causes are unlikely to fall neatly along the physical-psychological divide that some expect. The causes of chronic fatigue are undoubtedly many, both in a population and in any individual person, even when a discrete cause, such as depression or cancer, is identified. Social, behavioral, and psychological variables are important in both chronic fatigue and the chronic fatigue syndrome. Interventions that address these general variables can be successful, and currently they are often more successful than interventions directed at specific causes.
Wessely S.	Department of Psychological Medicine, Guy's King and St Thomas' School of Medicine, 103 Denmark Hill, London, England SE5 8AF. sphascw@iop.bpmf.ac.uk	Chronic fatigue syndrome-- trials and tribulations.	JAMA. 2001 Sep 19;286(11):1378-9. Comment on: JAMA. 2001 Sep 19;286(11):1360-8.	
White PD, Thomas JM, Kangro HO, Bruce-Jones WD, Amess J, Crawford DH, Grover SA, Clare AW.	Department of Psychological Medicine, St Bartholomew's and the Royal London School of Medicine and Dentistry, London, UK. P.D. White@qmul.ac.uk	Predictions and associations of fatigue syndromes and mood disorders that occur after infectious mononucleosis.	Lancet. 2001 Dec 8;358(9297):1946-54.	BACKGROUND: Certain infections can trigger chronic fatigue syndromes (CFS) in a minority of people infected, but the reason is unknown. We describe some factors that predict or are associated with prolonged fatigue after infectious mononucleosis and contrast these factors with those that predicted mood disorders after the same infection. METHODS: We prospectively studied a cohort of 250 primary-care patients with infectious mononucleosis or ordinary upper-respiratory-tract infections until 6 months after clinical onset. We sought predictors of both acute and chronic fatigue syndromes and mood disorders from clinical, laboratory, and psychosocial measures. FINDINGS: An empirically defined fatigue syndrome 6 months after onset, which excluded comorbid psychiatric disorders, was most reliably predicted by a positive Monospot test at onset (odds ratio 2.1 [95% CI 1.4-3.3]) and lower physical fitness (0.35 [0.15-0.8]). Cervical lymphadenopathy and initial bed rest were associated with, or predicted, a fatigue syndrome up to 2 months after onset. By contrast, mood disorders were predicted by a premorbid psychiatric history (2.3 [1.4-3.9]), an emotional personality score (1.21 [1.11-1.35]), and social adversity (1.7 [1.0-2.9]). Definitions of CFS that included comorbid mood disorders were predicted by a mixture of those factors that predicted either the empirically defined fatigue syndrome or mood disorders. INTERPRETATION: The predictors of a prolonged fatigue syndrome after an infection differ with both definition and time, depending particularly on the presence or absence of comorbid mood disorders. The particular infection and its consequent immune reaction may have an early role, but physical deconditioning may also be important. By contrast, mood disorders are predicted by factors that predict mood disorders in general.
Whiting P, Bagnall AM, Sowden AJ, Cornell JE, Mulrow CD, Ramirez G.	National Health Service Centre for Reviews and Dissemination, University	Interventions for the treatment and management of chronic fatigue	JAMA. 2001 Sep 19;286(11):1360-8. Erratum in: JAMA 2002	CONTEXT: A variety of interventions have been used in the treatment and management of chronic fatigue syndrome (CFS). Currently, debate exists among health care professionals and patients about appropriate strategies for management. OBJECTIVE: To assess the effectiveness of all interventions that have been evaluated for use in

	of York, York, England, YO10 5DD. pfw2@york.ac.uk	syndrome: a systematic review.	Mar 20;287(11):1401.	the treatment or management of CFS in adults or children. DATA SOURCES: Nineteen specialist databases were searched from inception to either January or July 2000 for published or unpublished studies in any language. The search was updated through October 2000 using PubMed. Other sources included scanning citations, Internet searching, contacting experts, and online requests for articles. STUDY SELECTION: Controlled trials (randomized or nonrandomized) that evaluated interventions in patients diagnosed as having CFS according to any criteria were included. Study inclusion was assessed independently by 2 reviewers. Of 350 studies initially identified, 44 met inclusion criteria, including 36 randomized controlled trials and 8 controlled trials. DATA EXTRACTION: Data extraction was conducted by 1 reviewer and checked by a second. Validity assessment was carried out by 2 reviewers with disagreements resolved by consensus. A qualitative synthesis was carried out and studies were grouped according to type of intervention and outcomes assessed. DATA SYNTHESIS: The number of participants included in each trial ranged from 12 to 326, with a total of 2801 participants included in the 44 trials combined. Across the studies, 38 different outcomes were evaluated using about 130 different scales or types of measurement. Studies were grouped into 6 different categories. In the behavioral category, graded exercise therapy and cognitive behavioral therapy showed positive results and also scored highly on the validity assessment. In the immunological category, both immunoglobulin and hydrocortisone showed some limited effects but, overall, the evidence was inconclusive. There was insufficient evidence about effectiveness in the other 4 categories (pharmacological, supplements, complementary/alternative, and other interventions). CONCLUSIONS: Overall, the interventions demonstrated mixed results in terms of effectiveness. All conclusions about effectiveness should be considered together with the methodological inadequacies of the studies. Interventions which have shown promising results include cognitive behavioral therapy and graded exercise therapy. Further research into these and other treatments is required using standardized outcome measures.
Wiesmuller GA, Ebel H, Hornberg C.	Institut für Hygiene und Umweltmedizin, Universitätsklinikums, RWTH Aachen. GA.Wiesmueller@post.rwth-aachen.de	[Syndromes in environmental medicine: variants of somatoform disorders] [Article in German]	Fortschr Neurol Psychiatr. 2001 Apr;69(4):175-88.	Concerning the syndromes in environmental medicine, like Multiple Chemical Sensitivities (MCS), Idiopathic Environmental Intolerances (IEI), Sick Building Syndrome (SBS), Chronic Fatigue Syndrome (CFS), Candida Syndrome (CS), and Burnout Syndrome (BS), scientific knowledge in etiology, pathology, pathophysiology, diagnosis, therapy, prevention and prognosis is still lacking until now. A critical comparison shows that it is still impossible to find a scientifically satisfying delimitation. Syndromes in environmental medicine show clinical similarities to somatoform disorders. Furthermore, there are the following possible explanations for the existence of these syndromes: Firstly, they may be a complex interaction of environmental impacts, individual predispositions, psychological influences, as well as processes of mental perception and interpretation. Secondly, they may be an effect of distress influenced by culture and social structures and/or thirdly, they may be an iatrogenic determination. A more comprehensive characterisation which better considers the complex clinical manifestations is overdue. Although there are neither scientifically validated procedures for diagnosis or therapy nor prophylactic measures, a hardly comprehensible number of partly unvalidated methods is in practical use. Until the syndromes are not finally defined the terms for the syndromes should not be applied to a certain disease. Despite all uncertainties in the evaluation of syndromes in environmental medicine, physicians have the duty to take the affected persons' problems seriously.
Wikland B, Lowhagen T, Sandberg PO.		Fine-needle aspiration cytology of the thyroid in chronic fatigue.	Lancet. 2001 Mar 24;357(9260):956-7. Comment in: Lancet. 2001 Jul 14;358(9276):151.	
Wilke WS.	Department of Rheumatology, Cleveland Clinic, U.S.A.	Can fibromyalgia and chronic fatigue syndrome be cured by surgery?	Cleve Clin J Med. 2001 Apr;68(4):277-9. Comment in: Cleve Clin J Med. 2002 Jan;69(1):89-91.	
Wilson A, Hickie I, Hadzi-Pavlovic D, Wakefield D, Parker G, Straus SE, Dale J, McCluskey D, Hinds G, Brickman A, Goldenberg D, Demitrack M, Blakely T, Wessely S, Sharpe M, Lloyd A.	University of New South Wales, Sydney, Australia.	What is chronic fatigue syndrome? Heterogeneity within an international multicentre study.	Aust N Z J Psychiatry. 2001 Aug;35(4):520-7.	OBJECTIVE: We sought to compare the characteristics of patients presenting with chronic fatigue (CF) and related syndromes in eight international centres and to subclassify these subjects based on symptom profiles. The validity of the subclasses was then tested against clinical data. METHOD: Subjects with a clinical diagnosis of CF completed a 119-item self-report questionnaire to provide clinical symptom data and other information such as illness course and functional impairment. Subclasses were generated using a principal components-like analysis followed by latent profile analysis (LPA). RESULTS: 744 subjects returned complete data sets (mean age 40.8 years, mean length of illness 7.9 years, female to male ratio 3:1). Overall, the subjects had a high rate of reporting typical CF symptoms (fatigue, neuropsychological dysfunction, sleep disturbance). Using LPA, two subclasses

				were generated. Class one (68% sample) was characterized by: younger age, lower female to male ratio; shorter episode duration; less premorbid, current and familial psychiatric morbidity; and, less functional disability. Class two subjects (32%) had features more consistent with a somatoform illness. There was substantial variation in subclass prevalences between the study centres (Class two range 6-48%). CONCLUSIONS: Criteria-based approaches to the diagnosis of CF and related syndromes do not select a homogeneous patient group. While substratification of patients is essential for further aetiological and treatment research, the basis for allocating such subcategories remains controversial.
Yunus MB.	College of Medicine at Peoria, University of Illinois, One Illini Drive, PO Box 1649, Peoria, IL 61656, USA. Yunus@uic.edu	The role of gender in fibromyalgia syndrome.	Curr Rheumatol Rep. 2001 Apr;3(2):128-34.	Fibromyalgia syndrome (FMS), characterized by widespread pain and tenderness on palpation (tender points), is much more common in women than in men in a proportion of 9:1. Two recent studies have shown important gender differences in various clinical characteristics of FMS. In a community and a clinic sample, women experienced significantly more common fatigue, morning fatigue, hurt all over, total number of symptoms, and irritable bowel syndrome. Women had significantly more tender points. Pain severity, global severity and physical functioning were not significantly different between the sexes, nor were psychologic factors, eg, anxiety, stress, and depression. Gender differences have also been observed in other related syndromes, eg, chronic fatigue syndrome, irritable bowel syndrome, and headaches. The mechanisms of gender differences in these illnesses are not fully understood, but are likely to involve an interaction between biology, psychology, and sociocultural factors.
Zaman R, Puri BK, Main J, Nowicky AV, Davey NJ.	Division of Neuroscience and Psychological Medicine, Imperial College School of Medicine, Charing Cross Hospital, London W6 8RF, UK.	Corticospinal inhibition appears normal in patients with chronic fatigue syndrome.	Exp Physiol. 2001 Sep;86(5):547-50.	The pathogenesis of chronic fatigue syndrome (CFS) remains unknown. Thresholds and latencies of motor evoked potentials (MEPs) in response to transcranial magnetic stimulation (TMS) are normal but intracortical inhibition has not been investigated. Eleven patients with CFS were compared with 11 control subjects. Each patient completed a questionnaire using visual analogue indices of pain, fatigue, anxiety and depression. Subjects released a button to initiate simple (SRTs) and choice reaction time (CRTs) tasks; for each task, movement times were measured between release of the initiation button and depression of a second button 15 cm away. Subjects held a 10 % maximum voluntary contraction in the thenar muscles of their dominant hand while TMS was applied to the motor cortex; the duration and extent of inhibition of surface electromyographic (EMG) activity were assessed at stimulus strengths above and below the threshold for MEPs. Patients had significantly ($P < 0.05$) higher mean indices of fatigue than of pain, anxiety or depression. Mean (+/- S.E.M.) SRTs (but not CRTs) were longer in patients (309 +/- 45 ms) than in controls (218 +/- 9 ms). Movement times were longer in patients for both SRTs and CRTs. TMS thresholds, expressed as a percentage of the maximum stimulator output, were not significantly ($P > 0.05$) different in both groups for both MEPs (patients, 34 +/- 3%; controls, 36 +/- 3%) and inhibition of voluntary contraction (patients, 29 +/- 2%; controls, 34 +/- 4%). The duration and extent of inhibition did not differ significantly between groups at any stimulus strength. The pattern of change in duration and extent of inhibition with increasing stimulus intensity was no different in the two groups. The duration and extent of corticospinal inhibition in patients with CFS did not differ from controls, adding further evidence to the notion that the feeling of fatigue and the slowness of movement seen in CFS is not manifest in corticospinal output pathways.