

Authors	Author Address	Title	Publication	Abstract
<b>Ablashi DV, Levine PH, De Vinci C, Whitman JE Jr, Pizza G, Viza D.</b>	Advanced Biotechnologies Inc., Columbia, MD 21046, USA.	Use of anti HHV-6 transfer factor for the treatment of two patients with chronic fatigue syndrome (CFS). Two case reports.	Biotherapy 1996;9(1-3):81-6	Specific Human Herpes virus-6 (HHV-6) transfer factor (TF) preparation, administered to two chronic fatigue syndrome patients, inhibited the HHV-6 infection. Prior to treatment, both patients exhibited an activated HHV-6 infection. TF treatment significantly improved the clinical manifestations of CFS in one patient who resumed normal duties within weeks, whereas no clinical improvement was observed in the second patient. It is concluded that HHV-6 specific TF may be of significant value in controlling HHV-6 infection and related illnesses.
<b>Anisman H, Baines MG, Berczi I, Bernstein CN, Blennerhassett MG, Gorczynski RM, Greenberg AH, Kisil FT, Mathison RD, Nagy E, Nance DM, Perdue MH, Pomerantz DK, Sabbadini ER, Stanisz A, Warrington RJ.</b>	Department of Psychology, Carleton University, Ottawa, Ont.	Neuroimmune mechanisms in health and disease: 2. Disease.	CMAJ 1996 Oct 15;155(8):1075-82	In the second part of their article on the emerging field of neuroimmunology, the authors present an overview of the role of neuroimmune mechanisms in defence against infectious diseases and in immune disorders. During acute febrile illness, immune-derived cytokines initiate an acute phase response, which is characterized by fever, inactivity, fatigue, anorexia and catabolism. Profound neuroendocrine and metabolic changes take place: acute phase proteins are produced in the liver, bone marrow function and the metabolic activity of leukocytes are greatly increased, and specific immune reactivity is suppressed. Defects in regulatory processes, which are fundamental to immune disorders and inflammatory diseases, may lie in the immune system, the neuro endocrine system or both. Defects in the hypothalamus-pituitary-adrenal axis have been observed in autoimmune and rheumatic diseases, chronic inflammatory disease, chronic fatigue syndrome and fibromyalgia. Prolactin levels are often elevated in patients with systemic lupus erythematosus and other autoimmune diseases, whereas the bioactivity of prolactin is decreased in patients with rheumatoid arthritis. Levels of sex hormones and thyroid hormone are decreased during severe inflammatory disease. Defective neural regulation of inflammation likely plays a pathogenic role in allergy and asthma, in the symmetrical form of rheumatoid arthritis and in gastrointestinal inflammatory disease. A better understanding of neuroimmunoregulation holds the promise of new approaches to the treatment of immune and inflammatory diseases with the use of hormones, neurotransmitters, neuropeptides and drugs that modulate these newly recognized immune regulators.
<b>Anon</b>		Chronic fatigue syndrome: any closer to an answer?	413: Consum Rep 1996 Sep;61(9):60-1	
<b>Arnetz BB.</b>	Department of Medicine, Karolinska Institute, Huddinge University Hospital, Sweden.	Causes of change in the health of populations: a biopsychosocial viewpoint.	Soc Sci Med 1996 Sep;43(5):605-8	In the current review, a biopsychosocial perspective is applied to current changes in the health of populations. It is proposed that the psychosocial environments either promote health or precipitate disease. Changes in the types of stress that people experience as well as its prevalence over time are discussed. In addition, possible biological mechanisms linking the psychosocial environments to health are presented. "Food for thought" is the possible interaction between the physical/chemical and the psychosocial environments and changes in health of individuals. Clearly, our traditional view of disease mechanisms is not sufficient to understand recent phenomena, such as environmental illness and chronic fatigue syndrome. Issues worthy of further discussions are the role of the "just-in-time" society, where individuals increasingly have to change jobs, cope with reorganizations and increased production pressure, and its impact on health and well-being. Further, in what way can we develop better models to truly assess the impact of an increasingly complex interaction between individual and environmental factors on health? A major obstacle to enhancing our understanding of causes of change in the health of populations is the use of inappropriate or outdated statistical analytical models. Finally, it is suggested that prospectively controlled studies of the impact on health of changes in the health and welfare systems are carried out. This would further add to our understanding of factors contributing to changes in the health of population.
<b>Aylward M.</b>		Government's expert group has reached consensus on prognosis of chronic fatigue syndrome.	BMJ 1996 Oct 5;313(7061):885	
<b>Baschetti R.</b>		Chronic fatigue syndrome and neurally mediated hypotension.	JAMA 1996 Feb 7;275(5):359; discussion 360 comment on: JAMA. 1995 Sep 27;274(12):961-7	
<b>Beard TC.</b>		Chronic fatigue syndrome and	JAMA 1996 Feb	

		neurally mediated hypotension.	7;275(5):359; discussion 360 comment on: JAMA. 1995 Sep 27;274(12):961-7	
<b>Bennett AL, Fagioli LR, Schur PH, Schacterle RS, Komaroff AL.</b>	Chronic Fatigue Syndrome Cooperative Research Center, Division of General Medicine and Primary Care, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.	Immunoglobulin subclass levels in chronic fatigue syndrome.	J Clin Immunol 1996 Nov;16(6):315-20	The levels of immunoglobulin subclasses were determined for 46 patients meeting the original Centers for Disease Control case definition of chronic fatigue syndrome and were compared to values obtained for 50 age- and gender-matched healthy volunteer blood donor controls. The levels of immunoglobulin subclasses in these groups were further compared to a third group of additional chronic fatigue syndrome cases from whom samples had been obtained and frozen prospectively over a period of 7 years. These data do not demonstrate significant immunoglobulin subclass deficiencies in patients with chronic fatigue syndrome.
<b>Bombardier CH, Buchwald D.</b>	Department of Rehabilitation Medicine, University of Washington, Seattle, USA.	Chronic fatigue, chronic fatigue syndrome, and fibromyalgia. Disability and health-care use.	795: Med Care 1996 Sep;34(9):924-30	<b>OBJECTIVES:</b> Disabling chronic fatigue that does not meet criteria for chronic fatigue syndrome (CFS) or fibromyalgia (FM) is a condition thought to be associated with substantial disability and an apparently high use of health-care services. The authors compare patients who have chronic fatigue, CFS, FM, or CFS and FM together (CFS+FM) on employment status, self-reported disability, number of medical care visits, type of services obtained, and other diagnoses received. <b>METHODS:</b> The authors studied 402 patients from a university-based chronic fatigue clinic. All patients underwent an initial structured diagnostic assessment. One hundred forty-seven patients met case criteria for CFS, 28 for FM, 61 for CFS+FM, and 166 fell in the residual chronic fatigue group. Of these patients, 388 completed a follow-up questionnaire an average of 1.7 years later. Chi-squared tests and analysis of variance were used to compare groups on follow-up measures of health-care use and disability. <b>RESULTS:</b> Patients with chronic fatigue, CFS, FM, and CFS+FM were similar in terms of disability and health-care use, though those with CFS+FM were significantly more likely to be unemployed and to use more chiropractic and "other" provider services. Rates of unemployment ranged from 26% (chronic fatigue) to 51% (CFS+FM). Overall, patients reported a mean of 21 visits to a wide variety health-care providers during the previous year, with no significant differences between groups. <b>CONCLUSIONS:</b> Chronic fatigue, CFS, and FM are associated with considerable personal and occupational disability and low rates of employment. The potentially large economic burden of these disorders underscores the need for accurate estimates of direct and indirect costs, the relative contribution of individual factors to disability, and the need to develop targeted rehabilitation programs.
<b>Borok G.</b>		Committee to investigate chronic fatigue syndrome.	S Afr Med J 1996 Oct;86(10):1301 comment on: S Afr Med J. 1995 Aug;85(8):780-2	
<b>Brown MT, Sam A. Fleishman, Manuel F. Casanova</b>		Gulf War Syndrome Polysomnographic Study of Eight Cases	Journal of Chronic Fatigue Syndrome 1996: 2(1): 41 - 51	Our purpose was to explore whether patients complaining of the "Gulf War Syndrome" might have hidden sleep disorders, or psychiatric disorders, similar to what has been described in patients with chronic fatigue syndrome and fibromyalgia. Eight consecutive Gulf War veterans from the VA Gulf War Registry and Evaluation program complaining of fatigue, as well as other symptoms, were psychiatrically and polysomnographically screened. One was found to have major depression and Post-traumatic Stress Disorder (PTSD), while another had PTSD alone. The sleep diagnoses assigned to the 8 patients were as follows: Three had sleep apnea syndrome, one of whom also had periodic limb movements of sleep disorder. Four others met criteria for periodic limb movements (PLMs) of sleep disorder. Four of the patients had clinically significant sleep state-misperceptions. All of the patients' symptoms were reported as occurring subsequent to Gulf War deployment, and not prior to deployment. As with the classic fatigue syndromes such as chronic fatigue syndrome and fibromyalgia, Gulf War Syndrome patients may benefit from a more thorough investigation of their sleep and psychiatric status. In view of these findings, consideration of polysomnographic screening would appear appropriate in Gulf War Veterans with fatigue or sleep-related complaints.
<b>Bruno RL, Nancy M. Frick, Susan Creange, Jerald R. Zimmerman, Todd Lewis</b>		Polioencephalitis and the Brain Fatigue Generator Model of Post-Viral Fatigue Syndromes	Journal of Chronic Fatigue Syndrome 1996: 2(2/3): 5 - 27	Fatigue is the most commonly reported and most debilitating Post-Polio Sequelae (PPS), affecting millions of polio survivors world-wide. Post-polio fatigue is associated with: (1) subjective reports of difficulty with attention, cognition, word-finding and maintaining wakefulness; (2) clinically significant deficits on neuropsychological tests of information processing speed and attention; (3) gray

				and white matter hyperintensities in the reticular activating system on magnetic resonance imaging of the brain; (4) neuroendocrine evidence of impaired activation of the HPA axis. Many of these findings are identical to those documented following a variety of viral encephalitides, including acute poliovirus infection, lethargic encephalitis, Iceland Disease, myalgic encephalomyelitis, and, most recently, Chronic Fatigue Syndrome. The clinical, historic, neuropsychologic, neuroanatomic and physiologic parallels between poliovirus infection, post-polio fatigue and post-viral fatigue syndromes (PVFS) will be explored in an attempt to describe the pathophysiology of PVFS. The disinhibition of a putative Brain Fatigue Generator will be implicated as a cause of the subjective symptoms and objective signs that accompany PVFS. The results of a pilot placebo-controlled study of a dopamine 2 receptor agonist to treat post-polio fatigue will also be described.
<b>Buchwald D, Ashley RL, Pearlman T, Kith P, Komaroff AL.</b>	Department of Medicine, University of Washington, Seattle, USA.	Viral serologies in patients with chronic fatigue and chronic fatigue syndrome.	J Med Virol 1996 Sep;50(1):25-30	Chronic fatigue syndrome (CFS) is an illness characterized by disabling fatigue associated with complaints of fevers, sore throat, myalgia, lymphadenopathy, sleep disturbances, neurocognitive difficulties, and depression. A striking feature of CFS is its sudden onset following an acute, presumably viral, illness and the subsequent recurrent "flu-like" symptoms. It has been speculated that both CFS and debilitating chronic fatigue (CF) that does not meet strict criteria for CFS may be the direct or indirect result of viral infections. We therefore tested 548 chronically fatigued patients who underwent a comprehensive medical and psychiatric evaluation for antibodies to 13 viruses. Our objectives were to compare the seroprevalence and/or geometric mean titer (GMT) of antibodies to herpes simplex virus 1 and 2, rubella, adenovirus, human herpesvirus 6, Epstein-Barr virus, cytomegalovirus, and Cox-sackie B virus, types 1-6 in patients with CF to healthy control subjects. Other goals were to determine if greater rates of seropositivity or higher GMTs occurred among subsets of patients with CFS, fibromyalgia, psychiatric disorders, a self-reported illness onset with a viral syndrome, and a documented temperature > 37 degrees C on physical examination. Differences in the seroprevalence or GMTs of antibodies to 13 viruses were not consistently found in those with CF compared with control subjects, or in any subsets of patients including those with CFS, an acute onset of illness, or a documented fever. These particular viral serologies were not useful in evaluating patients presenting with CF.
<b>Buchwald D, Pearlman T, Umali J, Schmalig K, Katon W.</b>	Department of Medicine, University of Washington, Seattle, USA.	Functional status in patients with chronic fatigue syndrome, other fatiguing illnesses, and healthy individuals.	Am J Med 1996 Oct;101(4):364-70	<b>BACKGROUND:</b> Chronic fatigue syndrome (CFS) is a condition that may be associated with substantial disability. The Medical Outcomes Study Short-Form General Health Survey (SF-36) is an instrument that has been widely used in outpatient populations to determine functional status. Our objectives were to describe the usefulness of the SF-36 in CFS patients and to determine if subscale scores could distinguish patients with CFS from subjects with unexplained chronic fatigue (CF), major depression (MD), or acute infectious mononucleosis (AIM), and from healthy control subjects (HC). An additional goal was to ascertain if subscale scores correlated with the signs and symptoms of CFS or the presence of psychiatric disorders and fibromyalgia. <b>DESIGN:</b> Prospectively collected case series. <b>SETTING:</b> Patients with CFS and CF were seen in a university-based referral clinic and had undergone a complete medical and psychiatric evaluation. Other study subjects were recruited from the community to participate in research studies. <b>PARTICIPANTS:</b> The study included 185 patients with CFS, 246 with CF, 111 with AIM, and 25 with MD. There were 99 HC subjects. <b>MEASURES:</b> The SF-36 and a structured psychiatric interview were used. The SF-36 contains 8 subscales: physical, emotional, social, and role functioning, body pain, mental health, vitality, and general health- and a structured psychiatric interview. <b>RESULTS:</b> Performance characteristics (internal reliability coefficients, convergent validity) of the SF-36 were excellent. A strikingly consistent pattern was found for the physical functioning, role functioning, social functioning, general health, and body pain subscales, with the lowest scores in CFS patients, intermediate scores in AIM patients, and the highest scores in the HC subjects. The CFS patients had significantly lower scores than patients with CF alone on the physical functioning ( $P < or = 0.01$ ), role functioning ( $P < or = 0.01$ ), and body pain ( $P < or = 0.001$ ) subscales. The emotional functioning and mental health scores were worst among those with MD. The presence of fibromyalgia, being unemployed, and increasing fatigue severity all were associated with additional functional limitations across multiple functional domains, with increasing fatigue appearing to have the greatest effect. <b>CONCLUSIONS:</b> The SF-36 is useful in assessing functional status in patients with fatiguing illnesses. Patients with CFS and CF have marked

				impairment of their functional status. The severity and pattern of impairment as documented by the SF-36 distinguishes patients with CFS and CF from those with MD and AIM, and from HC, but does not discriminate between CF and CFS.
<b>Buchwald D, Spero M, Manson , Tsilke Pearlman, Jovine Umali, Phalla Kith</b>		Race and Ethnicity in Patients with Chronic Fatigue	Journal of Chronic Fatigue Syndrome 1996; 2(1): 53 - 66	Purpose: Chronic fatigue (CF) is a common complaint in ambulatory settings. Chronic fatigue syndrome (CFS) is characterized by profound fatigue associated with other symptoms that is rarely reported in racial/ethnic minorities. Our objectives were to determine if differences exist between Caucasian and minority patients presenting with CF, particularly in the frequency meeting criteria for CFS. Patients: 690 patients with CF seen in a university-based referral clinic. Design/Methods: Demographic, historical, physical examination, laboratory, and psychosocial information was prospectively collected and compared. Psychosocial assessment consisted of a structured psychiatric interview, the Medical Outcomes Study Short-Form Health Survey to assess functional status, the General Health Questionnaire to ascertain psychological distress, and measures of health locus of control, illness attribution, social support, and coping. Results: With the exception of less social support from friends, no significant race/ethnicity-related differences were identified. Minority patients tended less commonly to report a moderate level of fatigue, and to have poorer social function, less social support from families, and lower rates of lifetime major depression and alcohol abuse. Conclusions: Demographic, clinical, and psychosocial factors do not distinguish Caucasian from minority CF patients. Help-seeking behaviors, access to care, and the significance attributed to the central complaints should be examined as potentially competing explanations for these findings.
<b>Buchwald D, Umali J, Pearlman T, Kith P, Ashley R, Wener M.</b>	Department of Medicine, University of Washington, Seattle, USA.	Postinfectious chronic fatigue: a distinct syndrome?	Clin Infect Dis 1996 Aug;23(2):385-7	Chronic fatigue syndrome (CFS) is often preceded by a viral illness and has recurrent "flu-like" symptoms. We compared demographic, clinical, and laboratory features (markers of inflammation and viral infection) among 717 patients with chronic fatigue (CF) with and without a self-reported postinfectious onset to identify associated clinical and biologic findings and to examine the subset of patients with CFS. Only subjective fever, chills, sore throat, lymphadenopathy, poorer functional status, and attribution of illness to a physical condition were significantly associated with a postinfectious onset. The features of patients with CFS were virtually identical to those of the broader category of patients with CF. We conclude that a postinfectious onset was not associated with a pattern of abnormalities across multiple psychosocial and biologic parameters.
<b>Buchwald D, Umali J, Stene M.</b>	Department of Medicine, University of Washington, Seattle, USA.	Insulin-like growth factor-I (somatomedin C) levels in chronic fatigue syndrome and fibromyalgia.	J Rheumatol 1996 Apr;23(4):739-42	OBJECTIVE. Fibromyalgia (FM) and chronic fatigue syndrome (CFS) are similar conditions characterized by substantial fatigue, diffuse myalgias, sleep disturbances and a variety of other symptoms. Many patients with CFS meet strict criteria for FM. Recently, low insulin-like growth factor-I (IGF-I) levels have been demonstrated in patients with FM, suggesting that disruption of the growth hormone-IGF-I axis might explain the link between the muscle pain and poor sleep. Our goal was to determine whether IGF-I levels are decreased in CFS, and whether such findings are restricted to patients with concurrent FM. METHODS. Radioimmunoassays were used to determine serum concentrations of IGF-I and its binding protein, (IGFBP-3). Subjects were 3 patients seen in a referral clinic for chronic fatigue: 15 patients with CFS, 15 who met criteria for both CFS and FM (CFS-FM), 27 with FM alone; and 15 healthy control (HC) subjects. RESULTS. Patients and control subjects had similar demographic and clinical characteristics. No significant differences were observed among any of the 3 patient groups and control subjects in the mean concentration of either IGF-I or IGFBP-3. Likewise, the proportion of subjects with values above or below the laboratory's reference range did not differ for IGF-I or IGFBP-3. CONCLUSIONS. These findings suggest the disruption of the growth hormone-IGF-I axis previously demonstrated in FM patients is not evident in a referral population of patients with CFS, CFS-FM, or FM.
<b>Buchwald D.</b>	Department of Medicine, University of Washington, Seattle, USA.	Fibromyalgia and chronic fatigue syndrome: similarities and differences.	Rheum Dis Clin North Am 1996 May;22(2):219-43	CFS and FM are clinical conditions characterized by a variety of nonspecific symptoms including prominent fatigue, myalgia, and sleep disturbances. There are no diagnostic studies or widely accepted, pathogenic, explanatory models for either illness. Despite remarkably different diagnostic criteria, CFS and FM have many demographic and clinical similarities. More specifically, few differences exist in the domains of symptoms, examination findings, laboratory tests, functional status, psychosocial features, and psychiatric disorders. FM appears to represent an additional burden of suffering among those with CFS, however, underscoring the importance of recognizing concurrent CFS and FM. Further clarification of the similarities (and differences) between CFS and FM may be

				useful in studies of prognosis and help define subsets of patients who may benefit from specific therapeutic interventions.
<b>Bujak DI, Weinstein A, Dornbush RL.</b>	Department of Medicine, New York Medical College, Valhalla 10595, USA.	Clinical and neurocognitive features of the post Lyme syndrome.	J Rheumatol 1996 Aug;23(8):1392-7	OBJECTIVE: To evaluate neurocognitive impairment in patients with persistent arthralgia, fatigue, and subjective memory loss in patients after Lyme disease (post-Lyme syndrome, PLS). METHODS: We compared the clinical, neurocognitive, and psychological features of 23 patients with PLS to 23 age, sex, and education matched recovered patients (REC). All met Centers for Disease Control criteria for Lyme disease, were ELISA positive at onset of Lyme disease and were previously treated with standard antibiotic regimens. RESULTS: Of the patients with PLS, 7 (30%) had fibromyalgia (FM), 3 (13%) had chronic fatigue syndrome, and 10 (43%) had similar but milder symptoms but did not meet the criteria for either. 22 of 23 patients with PLS complained of decreased memory or concentration problems. Patients with PLS had significantly lower scores on the attention/concentration scale ( $p = 0.012$ ) of the Wechsler Memory Scale-Revised (WMS-R), indicating lowered attention/concentration. 52% of patients with PLS and 35% in the REC group had significantly lower ( $p < 0.05$ ) WMS-R verbal memory scores than visual memory scores. The PLS group had subjectively more problems with sleep and mood changes and higher scores on several scales of Symptom Check List 90-R ( $p < 0.01$ ), indicating greater physical distress. Beck Depression Inventory scores were also higher for the PLS than the REC group ( $p < 0.005$ ), but were within the normal range. CONCLUSION: Despite antibiotic treatment, a sequelae of Lyme disease may be a PLS characterized by persistent arthralgia, fatigue, and neurocognitive impairment that is probably induced by Lyme disease.
<b>Burnet RB, Yeap BB, Chatterton BE, Gaffney RD.</b>		Chronic fatigue syndrome: is total body potassium important?	Med J Aust 1996 Mar 18;164(6):384 comment on: Med J Aust. 1995 Sep 18;163(6):314-8	
<b>Chagpar A.</b>		Chronic fatigue syndrome: a prodrome to psychosis?	Can J Psychiatry 1996 Oct;41(8):536-7 comment on: Can J Psychiatry. 1996 May;41(4):217-22	
<b>Chilton SA.</b>		Cognitive behaviour therapy for the chronic fatigue syndrome. Evening primrose oil and magnesium have been shown to be effective.	BMJ 1996 Apr 27;312(7038):1096; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
<b>Cleare AJ, O'Keane V.</b>		Re: Endocrine responses to fenfluramine challenge in chronic fatigue syndrome.	Can J Psychiatry 1996 Mar;41(2):129-31 comment on: Can J Psychiatry. 1995 Mar;40(2):93-6	
<b>Cleare AJ, Wessely SC.</b>	Department of Psychological Medicine, Institute of Psychiatry, London. Review Literature	Chronic fatigue syndrome: a stress disorder?	Br J Hosp Med 1996 May 1-14;55(9):571-4	
<b>Cleare AJ, Wessely SC.</b>		Fluoxetine and chronic fatigue syndrome.	Lancet 1996 Jun 22;347(9017):1770; discussion 1771-2	
<b>Conti F, Magrini L, Priori R, Valesini G, Bonini S.</b>	Universita di Roma La Sapienza, I Clinica Medica, Italy.	Eosinophil cationic protein serum levels and allergy in chronic fatigue syndrome.	Allergy 1996 Feb;51(2):124-7	Chronic fatigue syndrome (CFS) is a syndrome of uncertain etiopathogenesis characterized by disabling fatigue associated with a variable number of somatic and/or neuropsychologic symptoms. In patients with CFS, several immunologic abnormalities can be detected, including a higher prevalence of allergy. The aim of this study was to determine whether CFS patients, well studied for their allergy profile, show signs of eosinophil activation, as detectable by the measurement in serum of eosinophil cationic protein (ECP) levels. In 35 consecutive CFS outpatients (diagnosis based on the Centers for Disease Control case definition), ECP was measured in serum by a competitive enzyme immunoassay

				(ECP-FEIA kit, Kabi Pharmacia Diagnostics, Uppsala, Sweden). Fourteen disease-free subjects with no history of CFS or allergy were selected as controls. ECP serum levels were significantly higher in CFS patients than in controls (18.0 +/- 11.3 micrograms/l vs 7.3 +/- 2.1 micrograms/l; P < 0.01). In the CFS population, the prevalence of RAST positivity to one or more allergens was 77%, while no control showed positive RAST. Twelve of the 14 CFS patients with increased ECP serum levels were RAST-positive. However, CFS RAST-positive patients had no significantly higher ECP serum levels than CFS RAST-negative patients (19.3 +/- 12.4 micrograms/l vs 13.6 +/- 3.7 micrograms/l; P = 0.4). This is the first report of increased serum levels of ECP in CFS. On the basis of the available data, it is discussed whether eosinophil activation has a pathogenetic role in CFS or is linked to the frequently associated allergic condition, or, finally, whether a common immunologic background may exist for both atopy and CFS.
<b>Cope H, David AS.</b>		Neuroimaging in chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1996 May;60(5):471-3	
<b>Cope H, Mann A, Pelosi A, David A.</b>	Department of Psychological Medicine, King's College Hospital, London.	Psychosocial risk factors for chronic fatigue and chronic fatigue syndrome following presumed viral illness: a case-control study.	Psychol Med 1996 Nov;26(6):1197-209	This study investigated psychosocial morbidity, coping styles and health locus of control in 64 cases with and without chronic fatigue identified from a cohort of primary care patients recruited 6 months previously with a presumed, clinically diagnosed viral illness. A significant association between chronic fatigue and psychosocial morbidity, somatic symptoms and escape-avoidance coping styles was shown. Chronic fatigue cases were significantly more likely to have a past psychiatric history and a current psychiatric diagnosis based on a standardized clinical interview. Twenty-three of the cases fulfilled criteria for chronic fatigue syndrome (CFS). Such cases were significantly more fatigued than those not fulfilling criteria, but had little excess psychiatric disorder. A principal components analysis provided some evidence for chronic fatigue being separable from general psychosocial morbidity but not from the tendency to have other somatic complaints. Past psychiatric history and psychological distress at the time of the viral illness were risk factors for psychiatric 'caseness' 6 months later, while presence of fatigue, psychologising attributional style and sick certification were significant risk factors for CFS. These findings extend a previous questionnaire study of predictors of chronic 'post-viral' fatigue.
<b>Cordero DL, Sisto SA, Tapp WN, LaManca JJ, Pareja JG, Natelson BH.</b>	Fatigue Research Center, DVA Medical Center, East Orange, NJ 07018, USA.	Decreased vagal power during treadmill walking in patients with chronic fatigue syndrome.	Clin Auton Res 1996 Dec;6(6):329-33	The purpose of this study was to determine if patients with the chronic fatigue syndrome have less vagal power during walking and rest periods following walking, in comparison to a group of healthy controls. Eleven patients (ten women and one man) who fulfilled the case definition for chronic fatigue syndrome modified to reduce heterogeneity and eleven healthy, but sedentary, age- and sex-matched controls walked on a treadmill at 2.5 mph four times each for 4 min duration. Between each period of walking, subjects were given a 4-min seated rest period. Vagal power, a Fourier-based measure of cardiac, parasympathetic activity in the frequency range of 0.15 to 1.0 Hz, was computed. In each period of walking and in one period of rest, patients had significantly less vagal power than the control subjects despite there being no significant group-wise differences in mean heart rate, tidal volume, minute volume, respiratory rate, oxygen consumption or total spectrum power. Further, patients had a significant decline in resting vagal power after periods of walking. These results suggest a subtle abnormality in vagal activity to the heart in patients with the chronic fatigue syndrome and may explain, in part, their post-exertional symptom exacerbation.
<b>Crofford LJ, Demitrack MA.</b>	Department of Internal Medicine, University of Michigan, Ann Arbor, USA.	Evidence that abnormalities of central neurohormonal systems are key to understanding fibromyalgia and chronic fatigue syndrome.	Rheum Dis Clin North Am 1996 May;22(2):267-84	Fibromyalgia (FM) and chronic fatigue syndrome (CFS) fall into the spectrum of what might be termed stress-associated syndromes by virtue of frequent onset after acute or chronic stressors and apparent exacerbation of symptoms during periods of physical or emotional stress. These illnesses also share perturbation of the hypothalamic-pituitary-adrenal axis and sympathetic stress response systems. In this article, the authors discuss the specific neurohormonal abnormalities found in FM and CFS and potential mechanisms by which dysfunction of neurohormonal stress-response systems could contribute to vulnerability to stress-associated syndromes and to the symptoms of FM and CFS.
<b>Czarnowski D, Panasiuk B, Wiercinska-Drapalo A, Puzanowska B, Prokopowicz D.</b>	Klinika Obscrwacyjno-Zakazna Akademii Medycznj w Bialymstoku.	[Chronic fatigue syndrome]. [article in Polish]	Pol Arch Med Wewn 1996 Aug;96(2):161-4	
<b>David A, Wessely S.</b>		Chronic fatigue syndrome.	Lancet 1996 Nov	

			16;348(9038):1385 comment on: Lancet. 1996 Oct 12;348(9033):971	
<b>De Lorenzo F, Hargreaves J, Kakkar VV.</b>	Thrombosis Research Institute, London, UK.	Possible relationship between chronic fatigue and postural tachycardia syndromes.	Clin Auton Res 1996 Oct;6(5):263-4	Postural tachycardia syndrome refers to the development of symptoms such as light-headedness, visual blurring, palpitations and weakness on assuming an upright posture; these symptoms are relieved by resuming a supine posture. This syndrome is occasionally associated with idiopathic hypovolemia, impaired vasomotor tone, deconditioning and autonomic neuropathy, but has not been reported in association with chronic fatigue syndrome (CFS). We describe five patients who satisfied the CFS criteria of the Centres for Disease Control and Prevention. Upright tilt-table testing induced significant hypotension and increased heart rate in all five patients, consistent with clinical and autonomic manifestation of postural tachycardia syndrome.
<b>De Lorenzo F, Hargreaves J, Kakkar VV. Publication Types: Letter</b>		Lung function test findings in patients with chronic fatigue syndrome (CFS)	Aust N Z J Med 1996 Aug;26(4):563-4 comment in: Aust N Z J Med. 1997 Jun;27(3):346	
<b>De Lorenzo F, Kakkar VV.</b>		Twenty-four-hour urine analysis in patients with orthostatic hypotension and chronic fatigue syndrome (CFS)	Aust N Z J Med 1996 Dec;26(6):849-50	
<b>De Vinci C, Levine PH, Pizza G, Fudenberg HH, Orens P, Pearson G, Viza D.</b>	Immunodiagnosis and Immunotherapy Unit, 1st Division of Urology Sant'Orsola-Malpighi Hospital, Bologna, Italy.	Lessons from a pilot study of transfer factor in chronic fatigue syndrome.	Biotherapy 1996;9(1-3):87-90	Transfer Factor (TF) was used in a placebo controlled pilot study of 20 patients with chronic fatigue syndrome (CFS). Efficacy of the treatment was evaluated by clinical monitoring and testing for antibodies to Epstein-Barr virus (EBV) and human herpes virus-6 (HHV-6). Of the 20 patients in the placebo-controlled trial, improvement was observed in 12 patients, generally within 3-6 weeks of beginning treatment. Herpes virus serology seldom correlated with clinical response. This study provided experience with oral TF, useful in designing a larger placebo-controlled clinical trial. Randomized Controlled Trial
<b>Diamantis I.</b>	Department Innere Medizin, Medizinische Universitäts-Poliklinik, Basel.	[A case from practice (343). Chronic fatigue syndrome following Lyme borreliosis].[article in German]	Schweiz Rundsch Med Prax 1996 Feb 27;85(9):287-8	
<b>DiPino RK, Kane RL.</b>	Department of Psychology, Veterans Administration Medical Center, Baltimore, Maryland 21201, USA.	Neurocognitive functioning in chronic fatigue syndrome.	Neuropsychol Rev 1996 Mar;6(1):47-60	Although substantial research has been conducted on chronic fatigue syndrome (CFS) over the past decade, the syndrome remains poorly understood. The most recent case definition describes CFS as being characterized both by disabling fatigue and by subjective reports of difficulty with concentration and "short-term" memory. However, research into the neurocognitive and psychological functioning of individuals with CFS has provided mixed objective results. The current paper reviews studies that have examined the neurocognitive and/or psychological functioning of individuals with CFS. Changes in research design and instruments employed to study individuals with CFS are suggested.
<b>Djaldetti R, Ziv I, Achiron A, Melamed E.</b>	Department of Neurology, Beilinson Medical Center, Petah Tiqva 49100, Israel.	Fatigue in multiple sclerosis compared with chronic fatigue syndrome: A quantitative assessment.	Neurology 1996 Mar;46(3):632-5	Fatigue, a common complaint among patients with multiple sclerosis (MS), is poorly characterized. We developed a computerized method that quantitatively measures fatigue, and defined a fatigue index (FI), which is the ratio between the integral of muscle strength decay over time and maximal voluntary contraction. Thirty patients (mean age, 37.4 +/- 10.3 years) were examined - 20 patients with pyramidal tract involvement and 10 patients with involvement of other neurological systems. We evaluated 10 patients during relapse and 3 months afterwards, and compared their results with those of four patients with chronic fatigue syndrome (CFS) and 13 age-matched health subjects. The FI was significantly higher in the MS patients as compared with the CFS patients and normal controls: 34.2 +/- 6.4% versus 27.5 +/- 1.0% and 23.6 +/- 6.8%, p < 0.05. Within the MS group, the FI correlated with the presence of pyramidal signs- 43.5% compared with 33% in patients without pyramidal signs, p < 0.01. In MS patients, fatigue worsened during a relapse affecting the pyramidal tract, but not during a relapse in other systems. These results demonstrate that fatigue can be quantitatively measured in MS patients, and that pyramidal dysfunction leads to increased fatigability.

<b>Drago F, Ranieri E, Pastorino A, Casazza S, Crovato F, Rebori A.</b>	Department of Dermatology, University of Genoa, Italy.	Epstein-Barr virus-related primary cutaneous amyloidosis. Successful treatment with acyclovir and interferon-alpha.	Br J Dermatol 1996 Jan;134(1):170-4	Cutaneous lesions related to chronic active Epstein-Barr virus (EBV) infection have been rarely documented in immunocompetent patients. A 30-year-old woman, fulfilling the diagnostic criteria for the chronic fatigue syndrome, had a 10-year history of pruritic brownish macules and papules on her chest and back. Her EBV serology was abnormal; the EBV genome was present in the epidermis of lesions, in oral secretions, and in peripheral mononuclear cells (PMC). Her blood lymphocytes spontaneously outgrew in culture. Histology revealed deposits of amyloid in the papillary dermis. Treatment with acyclovir and interferon-alpha rapidly improved her condition, stopped the lymphocyte outgrowth in culture, and reduced the EBV DNA content in oral secretions and in PMC. These data support an endogenous reactivation of EBV infection and suggest a causal relationship with primary amyloidosis.
<b>Dunstan RH, Donohoe M, Taylor W, Roberts TK, Murdoch RN, Watkins JA, McGregor NR.</b>		Chlorinated hydrocarbons and chronic fatigue syndrome.	Med J Aust 1996 Feb 19;164(4):251 comment on: Med J Aust. 1995 Sep 18;163(6):285-6	
<b>Dyck D, Allen S, Barron J, Marchi J, Price BA, Spavor L, Tateishi S.</b>		Management of chronic fatigue syndrome: case study.	AAOHN J 1996 Feb;44(2):85-92	1. Chronic fatigue syndrome (CFS) is a complex disorder marked by incapacitating fatigue of uncertain etiology which has resulted in a least a 50% reduction in activity and is of at least 6 months' duration. 2. Definitive diagnosis can be very challenging. Because no markers objectively identify the presence of CFS, diagnosis depends heavily on the presence of subjective complaints. 3. The current philosophy of CFS management is to use a multidisciplinary approach incorporating these rehabilitation goals: restore a sense of self efficacy and control; gradually increase physical activity; and decrease the restrictions imposed by CFS.
<b>Eaton KK.</b>		Cognitive behaviour therapy for the chronic fatigue syndrome. Use an interdisciplinary approach.	BMJ 1996 Apr 27;312(7038):1097; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
<b>Euga R, Chalder T, Deale A, Wessely S.</b>	Academic Department of Psychological Medicine, King's College School of Medicine and Dentistry, London.	A comparison of the characteristics of chronic fatigue syndrome in primary and tertiary care.	Br J Psychiatry 1996 Jan;168(1):121-6	BACKGROUND: To evaluate the characteristics of Chronic Fatigue Syndrome (CFS) in primary and tertiary care. METHOD: A comparison of subjects fulfilling criteria for CFS, identified as part of a prospective cohort study in primary care, compared to 79 adults fulfilling the same criteria referred for treatment to a specialist CFS clinic. RESULTS: Hospital cases were more likely to belong to upper socio-economic groups, and to have physical illness attributions. They had higher levels of fatigue and more somatic symptoms, and were more impaired functionally, but had less overt psychological morbidity. Women were over-represented in both primary care and hospital groups. Nearly half of those referred to a specialist clinic did not fulfil operational criteria for CFS. CONCLUSION: The high rates of psychiatric morbidity and female excess that characterise CFS in specialist settings are not due to selection bias. On the other hand higher social class and physical illness attributions may be the result of selection bias and not intrinsic to CFS.
<b>Farmer A, Chubb H, Jones I, Hillier J, Smith A, Borysiewicz L.</b>		Screening for psychiatric morbidity in subjects presenting with chronic fatigue syndrome.	Br J Psychiatry 1996 Mar;168(3):354-8	BACKGROUND. There is a need for a valid self-rating questionnaire to screen for psychiatric morbidity in patients with chronic fatigue syndrome (CFS). This study had the aim of assessing the utility and validity of two commonly used measures. METHOD. Scores obtained on the General Health Questionnaire (GHQ) and the Beck Depression Inventory (BDI) were compared with various diagnostic and severity ratings obtained via a validating clinical interview, the Schedules for the Clinical Assessment of Neuropsychiatry (SCAN) in 95 consecutively referred subjects at a medical out-patient clinic who fulfilled standard criteria for CFS, and 48 healthy controls. Outcome measures were validating coefficients and receiver operating characteristics (ROC) for different thresholds and scoring on GHQ and BDI and index of definition (ID) as measured by SCAN; and Pearson and point by serial correlation coefficients for different diagnostic groups derived via SCAN and defined according to ICD-10 and DSM-III-R. RESULTS. GHQ and BDI perform poorly as screeners of psychiatric morbidity in CFS subjects when compared with various SCAN derived ratings although results for controls are comparable with other studies. CONCLUSIONS. Neither the GHQ nor BDI alone can be recommended as screeners for psychiatric morbidity in CFS subjects.
<b>Few J, Thompson NW,</b>	Department of Surgery,	Riedel's thyroiditis: treatment	Surgery 1996 Dec;120(6):993-	BACKGROUND: Riedel's thyroiditis is an often disabling disease with clinical and histologic

<p><b>Angelos P, Simeone D, Giordano T, Reeve T.</b></p>	<p>University of Michigan, Ann Arbor, USA.</p>	<p>with tamoxifen.</p>	<p>8; discussion 998-9</p>	<p>similarity to several other fibrous inflammatory disorders. Surgical treatment alone is often unsatisfactory in permanently alleviating airway compression, dysphagia, neck immobility, pain, or chronic fatigue syndrome. Investigation of drugs shown to be of benefit in the treatment of related fibrous disorders in which hormonal factors or inflammatory deregulation appear to be important is indicated. Tamoxifen has not been previously used in the treatment of Riedel's thyroiditis. METHODS: Four patients with clinical and histologic diagnoses of Riedel's thyroiditis were evaluated before and after treatment with tamoxifen. Each had progressive symptomatic disease of 3 to 16 years' duration despite one or more surgical procedures and steroid therapy. Subjective improvement was noted in all cases, and objective changes were confirmed by periodic physical and computed tomographic examinations. RESULTS: Patients have been monitored for 1 to 4 years with subjective improvement in 100% and objective disease regression ranging from 50% to 100% in all patients. One patient had complete regression within 6 months, and another had more than 50% regression within 3 months. All have returned to predisease activity levels. There were no significant side effects of the therapy. CONCLUSIONS: Tamoxifen has proved to be the most effective drug therapy available for managing Riedel's thyroiditis. Our studies suggest that this is unrelated to antiestrogen activity. Tamoxifen's effectiveness may be caused by a mechanism by which it stimulates the release of transforming growth factor-beta, which may inhibit the fibroblastic proliferation characteristic of Riedel's thyroiditis.</p>
<p><b>Fiedler N, Kipen H, Natelson B, Ottenweller J.</b></p>	<p>UMDNJ-Robert Wood Johnson Medical School, Environmental &amp; Occupational Health Sciences Institute, Piscataway 08855, USA.</p>	<p>Chemical sensitivities and the Gulf War: Department of Veterans Affairs Research Center in basic and clinical science studies of environmental hazards.</p>	<p>800: Regul Toxicol Pharmacol 1996 Aug;24(1 Pt 2):S129-38</p>	<p>The purpose of the New Jersey Center for Environmental Hazards Research is to define the illness referred to as Persian Gulf Syndrome (PGS). Our preliminary data indicated that more than half of the Persian Gulf Registry (PGR) veterans reported illness characterized by severe fatigue and symptoms consistent with chemical sensitivities. Therefore, our research approach focuses on investigations of veterans with chronic fatigue syndrome (CFS) and multiple chemical sensitivities (MCS). Project 1 is an epidemiological study of 2800 PGR veterans. Symptoms, indices of Chronic Fatigue (CF) and Chemical Sensitivity (CS), and risk factors will be surveyed with mailed questionnaires. Risk factors include demographics, past medical history, psychosocial variables, Gulf War experiences such as prophylactic medication use, occupational and environmental exposures, and pesticide exposures. Symptoms will be clustered to define Gulf War Syndromes. Significant associations between risk factors and these symptom clusters will also be investigated. Subjects identified as CF, CS, or both will be recruited into Projects 2 and 3. In Project 2, healthy veterans will be compared to veterans with CF, CS, and CF concurrent with CS. Veterans will undergo four studies: (1) viral-immunological, (2) psychiatric, psychological, behavioral, and neuropsychological, (3) autonomic dysregulation, and (4) marker of P4501A2 induction resulting from exposure to combusting material. The purpose of Project 3 is to test the autonomic, immunologic, neuropsychologic, and psychologic responses of veterans with CS or CF to two stressors: controlled chemical exposure and exercise. CS subjects will undergo chemical exposures in our Controlled Environment Facility (CEF) to assess their biologic and psychologic response to low-level exposure. CF subjects will undergo a maximal treadmill exercise test. Circadian patterns of catecholamines and axillary temperature, viral burden, and cardiovascular and endocrine reactivity will be measured in response to this physical stressor. Project 4 is an animal study evaluating the interaction between stress and pathology/physiology when rats are predisposed to disease by exposure to Soman or to Dioxin. Two strains of rats that differ in stress reactivity will be used to determine the interaction of hereditary factors and chemical exposure.</p>
<p><b>Fiedler N, Kipen H, Natelson B, Ottenweller J.</b></p>	<p>Environmental &amp; Occupational Health Sciences Institute, UMDNJ-Robert Wood Johnson Medical School, 681 Frelinghuysen Road, Piscataway, New Jersey, 08855</p>	<p>Chemical Sensitivities and the Gulf War: Department of Veterans Affairs Research Center in Basic and Clinical Science Studies of Environmental Hazards</p>	<p>Regul Toxicol Pharmacol 1996 Aug;24(1):S129-38</p>	<p>The purpose of the New Jersey Center for Environmental Hazards Research is to define the illness referred to as Persian Gulf Syndrome (PGS). Our preliminary data indicated that more than half of the Persian Gulf Registry (PGR) veterans reported illness characterized by severe fatigue and symptoms consistent with chemical sensitivities. Therefore, our research approach focuses on investigations of veterans with chronic fatigue syndrome (CFS) and multiple chemical sensitivities (MCS). Project 1 is an epidemiological study of 2800 PGR veterans. Symptoms, indices of Chronic Fatigue (CF) and Chemical Sensitivity (CS), and risk factors will be surveyed with mailed questionnaires. Risk factors include demographics, past medical history, psychosocial variables, Gulf War experiences such as prophylactic medication use, occupational and environmental exposures, and pesticide exposures. Symptoms will be clustered to define Gulf War Syndromes. Significant associations between risk</p>

				factors and these symptom clusters will also be investigated. Subjects identified as CF, CS, or both will be recruited into Projects 2 and 3. In Project 2, healthy veterans will be compared to veterans with CF, CS, and CF concurrent with CS. Veterans will undergo four studies: (1) viral-immunological, (2) psychiatric, psychological, behavioral, and neuropsychological, (3) autonomic dysregulation, and (4) marker of P4501A2 induction resulting from exposure to combusting material. The purpose of Project 3 is to test the autonomic, immunologic, neuropsychologic, and psychologic responses of veterans with CS or CF to two stressors: controlled chemical exposure and exercise. CS subjects will undergo chemical exposures in our Controlled Environment Facility (CEF) to assess their biologic and psychologic response to low-level exposure. CF subjects will undergo a maximal treadmill exercise test. Circadian patterns of catecholamines and axillary temperature, viral burden, and cardiovascular and endocrine reactivity will be measured in response to this physical stressor. Project 4 is an animal study evaluating the interaction between stress and pathology/physiology when rats are predisposed to disease by exposure to Soman or to Dioxin. Two strains of rats that differ in stress reactivity will be used to determine the interaction of hereditary factors and chemical exposure.
<b>Fiedler N, Kipen HM, DeLuca J, Kelly-McNeil K, Natelson B.</b>	Department of Environmental and Community Medicine, UMDNJ-Robert Wood Johnson Medical School, Piscataway, New Jersey 08855, USA.	A controlled comparison of multiple chemical sensitivities and chronic fatigue syndrome.	Psychosom Med 1996 Jan-Feb;58(1):38-49	The present study had two objectives: 1) to determine the characteristics that differentiated subjects with multiple chemical sensitivities (MCS), chemical sensitivities (CS), and chronic fatigue syndrome (CFS); and 2) to evaluate the psychiatric and neuropsychological complaints of these groups relative to normal controls. A cross-sectional comparison was made of the following groups matched for age, sex, and education: 1) patients whose sensitivities to multiple low level chemical exposures began with a defined exposure (MCS; N = 23); 2) patients with sensitivities to multiple chemicals without a clear date of onset (CS; N = 13); 3) patients meeting CDC criteria for Chronic Fatigue Syndrome (CFS; N = 18); and 4) normal controls (N = 18). Subjects with sensitivities to chemicals (MCS and CS) reported significantly more lifestyle changes due to chemical sensitivities and significantly more chemical substances that made them ill compared with chronic fatigue and normal controls. MCS, CS, and CFS patients had significantly higher rates of current psychiatric disorders than normal controls and reported significantly more physical symptoms with no medical explanation. Seventy-four percent of MCS and 61% of CFS did not qualify for any current Axis I psychiatric diagnosis. Chemically sensitive subjects without a defined date of onset (CS) had the highest rate of Axis I psychiatric disorders (69%). On the MMPI-2, 44% of MCS, 42% of CS, 53% of CFS, and none of the controls achieved clinically significant elevations on scales associated with somatoform disorders. With the exception of one complex test of visual memory, no significant differences were noted among the groups on tests of neuropsychological function. Standardized measures of psychiatric and neuropsychological function did not differentiate subjects with sensitivities to chemicals from those with chronic fatigue. Subjects with sensitivities to chemicals and no clear date of onset had the highest rate of psychiatric morbidity. Standardized neuropsychological tests did not substantiate the cognitive impairment reported symptomatically. Cognitive deficits may become apparent under controlled exposure conditions.
<b>Fischler B, D'Haenen H, Cluydts R, Michiels V, Demets K, Bossuyt A, Kaufman L, De Meirleir K.</b>	Department of Psychiatry, Academic Hospital, Free University of Brussels, Belgium.	Comparison of 99m Tc HMPAO SPECT scan between chronic fatigue syndrome, major depression and healthy controls: an exploratory study of clinical correlates of regional cerebral blood flow.	Neuropsychobiology 1996;34(4):175-83	An explorative analysis of the relationship between symptomatology and cerebral blood flow in the chronic fatigue syndrome (CFS) as assessed with 99mTc HMPAO SPECT scan reveals statistically significant positive correlations between frontal blood flow on the one hand and objectively and subjectively assessed cognitive impairment, self-rating of physical activity limitations and total score on Hamilton Depression Rating Scale on the other. A pathophysiological role of frontal blood flow in the cognitive impairment and physical activity limitations in CFS is hypothesized. A comparison of cerebral blood flow between CFS, major depression (MD) and healthy controls (HC) has been performed. A lower superofrontal perfusion index is demonstrated in MD as compared with both CFS and HC. There is neither a global nor a marked regional hypoperfusion in CFS compared with HC. Asymmetry (R > L) of tracer uptake at parietotemporal level is demonstrated in CFS as compared with MD.
<b>Fry AM, Martin M.</b>	University of Oxford Department of Psychiatry, Park Hospital for Children, U.K..	Cognitive idiosyncrasies among children with the chronic fatigue syndrome: anomalies in self-reported	J Psychosom Res 1996 Sep;41(3):213-23	The possibility that children with the chronic fatigue syndrome (CFS) and their parents tend to display idiosyncratic cognitive processing concerning levels of activity was examined by means of subjective and objective measures of current activity, together with subjective and objective measures of desired and expected future activity. The degree to which subjective reports of current activity level reflect

	AMFRY@VAX.OX.AC.UK	activity levels.		objectively measured activity level was examined in a group of children with CFS and a healthy control group. All subjects were assessed over a 3-day period by means of ambulatory activity monitoring, and self-reports and parent-reports of current activity level were collected by means of visual analog scales. Analysis of variance revealed a significant interaction between the method of measurement (objective versus subjective) and the participant group (CFS versus Healthy) with the CFS children and their parents underestimating actual level of activity relative to the healthy group. Desired and expected levels of future activity were also assessed by means of subjective report. Child and parent expected levels of future activity were compared with their desired levels. Although expected levels of future activity were similar in the two groups, the divergence between expected levels and corresponding desired levels was significantly greater in the CFS group. These results are discussed in terms of idiosyncratic cognitive processes, which are hypothesized to be associated with CFS and which may play a role in the maintenance of the disorder.
<b>Fry AM, Martin M.</b>	Department of Experimental Psychology, University of Oxford, UK. AMFRY@VAX.OX.AC.UK	Fatigue in the chronic fatigue syndrome: a cognitive phenomenon?	J Psychosom Res 1996 Nov;41(5):415-26	What is the source of the perception of excessive fatigue in the chronic fatigue syndrome (CFS)? Studies of physiological response to aerobic activity, of muscle pathology and muscle function in CFS, are reviewed, and suggest that the subjective report of fatigue is not due to any peripheral impairment. In addition, current technological methods such as electroencephalography have failed to uncover the nature of any abnormality in the central motor unit. A physiological model which proposes that patients with CFS possess a reduced threshold for sensory fatigue signals is rejected, because it fails to account for recent findings. Instead, it is suggested that the perception of fatigue in CFS is enhanced by idiosyncrasies in cognitive processing. The implications of this view to our understanding of the perpetuation of CFS as a whole are explored. Publication Types: Review Review Literature
<b>Fukazawa T, Sasaki H, Kikuchi S, Hamada T, Tashiro K.</b>	Hokuyukai Neurology Hospital, Sapporo, Japan.	Serum carnitine and disabling fatigue in multiple sclerosis.	Psychiatry Clin Neurosci 1996 Dec;50(6):323-5	The serum concentrations of total, free and acylcarnitine were compared in 25 patients with multiple sclerosis (MS) and among age- and sex-matched normal controls by the new enzymatic cycling method in order to clarify whether the fatigue in MS might be due to possible carnitine-related fatty acid metabolic abnormalities in the mitochondria of skeletal muscles. Patients with MS were divided into those with and those without excessive fatigue. Levels of total and free carnitine were not significantly different between MS patients and normal controls. Levels of acylcarnitine, whose decrease in chronic fatigue syndrome has been reported, were also similar between MS patients and normal controls. There was no difference in these carnitine levels between MS patients with and without excessive fatigue. We argue that acylcarnitine deficiency and fatty acid metabolic dysfunction in mitochondria are not relevant to the excessive fatigue in patients with MS, and further explanatory investigations are to be sought.
<b>Gibbons R, Macintyre A, Richards C.</b>		Cognitive behaviour therapy for the chronic fatigue syndrome. Patients were not representative of all patients with the syndrome.	BMJ 1996 Apr 27;312(7038):1096-7; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
<b>Goldenberg DL.</b>	Newton-Wellesley Hospital, Newton, MA 02162, USA.	Fibromyalgia, chronic fatigue syndrome, and myofascial pain.	Curr Opin Rheumatol 1996 Mar;8(2):113-23	The prevalence of fibromyalgia in the general population was found to be 2% and increased with age. Multiple traumatic factors, including sexual and physical abuse, may be important initiating events. The most important pathophysiologic studies in fibromyalgia included evidence of altered blood flow to the brain and hypothalamic-pituitary-adrenal dysfunction. The prevalence of chronic fatigue syndrome is much less than that of fibromyalgia. Epidemiologic studies demonstrated that chronic fatigue and symptoms of fibromyalgia are distributed as continuous variables in the general population. No association between chronic fatigue and initial infections was seen in primary care practices.
<b>Gonzalez MB, Cousins JC, Doraiswamy PM.</b>	Department of Psychiatry, Duke University Medical Center, Durham, NC, USA.	Neurobiology of chronic fatigue syndrome.	Prog Neuropsychopharmacol Biol Psychiatry 1996 Jul;20(5):749-59	1. Chronic fatigue syndrome (CFS) is characterized by a new onset of significant fatigue for a period of six months or longer usually following an infection, injury or period of high stress. 2. The exact etiology of CFS is not known and a diagnostic test is not available. Hence, the diagnosis is made by exclusion of other explanations for the patient's symptoms and by meeting the CDC research case definitions. Early studies supported an infectious or immune dysregulation hypothesis for the pathophysiology of CFS. 3. Subsequent studies documented that neurological, affective and cognitive symptoms also occur at high rates in CFS patients. Neuropsychological, neuroendocrine studies and

				brain imaging have now confirmed the occurrence of neurobiological abnormalities in most patients with CFS. 4. In this article, the authors review these findings in relation to the clinical neurobiology of CFS and their potential relevance to biological psychiatry.
<b>Goodnick PJ.</b>		Treatment of chronic fatigue syndrome with venlafaxine.	Am J Psychiatry 1996 Feb;153(2):294	
<b>Grant JE, Veldee MS, Buchwald D.</b>	University of Washington Medical Center, Seattle, 98104, USA.	Analysis of dietary intake and selected nutrient concentrations in patients with chronic fatigue syndrome.	J Am Diet Assoc 1996 Apr;96(4):383-6	
<b>Griffiths RA, Beumont PJ, Moore GM, Touyz SW.</b>	Department of Psychological Medicine, University of Sydney, New South Wales, Australia.	Chronic fatigue syndrome and dieting disorders: diagnosis and management problems.	Aust N Z J Psychiatry 1996 Dec;30(6):834-8	OBJECTIVE: This paper illustrates the importance of conducting an initial and ongoing psychiatric assessment of patients with chronic fatigue syndrome in order to diagnose dieting disorders. The diagnostic issues and management problems of three case vignettes, two with anorexia nervosa and one with bulimia nervosa, are described. METHOD: The treatment response of dieting disordered patients is generally prolonged after a previous diagnosis of chronic fatigue syndrome has been made and the patient and family favour a disease diagnosis. RESULTS: Several management problems arise and family members may also be reluctant to accept a dieting disorder diagnosis. CONCLUSIONS: Early detection of dieting disorders by adequate screening and assessment is necessary so that a significant reduction in morbidity may occur.
<b>Gruber AJ, Hudson JI, Pope HG Jr.</b>	Biological Psychiatry Laboratory, McLean Hospital, Belmont, Massachusetts, USA.	The management of treatment-resistant depression in disorders on the interface of psychiatry and medicine. Fibromyalgia, chronic fatigue syndrome, migraine, irritable bowel syndrome, atypical facial pain, and premenstrual dysphoric disorder.	Psychiatr Clin North Am 1996 Jun;19(2):351-69	We have reviewed studies examining the efficacy of various psychotropic medications, primarily antidepressant agents, in the treatment of a group of disorders that appear to exhibit some phenomenologic and genetic relationship to major depression. These disorders all appear to benefit (albeit to varying degrees) from antidepressant medications of several different chemical families. This observation has important theoretical and clinical implications. From a theoretical perspective, these results invite the hypothesis that these various disorders may share some particular etiologic "step" in common with major depression-and that the various antidepressant classes benefit these various disorders and major depression via a common action at this hypothetical "step". Although there is an appealing parsimony to this hypothesis, several reservations must be considered. First, it must be recognized that the quality of the available studies varies widely. As noted in the text, these studies used numerous different designs, varying diagnostic criteria for the disorders under study, and diverse methods of rating outcome. Interpretation is further complicated by the fact that many studies included other concomitant medications or therapeutic interventions in addition to the psychotropic drugs administered. Also, the dose of antidepressant medications administered in many of these studies, especially those using TCAs, was often much less than that normally administered in the treatment of major depressive disorder itself. Finally, many of the studies did not systematically evaluate improvement in both the physical and psychological symptoms of a given disorder. For all of these reasons, any theoretic discussion of the results must be tentative. Nevertheless, the overall tally of results strongly favors the hypothesis that antidepressant agents, regardless of their chemical class, are generally useful in the treatment of these disorders. At a minimum, therefore, we can conclude that antidepressant treatment in these disorders deserves aggressive further investigation in studies with modern, rigorous designs. Second, even allowing that multiple antidepressant agents are effective in these various disorders, it still may be premature to conclude that these disorders are related to major depressive disorder. In particular, many of the studies found little correlation between improvement in psychological symptoms and physical symptoms of a given disorder. This observation would seem to argue against a relationship with major depressive disorder. The alternative hypothesis, however, namely, that these disorders do not share a common etiologic "step," seems even less attractive. It would be a remarkable coincidence if, say, fluoxetine possessed an antidepressant property, an independent antimigraine property, and a third, independent, antipremenstrual dysphoric disorder property. And it would be even more peculiar if various other antidepressant medications chemically unrelated to fluoxetine also, by chance alone, benefited all of these same disorders via still other independent mechanisms. Although we cannot, of course, rule out the possibility of multiple mechanisms and multiple causes, the experience of scientific research often has been that the simpler explanation of a phenomenon has proved to be correct. Therefore, the possibility of a link among these

				various antidepressant-responsive disorders deserves investigation. From a clinical perspective, too, these results are important. They suggest that trials of antidepressant medications should be strongly considered in patients with these disorders. Furthermore, other types of psychotropic medication appear to have a role in the treatment of individual disorders, as discussed in the corresponding sections.(ABSTRACT TRUNCATED) Review Literature
<b>Gushue J.</b>		Increasing workplace stress means occupational medicine will be a growth area.	CMAJ 1996 Nov 1;155(9):1310-3	Physicians attending a recent annual meeting on occupational medicine heard wide-ranging discussions about chronic fatigue syndrome and the effect of increased stress on workers. They also learned that occupational medicine is likely to be one of the growth specialties in the coming decade.
<b>Hakimi R.</b>	Stabsabteilung arztlicher Dienst der Hallesche-Nationale Krankenversicherung a.G Stuttgart.	[Chronic fatigue syndrome--also an insurance medicine problem].[article in German]	Versicherungsmedizin 1996 Apr 1;48(2):59-61	Not everybody who is chronically tired has a chronic fatigue syndrome. The diagnosis of the chronic fatigue syndrome is still a problem, and is becoming a problem in health insurance medicine too. There is a lack of knowledge concerning the causes, the diagnosis and the therapy of the chronic fatigue syndrome. And there is still the question if the chronic fatigue syndrome is an entity of its own. For these reasons we should apply the few facts we really know about the chronic fatigue syndrome. This is the working case definition of Kaplan et al. from 1988. Otherwise there will be done hundreds of expensive laboratory tests, which are useless for the patient and very costly for the health insurance companies.
<b>Hall SR, Smith AP.</b>	School of Psychology, University of Birmingham, UK.	Behavioural effects of infectious mononucleosis.	Neuropsychobiology 1996;33(4):202-9	The aim of the present study was to provide preliminary information on the acute and chronic effects of infectious mononucleosis (IM) on memory, attention, psychomotor performance and mood. These issues were examined by comparing individuals with acute IM, those who had the initial illness some months before, and matched healthy controls. Objective measures of memory, attention, motor skills and visual functions were obtained, as were subjective reports of mood. The results showed selective effects of acute IM on performance and mood, with the profile of impairments being very similar to those observed in previous studies of influenza. Different impairments were observed in subjects who had the primary illness several months before, and the effects observed in this group were similar to those observed in recent studies of chronic fatigue syndrome patients. Both acute and chronic IM subjects reported similar levels of symptoms and psychopathology, with both groups having greater scores than the controls. However, the performance impairments did not reflect symptoms or psychopathology. One may conclude that the study of IM will provide important data on both the acute and longer lasting effects of viral infections on the brain and behaviour.
<b>Hamre HJ.</b>		[Chronic fatigue syndrome and cognitive therapy].[article in Norwegian]	Tidsskr Nor Laegeforen 1996 May 10;116(12):1503 comment in: Tidsskr Nor Laegeforen. 1996 May 20;116(13):1615 comment on: Tidsskr Nor Laegeforen. 1996 Mar 10;116(7):861-4	
<b>Hana I, Vrabel J, Pekarek J, Cech K.</b>	Dept. of Immunology, Institute for Clinical and Experimental Medicine, Prague, Czechia.	The influence of age on transfer factor treatment of cellular immunodeficiency, chronic fatigue syndrome and/or chronic viral infections.	Biotherapy 1996;9(1-3):91-5	A group of 222 patients suffering from cellular immunodeficiency (CID), frequently combined with chronic fatigue syndrome (CFS) and/or chronic viral infections by Epstein-Barr virus (EBV) and/or cytomegalovirus (CMV), were immunologically investigated and treated with transfer factor (TF). The age range was 17-77 years. In order to elucidate the influence of aging on the course of the disease and on treatment, 3 subgroups were formed: 17-43 years, 44-53 years, and 54-77 years. Six injections of Immodin (commercial preparation of TF by SEVAC, Prague) were given in the course of 8 weeks. When active viral infection was present, IgG injections and vitamins were added. Immunological investigation was performed before the start of therapy, and subsequently according to need, but not later than after 3 months. The percentages of failures to improve clinical status of patients were in the individual subgroups, respectively: 10.6%, 11.5% and 28.9%. The influence of increasing age on the percentage of failures to normalize low numbers of T cells was very evident: 10.6%, 21.2% and 59.6%. In individuals unaffected by therapy, persistent absolute lymphocyte numbers below 1,200 cells were found in 23.1%, 54.5% and 89.3% in the oldest group. Statistical analysis by Pearson's Chi-square test, and the test for linear trend proved that the differences among the individual age groups were significant. Neither sex, nor other factors seemed to influence the results. The results of this pilot study show that age substantially influences the failure rate of CID treatment using TF. In older

				people, it is easier to improve the clinical condition than CID: this may be related to the diminished number of lymphocytes, however, a placebo effect cannot be totally excluded.
<b>Hausotter W.</b>		[Expert assessment of chronic fatigue syndrome].[article in German]	Versicherungsmedizin 1996 Apr 1;48(2):57-9	The Chronic-Fatigue-Syndrome (CFS) has been first described in 1988 and has been also in Germany recently more frequently diagnosed. It is similar to a lot of other terms, especially to "neurasthenia", which has been introduced 1869 from Beard and is now again content of ICD-10. CFS is defined by primary and secondary criteria, which are however largely subjective. There are no objective signs. It is unknown if this syndrome represents a disease entity of its own. The explanation is either exclusive organic based on immunological and virological findings or exclusive psychogenic as a special form of anxiety psychosis. Possibly are both factors involved as part of "psycho-neuro-immunology". CFS is increased subject of medical certification. It has been tried to give a practical guidance to the assessment of CFS.
<b>Hilgers A, Johannes Frank</b>		Chronic Fatigue Syndrome Evaluation of a 30-Criteria-Score and Correlation with Immune Activation	Journal of Chronic Fatigue Syndrome 1996; 2(4): 35 - 47	Objective: The development of a score for severity of Chronic Fatigue Syndrome (CFS), the correlation of CFS with parameters of immune activation and the association with pathogens. Methods: Five hundred five patients with suspicion of Chronic Fatigue Syndrome and no other definitive diagnosis were checked by a 45-criteria-score, basic laboratory programs and immunological profiles. In most of the patients further tests concerning complement system, immune activation markers, hormones and serology of herpesviruses, Chlamydia and Borrelia could be evaluated. Comparison of the symptoms of CFS patients with healthy controls lead to a 30-criteria-score and this score was correlated with laboratory parameters (Spearman rank-correlation-coefficients, ties corrected). Results: Three hundred eighty-five patients fulfilling stronger criteria according to the Centers for Disease Control (CDC) definition showed significant differences to 53 healthy controls in 40 of the 45 criteria ( $p < 0.001$ , twitches and food allergies $p < 0.05$ ). Thirteen symptoms corresponding to CDC criteria were all significant ( $p < 0.001$ ), 17 further significant criteria of descending precision were added: respiratory infections, palpitations, dizziness, dyspepsia, dryness of mouth/eyes, allergies, nausea, paresthesia, loss of hair, skin alterations, dyscoordination, chest pain, personality changes, eczema, general infections, twitches, urogenital infections. A correlation between the 30-criteria-score and immunological parameters could be evaluated in 472 of the 505 patients. Significant positive correlation with the 30-criteria-score was found in numbers of CD8+ T-lymphocytes, HLA-DR+ T-lymphocytes, gamma globulins, IgM, IgG, and for the number of types of autoantibodies (mainly ANA, ACA, antithyroid and antiparietal cell antibodies). Significant negative correlation was found in albumin-globulin-ratio, eosinophils and IgE. Most of these parameters also correlated with one another. On the other hand, in subgroups of the 505 patients the Frequency of positivity in serological tests for HHV-6 (49.9%), EBV (35.4%), HSV (29.2%), CMV (12.5%) and Chlamydia (35.0%) was striking. Borrelia Western blots showed 3 or more specific IgG-bands in 54 of 131 patients (41.2%). In some cases infection with EBV, HHV-6 and CMV, respectively, was confirmed by DNA-PCR-test and antigen detection. Summary: In increasingly larger groups of patients with CFS and related constellations we often see clinical signs and longer anamnesis of other symptoms besides the classical criteria of CFS, especially a high prevalence of local and general susceptibility to infections and hints to prolonged inflammation processes. Together with other results, the data confirm the hypothesis that a reduced or unstable immune control or delayed immune reaction to persisting viruses or bacterial intracellular pathogens, possibly triggered by common infections or other environmental factors, can lead to a chronic neuroimmune activation state and auto-immune disorders. Hypersensitivity symptoms of the patients might not be mediated by classical allergies alone but also result from a type-IV-hypersensitivity.
<b>Ho-Yen DO.</b>		Cognitive behaviour therapy for the chronic fatigue syndrome. Patients' beliefs about their illness were probably not a major factor.	BMJ 1996 Apr 27;312(7038):1097-8 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
<b>Hoffmann A, Linder R, Kroger B, Schnabel A, Kruger GR.</b>	Medizinische Universitätsklinik Lubeck.	[Fibromyalgia syndrome and chronic fatigue syndrome. Similarities and	Dtsch Med Wochenschr 1996 Sep 20;121(38):1165-8	

		differences].[article in German]		
<b>Hotopf M, Noah N, Wessely S.</b>	Institute of Psychiatry, Denmark Hill, London, UK.	Chronic fatigue and minor psychiatric morbidity after viral meningitis: a controlled study.	J Neurol Neurosurg Psychiatry 1996 May;60(5):504-9	OBJECTIVE--To test the hypotheses that patients exposed to viral meningitis would be at an increased risk of developing chronic fatigue syndrome and would have an excess of neurological symptoms and physical impairment. METHODS--Eighty three patients were followed up 6-24 months after viral meningitis and a postal questionnaire was used to compare outcome with 76 controls who had had non-enteroviral, non-CNS viral infections. RESULTS--For the 159 patients and controls the prevalence of chronic fatigue syndrome was 12.6%, a rate higher than previously reported from primary care attenders, suggesting that moderate to severe viral infections may play a part in the aetiology of some fatigue states. Those with a history of meningitis showed a slight, non-significant increase in prevalence of chronic fatigue syndrome (OR 1.4; 95% CI 0.5-3.6) which disappeared when logistic regression and analysis was used to correct for age, sex, and duration of follow up (OR 1.0; 95% CI 0.3-2.8). Controls showed marginally higher psychiatric morbidity measured on the general health questionnaire-12 (adjusted OR 0.6; 95% CI 0.3-1.3) Both groups had similar rates of neurological symptoms and physical impairment. The best predictor of chronic fatigue was a prolonged duration time of off work after the illness (OR 4.93, 95% CI 1.3-18.8). The best predictor of severe chronic fatigue syndrome diagnosed by Center for Disease Control criteria was past psychiatric illness (OR 7.82, 95% CI 1.8-34.3). Duration of viral illness, as defined by days in hospital, did not predict chronic fatigue syndrome. CONCLUSIONS--(1) The prevalence of chronic fatigue syndrome is higher than expected for the range of viral illnesses examined; (2) enteroviral infection is unlikely to be a specific risk factor for its development; (3) onset of chronic fatigue syndrome after a viral infection is predicted by psychiatric morbidity and prolonged convalescence, rather than by the severity of the viral illness itself.
<b>Hyams KC, Wignall FS, Roswell R.</b>	U.S. Naval Medical Research Institute, Rockville, Maryland, USA.	War syndromes and their evaluation: from the U.S. Civil War to the Persian Gulf War.	Ann Intern Med 1996 Sep 1;125(5):398-405	PURPOSE: To better understand the health problems of veterans of the Persian Gulf War by analyzing previous war-related illnesses and identifying possible unifying factors. DATA SOURCE: English-language articles and books on war-related illnesses published since 1863 that were located primarily through a manual search of bibliographies. DATA EXTRACTION: Publications were assessed for information on the clinical characteristics of war-related illnesses and the research methods used to evaluate such illnesses. DATA SYNTHESIS: Poorly understood war syndromes have been associated with armed conflicts at least since the U.S. Civil War. Although these syndromes have been characterized by similar symptoms (fatigue, shortness of breath, headache, sleep disturbance, forgetfulness, and impaired concentration), no single recurring illness that is unrelated to psychological stress is apparent. However, many types of illness were found among evaluated veterans, including well-defined medical and psychiatric conditions, acute combat stress reaction, post-traumatic stress disorder, and possibly the chronic fatigue syndrome. No single disease is apparent, but one unifying factor stands out: A unique population was intensely scrutinized after experiencing an exceptional, life-threatening set of exposures. As a result, research efforts to date have been unable to conclusively show causality, have been subject to reporting bias, and have lacked similar control populations. In addition to research limitations, war syndromes have involved fundamental, unanswered questions about the importance of chronic somatic symptoms and the factors that create a personal sense of ill health. CONCLUSION: Until we can better understand what constitutes health and illness in all adult populations, we risk repeated occurrences of unexplained symptoms among veterans after each war.
<b>James LC, Folen RA.</b>	Department of Psychology, Tripler Army Medical Center, Honolulu, USA.	EEG biofeedback as a treatment for chronic fatigue syndrome: a controlled case report.	Behav Med 1996 Summer;22(2):77-81	EEG neurofeedback has been identified as a potential diagnostic and treatment protocol with chronic fatigue syndrome (CFS) symptoms. In the present case study, the authors applied an EEG neurofeedback biofeedback paradigm as a treatment modality with a CFS patient. Baseline data were acquired using the Wechsler Adult Intelligence Scale-Revised and qualitative and subjective ratings of cognitive improvement. Test results and clinical findings revealed improvements in the patient's cognitive abilities, functional skill level, and quality of life. The patient showed significant differences in pre- and posttest levels on the Wechsler scale.
<b>Jason LA, Ferrari JR, Taylor RR, Slavich SP,</b>	Department of Psychology, DePaul University, Chicago,	A national assessment of the service, support, and housing	Eval Health Prof 1996 Jun;19(2):194-207	Persons with Chronic Fatigue Syndrome (PWCs) completed and returned by mail a brief survey of open- and closed-ended items designed to assess their utilization and preferences for a variety of

<b>Stenzel CL.</b>	IL 60614, USA.	preferences by persons with chronic fatigue syndrome. Toward a comprehensive rehabilitation program.		services. A total of 984 middle-aged adults diagnosed with Chronic Fatigue Syndrome (CFS) from across North America returned the survey. During the past 12 months, many of these PWCs reported utilization of a primary care physician, gynecologist, CFS specialist, and self-help group to assist in their recovery from CFS. Most PWCs believed it was important to educate both health-care practitioners and the general public about CFS. In terms of their desire for specific recovery needs, factor analysis of responses indicated that these PWCs preferred self-help/social support services and general advocacy services in the treatment of their illness. The implications of these results for developing rehabilitation programs for PWCs are discussed.
<b>Johnson SK, DeLuca J, Diamond BJ, Natelson BH.</b>	Chronic Fatigue Syndrome Research Center, Research Department, Kessler Institute for Rehabilitation, West Orange, NJ 07052, USA.	Selective impairment of auditory processing in chronic fatigue syndrome: a comparison with multiple sclerosis and healthy controls.	Percept Mot Skills 1996 Aug;83(1):51-62	The most consistent deficit observed in individuals with Chronic Fatigue Syndrome has been in efficiency of information processing. To examine the possibility of a modality-specific impairment, the present study examined subjects with Chronic Fatigue Syndrome, multiple sclerosis, and healthy controls on an auditory-versus visual-paced serial-addition test. 20 subjects with Chronic Fatigue Syndrome, 20 subjects with clinically definite Multiple Sclerosis, and 20 sedentary healthy controls were compared. One-half of the subjects in each group were administered the Paced Auditory Serial Addition Test and the other half were administered the Paced Visual Serial Addition Test. The group with Chronic Fatigue Syndrome was differentially impaired on the auditory relative to the visual processing task. The group with Multiple Sclerosis was equally impaired on both versions of the task. The results are discussed within the framework of Baddeley's model of working memory.
<b>Johnson SK, DeLuca J, Natelson BH.</b>	Research Department, Kessler Institute for Rehabilitation, West Orange, N.J. 07052, USA.	Assessing somatization disorder in the chronic fatigue syndrome.	Psychosom Med 1996 Jan-Feb;58(1):50-7	This study was conducted to examine the rates of somatization disorder (SD) in the chronic fatigue syndrome (CFS) relative to other fatiguing illness groups. It further addressed the arbitrary nature of the judgments made in assigning psychiatric vs. physical etiology to symptoms in controversial illnesses such as CFS. Patients with CFS (N = 42), multiple sclerosis (MS) (N = 18), and depression (N = 21) were compared with healthy individuals (N = 32) on a structured psychiatric interview. The SD section of the Diagnostic Interview Schedule (DIS) III-R was reanalyzed using different criteria sets to diagnose SD. All subjects received a thorough medical history, physical examination, and DIS interview. CFS patients received diagnostic laboratory testing to rule out other causes of fatigue. This study revealed that changing the attribution of SD symptoms from psychiatric to physical dramatically affected the rates of diagnosing SD in the CFS group. Both the CFS and depressed subjects endorsed a higher percentage of SD symptoms than either the MS or healthy groups, but very few met the strict DSM-III-R criteria for SD. The present study illustrates that the terminology used to interpret the symptoms (ie, psychiatric or physical) will determine which category CFS falls into. The diagnosis of SD is of limited use in populations in which the etiology of the illness has not been established.
<b>Johnson SK, DeLuca J, Natelson BH.</b>	Chronic Fatigue Syndrome Research Center, West Orange, NJ 07052, USA.	Personality dimensions in the chronic fatigue syndrome: a comparison with multiple sclerosis and depression.	J Psychiatr Res 1996 Jan-Feb;30(1):9-20 comment in: J Psychiatr Res. 1996 Jan-Feb;30(1):3-7	This study investigated the relative rates of personality disturbance in chronic fatigue syndrome (CFS). Individuals who met the CDC criteria for CFS were compared to two other fatiguing illness groups, mild multiple sclerosis and depression, as well as sedentary healthy controls. Subjects were administered a structured psychiatric interview to determine Axis I psychiatric disorders and two self-report instruments to assess Axis II personality disorders and the personality trait of neuroticism. The depressed group had significantly more personality disorders and elevated neuroticism scores compared with the other three groups. The CFS and MS subjects had intermediary personality scores which were significantly higher than healthy controls. The CFS group with concurrent depressive disorder (34% of the CFS group) was found to account for most of the personality pathology in the CFS sample. The results are discussed in the context of the relationship between personality variables and fatiguing illness.
<b>Johnson SK, DeLuca J, Natelson BH.</b>	Chronic Fatigue Syndrome Center, University of Medicine and Dentistry of New Jersey--New Jersey Medical School, West Orange, USA.	Depression in fatiguing illness: comparing patients with chronic fatigue syndrome, multiple sclerosis and depression.	J Affect Disord 1996 Jun 20;39(1):21-30	Because depression is commonly observed in the chronic fatigue syndrome (CFS), the present study sought to determine whether the symptom pattern is similar to that seen in clinically depressed subjects (DEP). Individuals with multiple sclerosis (MS) were chosen as an additional comparison group because MS is a fatiguing illness of known organic etiology. The Beck Depression Inventory (BDI) was used to compare categories of depressive symptomatology. Absolute scores on the BDI were higher for the depressed group on mood and self-reproach symptoms, but were not higher than the CFS group on somatic and vegetative items. Analysis of symptoms as a percentage of total BDI score revealed no significant differences in mood or vegetative items among the three groups. The CFS and MS groups exhibited a significantly lower percentage of self-reproach symptoms than DEP,

				whereas the DEP group showed a lower percentage of somatic symptoms than the CFS and MS groups.
<b>Josevic M, Nikolic S, Dulovic O, Jovanovic L, Zerjav S, Radivojevic M.</b>	Dr. Kosta Todorovitsh Institute of Infectious and Tropical Diseases, Belgrade.	[Neural manifestations in Lyme disease (Lyme borreliosis of the nervous system)].[article in Serbo- Croatian (Cyrillic)]	Srp Arh Celok Lek 1996 Mar- Apr;124(3-4):87-92	The involvement of the nervous system is common during Lyme's disease, and the term neuroborreliosis has been established. All structures of the nervous system, from meninges to periferial nerves, can be involved. Neurological manifestations are most common in the second stage (dissemination). The article deals with the most important neurological manifestations, as well as with the contemporary pathogenetic considerations and therapy. Eleven patients with neuroborreliosis who were treated at Dr. Kosta Todorovitsh Institute of Infectious and Tropical Diseases, are reviewed. Five of them had acute meningoencephalitis, of whom two had concurrent neuritis; one patient had Banawart's syndrome with arthralgias, arthritis and fatigue syndrome; two patients had neuritis; one had bilateral facial palsy; two had chronic fatigue syndrome.
<b>Joyce E, Blumenthal S, Wessely S.</b>	Academic Department of Psychiatry, Charing Cross and Westminster Medical School, London, UK.	Memory, attention, and executive function in chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1996 May;60(5):495-503	OBJECTIVES--To examine cognitive function in chronic fatigue syndrome. METHODS--Twenty patients with chronic fatigue syndrome recruited from primary care and 20 matched normal controls were given CANTAB computerised tests of visuospatial memory, attention, and executive function, and verbal tests of letter and category fluency and word association learning. RESULTS: Patients with chronic fatigue syndrome were impaired, predominantly in the domain of memory but their pattern of performance was unlike that of patients with amnesic syndrome or dementia. They were normal on tests of spatial pattern recognition memory, simultaneous and delayed matching to sample, and pattern-location association learning. They were impaired on tests of spatial span, spatial working memory, and a selective reminding condition of the pattern-location association learning test. An executive test of planning was normal. In an attentional test, eight subjects with chronic fatigue syndrome were unable to learn a response set; the remainder exhibited no impairment in the executive set shifting phase of the test. Patients with chronic fatigue syndrome were also impaired on verbal tests of unrelated word association learning and letter fluency. CONCLUSION--Patients with chronic fatigue syndrome have reduced attentional capacity resulting in impaired performance on effortful tasks requiring planned or self ordered generation of responses from memory.
<b>Kendell R, Turnberg L, Toby J.</b>		Chronic fatigue syndrome.	Lancet 1996 Nov 16;348(9038):1384 comment on: Lancet. 1996 Oct 12;348(9033):971	
<b>Kitani T, Kuratsune H, Fuke I, Nakamura Y, Nakaya T, Asahi S, Tobiume M, Yamaguti K, Machii T, Inagi R, Yamanishi K, Ikuta K.</b>	Department of Hematology and Oncology, Osaka University Medical School, Japan.	Possible correlation between Borna disease virus infection and Japanese patients with chronic fatigue syndrome.	Microbiol Immunol 1996;40(6):459-62	Borna disease virus (BDV) is a neurotropic, as yet unclassified, non-segmented, negative-sense, single-strand RNA virus. Natural infection with this virus has been reported to occur in horses and sheep. In addition, antibodies to BDV in plasma or BDV RNA in peripheral blood mononuclear cells (PBMCs) were also found in patients with neuropsychiatric diseases. We describe here the possible link between the patients with chronic fatigue syndrome (CFS) and infection with BDV.
<b>Klonoff DC.</b>		Chronic fatigue syndrome and neurally mediated hypotension.	JAMA 1996 Feb 7;275(5):359-60 comment on: JAMA. 1995 Sep 27;274(12):961-7	
<b>Kodama M, Kodama T, Murakami M.</b>	Kodama Research Institute of Preventive Medicine, Nagoya, Japan.	The value of the dehydroepiandrosterone- annexed vitamin C infusion treatment in the clinical control of chronic fatigue syndrome (CFS). I. A Pilot study of the new vitamin C infusion treatment with a volunteer CFS patient.	In Vivo 1996 Nov- Dec;10(6):575-84	A series of publications from our laboratory have indicated that the practice of megadose vitamin C drip infusion treatment enhanced the activity of endogenous glucocorticoids in such a way as to improve the clinical course of allergy and autoimmune disease-a disease entity that is known to respond to the therapeutic effect of glucocorticoids. The present paper represents an extension of our vitamin C studies, and intends to investigate the problem whether or not chronic fatigue syndrome (CFS), an acquired immunodeficiency disease, can also be counted as one of the candidate diseases for the vitamin C infusion treatment. We prepared two kinds of vitamin C infusion sets for the clinical use: the dehydroepiandrosterone-annexed vitamin C infusion set (the new set) and the annex-free vitamin C infusion set (the old set). The new set was expected to enhance the endogenous activities of both glucocorticoids and gonadal steroids. We followed the clinical course of a male CFS patient using the old and new vitamin C infusion sets, and with and without the oral intake of erythromycin and chloramphenico. Results obtained are as follows: a) the observation period of a study subject covered a period of August 1995 to May 1996. Combination of pneumonia signs and dermatomyositis

				<p>signs marked the onset of his CFS. b) Old infusion treatment together with the short term antibiotics treatment was found effective for the control of pneumonia in the first stage of the disease (from August to October, 1995). c) Signs of pneumonia recurrence gradually became eminent in the second stage of disease (from November, 1995, to January, 1996) in spite of the moderate frequency of the old treatment together with stepwise prolongation of the antibiotics treatment. d) The alternate practice of the old and new infusion treatments together with the long-term antibiotics treatment, as conducted in the 3rd stage of disease (from February to May, 1996) led to substantial extinction of pneumonia signs (leucocytosis, tachycardia etc). e) The practice of the new infusion treatment markedly increased the excretion of both 17-ketosteroids and 17-hydroxycorticosteroids in the urine. Evidence was also available to indicate that the dehydroepiandrosterone annex was converted to testosterone, which in turn made a contribution to the control of CFS. f) The immunological survey of lymphocyte subsets including NK cell percent failed to find a coherent change in a study subject with CFS. In conclusion, the above results could be taken as evidence to indicate that the new vitamin C infusion treatment effectuates the clinical control of CFS by fortifying the endogenous activities of both cortisol and testosterone. The significance of parallelism between pulmonary infection and CFS, as observed in the clinical course of the test subject, was discussed in the light of the focal infection theory of nephritis.</p>
<p><b>Kodama M, Kodama T, Murakami M.</b></p>	<p>Kodama Research Institute of Preventive Medicine, Nagoya, Japan.</p>	<p>The value of the dehydroepiandrosterone-annexed vitamin C infusion treatment in the clinical control of chronic fatigue syndrome (CFS). II. Characterization of CFS patients with special reference to their response to a new vitamin C infusion treatment.</p>	<p>In Vivo 1996 Nov-Dec;10(6):585-96</p>	<p>This study is a counterpart of the pilot study on the clinical management of chronic fatigue syndrome (CFS) by the combined use of the old (annex-free) and the new (dehydro-epiandrosterone- annexed) vitamin C infusion treatments with and without oral intake of erythromycin and chloramphenicol. We were motivated to start this clinical study by 2 reasons: i) we have made a success in the clinical management of autoimmune disease and allergy by use of the old megadose vitamin C infusion treatment, and we therefore took up CFS as a good candidate for vitamin C infusion treatment; ii) In 1995, we received a total of 313 chronic pneumonia patients whose clinical course showed a good fitness to the criteria of CFS. We assessed the nature of the disease by investigating the clinicoepidemiological aspect of our patients on the one hand and the response of the disease to both the old and new vitamin C infusion treatments with and without the use of 2 antibiotics on the other hand. Results are summarized as follows: a) the analysis of the medical records of our outpatients revealed that chronic type pneumonia epidemic in Nagoya Japan, with its onset of January 1995, showed no sign of its extinction by the end of May 1996. The patient population contained no patients under 15 years of age, and showed a distinct female predominance in the patient number (207 females versus 106 males). In 1995, we also experienced a simple cold epidemic with its onset of January 1995 (162 males and 224 females). The majority of simple cold patients were under 25 years of age in both sexes. b) A chronic type pneumonia patient was distinguished from a simple cold patient in 2 respects: firstly the former required prolonged medical care (over 1 month) resulting in an incomplete cure and return to medical care upon the recurrence of disease, whereas the latter required short-term medical care (mostly within 1 week) ending up with complete cure. Secondly, the former required the long term use of 2 antibiotics (erythromycin and chloramphenicol) together with regular practice of the old and new vitamin C infusion treatments for disease control, whereas the latter recovered from the disease after the short time use of a set of conventional cold remedies. c) The clinical manifestations of our chronic pneumonia patients showed good fitness to the criteria of CFS. d) CFS was distinguished from autoimmune disease-allergy complex by the method of clinical control: the former required the long-term use of 2 antibiotics together with regular practice of the old and new vitamin C infusion treatments, whereas the latter was controllable by the single use of the old vitamin C infusion treatment. e) The combined use of the old and new vitamin C infusion treatments rather than the single use of the old vitamin C infusion treatment was more effective for the control of CFS-a finding which suggests that deficient activities of both endogenous glucocorticoid and endogenous androgen in a CFS patient are somehow related to the genesis and further development of CFS. f) Evidence was available to indicate that the sole use of the new vitamin C infusion treatment may induce a state of gonadal steroid excess together with various other problems in the recipient. The maintenance of a good balance between the old vitamin C infusion set (glucocorticoid-inducer) and the new vitamin C infusion set (inducer of both glucocorticoid and gonadal steroids) in their use was of prime importance for the successful control of CFS. g) The historical significance of CFS epidemic in 1995, and in</p>

<p><b>Komaroff AL, Fagioli LR, Doolittle TH, Gandek B, Gleit MA, Guerriero RT, Kornish RJ 2nd, Ware NC, Ware JE Jr, Bates DW.</b></p>	<p>Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.</p>	<p>Health status in patients with chronic fatigue syndrome and in general population and disease comparison groups.</p>	<p>Am J Med 1996 Sep;101(3):281-90</p>	<p>Nagoya-Japan, is discussed in the light of the new infection concept.</p> <p>PURPOSE: To measure the functional status and well-being of patients with chronic fatigue syndrome (CFS), and compare them with those of a general population group and six disease comparison groups. PATIENTS AND METHODS: The subjects of the study were patients with CFS (n = 223) from a CFS clinic, a population-based control sample (n = 2,474), and disease comparison groups with hypertension (n = 2,089), congestive heart failure (n = 216), type II diabetes mellitus (n = 163), acute myocardial infarction (n = 107), multiple sclerosis (n = 25), and depression (n = 502). We measured functional status and well-being using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), which is a self-administered questionnaire in which lower scores are indicative of greater impairment. RESULTS: Patients with CFS had far lower mean scores than the general population control subjects on all eight SF-36 scales. They also scored significantly lower than patients in all the disease comparison groups other than depression on virtually all the scales. When compared with patients with depression, they scored significantly lower on all the scales except for scales measuring mental health and role disability due to emotional problems, on which they scored significantly higher. The two SF-36 scales reflecting mental health were not correlated with any of the symptoms of CFS except for irritability and depression. CONCLUSION: Patients with CFS had marked impairment, in comparison with the general population and disease comparison groups. Moreover, the degree and pattern of impairment was different from that seen in patients with depression.</p>
<p><b>Komaroff AL, Fagioli LR, Geiger AM, Doolittle TH, Lee J, Kornish RJ, Gleit MA, Guerriero RT.</b></p>	<p>Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.</p>	<p>An examination of the working case definition of chronic fatigue syndrome.</p>	<p>Am J Med 1996 Jan;100(1):56-64</p>	<p>PURPOSE: Chronic fatigue syndrome (CFS) currently is defined by a working case definition developed under the leadership of the United States Centers for Disease Control and Prevention (CDC) based on a consensus among experienced clinicians. We analyzed the experience from one large center to examine the adequacy of the case definition. PATIENTS AND METHODS: Predefined clinical and laboratory data were collected prospectively from 369 patients with debilitating fatigue, of whom 281 (76%) met the major criteria of the original CDC case definition for CFS: (1) fatigue of at least 6 months' duration, seriously interfering with the patient's life; and (2) without evidence of various organic or psychiatric illnesses that can produce chronic fatigue. The same clinical data were obtained from 311 healthy control subjects and two comparison groups with diseases that can present in a similar fashion; relapsing-remitting multiple sclerosis (n = 25) and major depression (n = 19). RESULTS: All of the minor criteria symptoms from the original CDC case definition distinguished patients with debilitating chronic fatigue from healthy control subjects, and many distinguished the patients with chronic fatigue from the comparison groups with multiple sclerosis and depression: myalgias, postexertional malaise, headaches, and a group of infectious-type symptoms (ie, chronic fever and chills, sore throat, swollen glands in the neck or underarm areas). In addition, two other symptoms not currently part of the case definition discriminated the chronic fatigue patients from the control/comparison groups: anorexia and nausea. Physical examination criteria only infrequently contributed to the diagnosis. Patients meeting the CDC major criteria for CFS also met the minor criteria in 91% of cases. CONCLUSION: Patients meeting the major criteria of the current CDC working case definition of CFS reported symptoms that were clearly distinguishable from the experience of healthy control subjects and from disease comparison groups with multiple sclerosis and depression. Eliminating three symptoms (ie, muscle weakness, arthralgias, and sleep disturbance) and adding two others (ie, anorexia and nausea) would appear to strengthen the CDC case definition of CFS.</p>
<p><b>Konstantinov K, von Mikecz A, Buchwald D, Jones J, Gerace L, Tan EM.</b></p>	<p>Autoimmune Disease Center and Department of Cell Biology, The Scripps Research Institute, La Jolla, California 92037, USA.</p>	<p>Autoantibodies to nuclear envelope antigens in chronic fatigue syndrome.</p>	<p>J Clin Invest 1996 Oct 15;98(8):1888-96</p>	<p>We have identified and partially characterized the autoantibodies in sera of 60 patients with chronic fatigue syndrome. Approximately 52% of the sera were found to react with nuclear envelope antigens. The combination of nuclear rim staining observed in immunofluorescence microscopy and immunoblot analysis of highly purified nuclear envelope proteins provided initial characterization of these autoantibodies. Further characterization showed that some sera immunoprecipitated the in vitro transcription and translation product of a human cDNA clone encoding the nuclear envelope protein lamin B1. The autoantibodies were of the IgG isotype. The occurrence of autoantibodies to a conserved intracellular protein like lamin B1 provides new laboratory evidence for an autoimmune component in chronic fatigue syndrome.</p>

<b>Krupp LB, Pollina D.</b>	Department of Neurology, SUNY at Stony Brook 11794- 8121, USA.	Neuroimmune and neuropsychiatric aspects of chronic fatigue syndrome.	Adv Neuroimmunol 1996;6(2):155-67	
<b>Lawrie SM.</b>		Cognitive behaviour therapy for the chronic fatigue syndrome. Essential elements of the treatment must be identified.	BMJ 1996 Apr 27;312(7038):1097; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
<b>Leese G, Chattington P, Fraser W, Vora J, Edwards R, Williams G.</b>	Department of Medicine, University of Liverpool, United Kingdom.	Short-term night-shift working mimics the pituitary- adrenocortical dysfunction in chronic fatigue syndrome.	J Clin Endocrinol Metab 1996 May;81(5):1867-70	The purpose of this study was to determine whether a short period (5 days) of night-shift work affected the pituitary-adrenal responses to CRH. Ten nurses (8 female and 2 male; age 28.1 +/- 1.7 yr: mean +/- SEM) working at the Royal Liverpool University Hospital, and who regularly undertook periods of night and day shift work were enrolled. Measurements were made of basal ACTH and cortisol concentrations, and their responses to iv ovine CRH (1 microgram.kg-1). Basal ACTH concentrations were higher during the night shift than during the day shift (12.9 +/- 5.1 pmol.L-1 vs. 4.7 +/- 1.2 pmol.L-1, P < 0.01) whereas cortisol concentrations were lower (551 +/- 48 nmol.L - 1 vs. 871 +/- 132 nmol.L - 1, P < 0.01). After CRH injection, ACTH concentrations remained consistently higher during the night shift, but the integrated increase in ACTH concentration was lower (P < 0.05) than during the day shift. Conversely, the increase in cortisol concentration was greater during the night shift than the day shift (283 +/- 53 nmol.L-1 vs. 134 +/- 41 nmol.L-1, P < 0.05). We conclude that the pituitary-adrenal responses to CRH are markedly disrupted after only 5 days of nighttime work. These abnormalities mimic those previously observed in patients with chronic fatigue syndrome. Neuroendocrine abnormalities reported to be characteristic of chronic fatigue syndrome may be merely the consequence of disrupted sleep and social routine.
<b>Lemke MR.</b>	Psychiatrische Klinik, Klinikum Ingolstadt.	[Chronic fatigue syndrome-- psychiatric aspects].[article in German]	Fortschr Neurol Psychiatr 1996 Apr;64(4):132-41	Diagnosis of the chronic fatigue syndrome depends on various somatic and psychopathological symptoms. Somatic symptoms of the syndrome have been subject of an extensive body of literature. In comparison, psychiatric aspects have caught relatively less attention. Psychiatric aspects of etiological, diagnostic, and therapeutic concepts are essential for evaluation of the syndrome. Application of CDC-criteria to a well known disease does not solve the nosological problem, but may define the syndrome more accurately. In this respect, issues including psychiatric comorbidity and specificity of neuropathological symptoms are discussed. Psychological variables seem to have a high predictor value for time course and outcome of the symptoms. Etiological concepts emphasize on biological or psychosocial factors. Alterations of biological parameters including immune functions, sleep regulation, and hypothalamic-pituitary-adrenocortical function have been reported. The role of cultural factors has been discussed extensively. Somatic and psychological stress may result in the same clinical syndrome via psychoimmunological mechanisms. An integrated, interdisciplinary approach to further refine diagnostic criteria, understanding of etiology and development of adequate therapeutic measures seems necessary.
<b>Levine PH</b>		The Elusive Gulf War Syndrome	Journal of Chronic Fatigue Syndrome 1996: 2(2/3): 55 - 63	In 1990/1991, approximately 697,000 U.S. service members joined coalition forces in the Middle East for Operations Desert Shield and Desert Storm (ODS/S). Following the military action, a number of service men and women reported a variety of signs and symptoms which they attributed to their participation in the operation; the term Gulf War Syndrome was proposed to facilitate evaluation of what was perceived as a possible new entity. Subsequent studies failed to identify a discrete syndrome, and a series of reports have raised questions as to whether or not Gulf War Syndrome exists or if indeed any of the reported disorders can be attributed to participation in ODS/S. This report reviews the history of U.S. participation in the Gulf War, the medical threats and exposures considered by the U.S. Armed Services, and the U.S. Government's approach to investigating the complaints of the returning servicemen. In the context of the reports from non-U.S. veterans with similar complaints, the elusive Gulf War Syndrome is an important unresolved issue that could provide a model for a number of disorders, including chronic fatigue syndrome.
<b>Levine PH, Dale JK, Benson-Grigg E, Fritz S, Grufferman S, Straus SE.</b>	Division of Cancer Etiology, National Cancer Institute, National Institutes of Health,	A cluster of cases of chronic fatigue and chronic fatigue syndrome: clinical and	Clin Infect Dis 1996 Aug;23(2):408-9	

	Bethesda, Maryland 20892-1888, USA.	immunologic studies.		
<b>Levine PH.</b>	Viral Epidemiology Branch, National Cancer Institute, Bethesda, MD, USA.	The use of transfer factors in chronic fatigue syndrome: prospects and problems.	Biotherapy 1996;9(1-3):77-9	Chronic fatigue syndrome (CFS) is a heterogeneous disorder characterized by severe prolonged unexplained fatigue and a variety of associated symptoms such as arthralgias, myalgias, cognitive dysfunction, and severe sleep disturbances. Many patients initially present with an acute onset of apparent infectious origin with either an upper respiratory or gastrointestinal illness, fever, chills, tender lymphadenopathy, and malaise suggestive of a flu-like illness. In some cases, specific viral infections can be identified at the outset, particularly herpes viruses such as Epstein-Barr virus (EBV), human herpes virus-6 (HHV-6), and cytomegalovirus (CMV). Transfer factors (TF) with specific activity against these herpes viruses has been documented. With some studies suggesting that persistent viral activity may play a role in perpetuation of CFS symptoms, there appears to be a rationale for the use of TF in patients with CFS and recent reports have suggested that transfer factor may play a beneficial role in this disorder. This report focuses on the heterogeneity of CFS, the necessity for randomized coded studies, the importance of patient selection and sub-classification in clinical trials, and the need to utilize specific end-points for determining efficacy of treatment.
<b>Lieb K, Dammann G, Berger M, Bauer J.</b>	Universitätsklinik für Psychiatrie und Psychosomatik, Universität, Freiburg.	[Chronic fatigue syndrome. Definition, diagnostic measures and therapeutic possibilities].[article in German]	Nervenarzt 1996 Sep;67(9):711-20 comment in: Nervenarzt. 1997 Nov;69(11):924-5	This article reviews the chronic fatigue syndrome (CFS), a disorder whose etiology is unknown. The diagnostic criteria proposed in 1994 by the CDC and the International Chronic Fatigue Syndrome Study Group are introduced. In contrast to widespread belief, there are no laboratory tests available to underpin the diagnosis of CFS; the diagnosis is made solely on the basis of clinical criteria. In the differential diagnosis, the exclusion of other conditions that can cause chronic fatigue, such as neuropsychiatric or sleep disorders, is of critical importance. In this context, the question as to whether CFS is a clinical entity that can be differentiated from psychiatric diagnoses, such as depression, somatoform disorder, or neurasthenia, is discussed. At the moment, there is no specific therapy for CFS. Therefore, therapeutic approaches are limited to symptomatic management of the concomitant sleep disturbances, pain, or psychiatric symptoms, such as depression. Patients may benefit from cognitive behavioral therapy, as this may help them to identify and exclude factors contributing to and maintaining chronic fatigue. An integrated medical and psychological approach should be adopted, with the aim of preventing significant secondary negative results of the illness, such as interpersonal conflicts or chronic disability.
<b>Lindal E, Bergmann S, Thorlacius S, Stefansson JG.</b>	Department of Psychiatry, National University Hospital, Reykjavik, Iceland. elindal@rsp.is	The localization of pain in chronic fatigue syndrome on a pain drawing according to grid areas.	Percept Mot Skills 1996 Oct;83(2):508-10	
<b>Lindh G, Samuelson A, Hedlund KO, Evengard B, Lindquist L, Ehrnst A.</b>	Division of Infectious Diseases, Huddinge University Hospital, Karolinska Institutet, Stockholm, Sweden.	No findings of enteroviruses in Swedish patients with chronic fatigue syndrome.	Scand J Infect Dis 1996;28(3):305-7	Enteroviruses have been proposed to cause an immune complex disease in the chronic fatigue syndrome. Altogether 34 patients with the chronic fatigue syndrome, according to criteria of the Centers for Disease Control, USA, were studied evenly over the seasons for the possible presence of a chronic enterovirus infection. In 11 patients, 1-5 faecal samples were collected at about 6 month intervals for virus isolation before and after acid treatment, followed by ultracentrifugation at pH 3 to dissolve possible enterovirus-antibody complexes. Another 14 faecal samples were subjected to routine virus isolation alone. Seven pairs of serum-cerebrospinal fluid samples were analysed for cross-reactive IgG antibody activity to enteroviruses. In 29 patients a muscle biopsy was collected for enterovirus polymerase chain reaction (PCR). We were unable to identify enteroviruses in any of these samples by any of these techniques. Our study does not confirm evidence for persistent enterovirus infection in the chronic fatigue syndrome.
<b>Lohmann K, Prohl A, Schwarz E.</b>	Schleswig, Christian-Albrechts-Universität, Kiel.	[Multiple chemical sensitivity disorder in patients with neurotoxic illnesses].[article in German]	Gesundheitswesen 1996 Jun;58(6):322-31 comment in: Gesundheitswesen. 1997 Jan;59(1):56	The data of 466 subjects suffering from neurologic disorders which are suggested to be caused by neurotoxic agents in their environment retrospectively was evaluated and documented. Among these cases there were 151 subjects with symptoms of Multiple Chemical Sensitivity Disorder (MCS). The relationship between the neurological health impairments and neurotoxic agents in the environment of these patients was characterised using five different categories (probable = A, possible = B, uncertain = C, unclarified = D, not probable = E). From the 466 patients 320 subjects (69%) could be assigned to the categories A and B, respectively. Within these 320 cases with chronic neurotoxic health impairments 136 subjects (79 females and 57 males) showed signs of MCS. Age and gender of cases

				as well as duration and character of exposure to neurotoxic substances retrospectively were assessed from the explicit files of the patients, which had been made anonymous for this purpose. Frequency of characteristic symptoms of neurotoxicity were analysed. Results are given for patients with neurotoxic health impairments with MCS (n = 136) and without MCS (n = 184). Neurotoxic substances which were used as indoor wood preservatives (mainly Pentachlorophenol and/or Lindane) were found to be the causative agents in 63% of the cases with neurotoxic health impairments and MCS. Other important neurotoxic substances to which the patients were mainly exposed were organic solvents (25%), formaldehyde (15%), dental materials (15%), pyrethroids (13%), and other biocides (19%) (multiple exposures were possible). The time of exposure was calculated as being > or = 10 years for 55% of the patients with MCS and for 50% of the group with neurotoxic health impairments but without MCS. Out of the 184 cases with neurotoxic health impairments but without MCS there were 22%, and out of the 136 cases with MCS there were 39% who showed all symptoms of chronic fatigue syndrome. 53% of the cases with MCS had an allergic disposition compared to only 20% of the cases without MCS. This work is not a controlled epidemiological study but a retrospective documentation and evaluation of data related to environmental medicine. With the present documentation in this purely descriptive manner the proof of a causal relationship was not possible or intended. But because corresponding epidemiological studies are lacking, this documentation can give important information on characteristic features of Multiple Chemical Sensitivity Disorder and chronic neurotoxic health impairments. Such information is essential for planning and carrying out epidemiological studies urgently needed in this field.
<b>Lynch S, Seth R.</b>		Fluoxetine and chronic fatigue syndrome.	Lancet 1996 Jun 22;347(9017):1771; discussion 1171-2	
<b>MacDonald KL, Osterholm MT, LeDell KH, White KE, Schenck CH, Chao CC, Persing DH, Johnson RC, Barker JM, Peterson PK.</b>	Minnesota Department of Health, Minneapolis, 55440-9441, USA.	A case-control study to assess possible triggers and cofactors in chronic fatigue syndrome.	Am J Med 1996 May;100(5):548-54 Comment in: Am J Med. 1997 Apr;102(4):422-3	PURPOSE: To assess possible triggers and cofactors for chronic fatigue syndrome (CFS) and to compare levels of selected cytokines between cases and an appropriately matched control group. PATIENTS AND METHODS: We conducted a case-control study of 47 cases of CFS obtained through a regional CFS research program maintained at a tertiary care medical center. One age-, gender-, and neighborhood-matched control was identified for each case through systematic community telephone sampling. Standardized questionnaires were administered to cases and controls. Sera were assayed for transforming growth factor-beta (TGF-beta), interleukin-1 beta, interleukin-6, tumor necrosis factor-alpha, and antibody to Borrelia burgdorferi and Babesia microti. RESULTS: Cases were more likely to have exercised regularly before illness onset than controls (67% versus 40%; matched odds ratio (MOR) = 3.4; 95% CI = 1.2 to 11.8; P = 0.02). Female cases were more likely to be nulliparous prior to onset of CFS than controls (51% versus 31%; MOR = 8.0; 95% CI = 1.03 to 170; P = 0.05). History of other major factors, including silicone-gel breast implants (one female case and one female control), pre-morbid history of depression (15% of cases, 11% of controls) and history of allergies (66% of cases, 51% of controls) were similar for cases and controls. However, cases were more likely to have a diagnosis of depression subsequent to their diagnosis of CFS compared to a similar time frame for controls (MOR = undefined; 95% CI lower bound = 2.5; P < 0.001). Positive antibody titers to B burgdorferi (one case and one control) and B microti (zero cases and two controls) were also similar. CONCLUSIONS: Further investigation into the role of prior routine exercise as a cofactor for CFS is warranted. This study supports the concurrence of CFS and depression, although pre-morbid history of depression was similar for both groups.
<b>MacFarlane JG, Shahal B, Mously C, Moldofsky H.</b>	University of Toronto, Centre for Sleep and Chronobiology, Toronto Hospital (Western Division), Ontario, Canada.	Periodic K-alpha sleep EEG activity and periodic limb movements during sleep: comparisons of clinical features and sleep parameters.	Sleep 1996 Apr;19(3):200-4	The K-alpha sleep electroencephalographic (EEG) phenomenon is characterized by periodic (approximately 20-40 seconds) K-complexes, immediately followed by alpha-EEG activity (7.5-11 Hz) of 0.5- to 5.0-second duration. A group of 14 subjects with the periodic K-alpha anomaly was found to have a similar distribution pattern of interevent intervals as compared with previously published data for sleep-related periodic limb movements during sleep (PLMS). Sleep parameters and somatic symptoms of 30 patients with K-alpha were compared with 30 patients with PLMS. The periodic K-alpha group was predominantly female, younger, exhibiting more slow-wave sleep, gastrointestinal symptoms and muscular complaints and fewer movement arousals on overnight polysomnography. The K-alpha group presented uniformly with complaints of unrefreshing sleep,

				often associated with fibromyalgia and chronic fatigue syndrome. The PLMS group was predominantly male, showed greater sleep disruption and presented with a variety of sleep-related symptoms.
<b>Manu P, Affleck G, Tennen H, Morse PA, Escobar JI.</b>	Department of Psychiatry, Long Island Jewish Medical Center, New Hyde Park, N.Y., USA.	Hypochondriasis influences quality-of-life outcomes in patients with chronic fatigue.	Psychother Psychosom 1996 Mar-Apr;65(2):76-81	BACKGROUND: To determine how hypochondriacal symptoms influence the quality-of-life outcomes of patients with a chief complaint of chronic fatigue. METHODS: Cross-sectional cohort study of a consecutive sample of 71 patients (mean duration of fatigue of 4.1 years). Forty-eight (68%) patients met criteria for current major depression and 32 (45%) met criteria for chronic fatigue syndrome (CFS). All patients received a comprehensive medical and psychiatric evaluation. Quality-of-life and physical, depressive and hypochondriacal symptom scores were assessed through reliable self-report questionnaires and a structured interview. A path model expressing the relation between predictor variables (hypochondriasis and depression), intervening variables (physical symptoms) and quality of life was postulated and evaluated using structural equation methods. RESULTS: The paths linking hypochondriasis with physical symptoms and mental health and the path connecting physical symptoms and quality of life were each statistically significant. The model applied especially well to patients who fulfilled CFS criteria. CONCLUSIONS: The quality of life of chronic fatigue patients correlates with the severity of their physical symptoms and their hypochondriacal disposition toward illness.
<b>Marcel B, Komaroff AL, Fagioli LR, Kornish RJ 2nd, Albert MS.</b>	Department of Psychiatry, Massachusetts General Hospital, Charlestown, MA 02129, USA.	Cognitive deficits in patients with chronic fatigue syndrome.	Biol Psychiatry 1996 Sep 15;40(6):535-41	Twenty-nine subjects with chronic fatigue syndrome (CFS) and 25 healthy control subjects were administered a lengthy neuropsychological battery that included standard neuropsychological tests and a computerized set of tasks that spanned the same areas of ability. The primary significant differences between patients and controls were found on tests of learning and memory. These differences remained when the degree of psychiatric symptomatology in the subjects was covaried. Patients on and off psychoactive medications did not differ in their performance on these tasks. These results suggest that at least a subset of CFS patients may experience significant impairments in learning and memory.
<b>Marsh S, Kaplan M, Asano Y, Hoekzema D, Komaroff AL, Whitman JE Jr, Ablashi DV.</b>	Advanced Biotechnologies Inc, Columbia, MD 21046, USA.	Development and application of HHV-6 antigen capture assay for the detection of HHV-6 infections.	J Virol Methods 1996 Sep;61(1-2):103-12	An HHV-6 antigen capture assay measuring gp116/64/54 antigen was developed. This ELISA is specific for HHV-6 Variants A and B, does not cross react with other human herpesviruses, is sensitive, stable, quantitative, and can detect antigen in body fluids and cell cultures. Relative to virus isolation or techniques for measuring HHV-6 nucleic acids, the assay is much simpler and less expensive to perform. Plasmas/sera (413) obtained from healthy donors, children with Exanthem subitum, febrile illnesses, patients with Chronic Fatigue Syndrome, and AIDS patients tested by antigen capture assay demonstrated that the assay is useful in clinical laboratory settings. The capture assay can also be used to monitor cell cultures for virus isolation, production, quantitation, and antiviral agent screening.
<b>Marshall PS, Watson D, Steinberg P, Cornblatt B, Peterson PK, Callies A, Schenck CH.</b>	Department of Psychiatry, Hennepin County Medical Center, Minneapolis, MN 55415, USA.	An assessment of cognitive function and mood in chronic fatigue syndrome.	Biol Psychiatry 1996 Feb 1;39(3):199-206	Data were gathered regarding the associates of chronic fatigue syndrome (CFS) with: (1) speed of cognitive processing, (2) motor speed, (3) ability to sustain attention, and (4) mood. Patients were given a brief neuropsychological test battery before and after double-blind treatment with terfenadine or placebo and completed a daily mood rating scale (Positive and Negative Affect Schedule) during the study. CFS patients exhibited slower cognitive processing and motor speed and lower positive affect, as compared to data reported from previous studies of healthy subjects and other patient groups; however, CFS patients did not exhibit deficits in sustained attention in comparison to other groups. The CFS patients' ability to attend to verbal versus figural stimuli and mood ratings were different from those reported in studies of patients with depression. Because of methodological limitations, these findings are preliminary, but they encourage further assessment of cognitive dysfunction and mood in CFS.
<b>Martin WJ.</b>	Center for Complex Infectious Diseases, Rosemead, Calif 91770, USA.	Severe stealth virus encephalopathy following chronic-fatigue-syndrome-like illness: clinical and histopathological features.	Pathobiology 1996;64(1):1-8	The clinical histories and brain biopsy findings of 3 patients with severe stealth virus encephalopathy are reviewed. The patients initially developed symptoms consistent with a chronic fatigue syndrome. One patient has remained in a vegetative state for several years, while the other 2 patients have shown significant, although incomplete, recovery. Histological and electron-microscopic studies revealed vacuolated cells with distorted nuclei and various cytoplasmic inclusions suggestive of incomplete viral expression. There was no significant inflammatory response. Viral cultures provided further evidence of stealth viral infections occurring in these patients.

<b>Martin WJ.</b>	Center for Complex Infectious Diseases, Rosemead, Calif 91770, USA.	Genetic instability and fragmentation of a stealth viral genome.	Pathobiology 1996;64(1):9-17	Partial sequencing was performed on cloned DNA obtained from cultures of a stealth virus isolated from a patient with the chronic fatigue syndrome. The results extend earlier findings showing regions of homology to cytomegalovirus (CMV). Although the virus is much more closely related to simian CMV than to human CMV, many of the cloned viral segments could be aligned with the human CMV genome. The aggregate size of the aligned segments exceeds 100 kilobase pairs (kbp). Undigested viral DNA has a mobility in agarose gel electrophoresis corresponding to approximately 20 kbp. The virus, therefore, apparently exists in multiple fragments. Considerable sequence variation exists between individual clones which overlap to similar regions of the human CMV genome. The fragmented genome and sequence microheterogeneity suggest that both the processivity and the fidelity of replication of the viral genome are defective. An unstable viral genome may provide a potential mechanism of recovery from stealth viral illness.
<b>Martin WJ.</b>	Center for Complex Infectious Diseases, Rosemead, CA 91770, USA.	Simian cytomegalovirus-related stealth virus isolated from the cerebrospinal fluid of a patient with bipolar psychosis and acute encephalopathy.	Pathobiology 1996;64(2):64-6	A cytopathic 'stealth' virus was cultured from the cerebrospinal fluid of a patient with a bipolar psychotic disorder who developed a severe encephalopathy leading to a vegetative state. DNA sequencing of a polymerase chain reaction-amplified product from infected cultures has identified the virus as an African green monkey simian cytomegalovirus (SCMV)-related stealth virus. The virus is similar to the SCMV-related stealth virus isolated from a patient with chronic fatigue syndrome. The findings support the concepts that stealth viruses can account for a spectrum of dysfunctional brain diseases and that some of these viruses may have arisen from live polio viral vaccines.
<b>Mayou R.</b>		Chronic fatigue syndrome.	Lancet 1996 Nov 16;348(9038):1384-5 comment in: Lancet. 1997 Jan 4;349(9044):57-8 comment on: Lancet. 1996 Oct 12;348(9033):971	
<b>McArdle A, McArdle F, Jackson MJ, Page SF, Fahal I, Edwards RH.</b>	Department of Medicine, University of Liverpool, U.K.	Investigation by polymerase chain reaction of enteroviral infection in patients with chronic fatigue syndrome.	Clin Sci (Colch) 1996 Apr;90(4):295-300	1. Chronic fatigue syndrome is characterized by muscle fatigue and pain at rest, symptoms which are usually exacerbated with exercise. Although various studies have shown minor, non-specific morphological and biochemical changes in muscle of patients with chronic fatigue syndrome, no consistent defect has been identified. Some have suggested that an enteroviral infection in muscle may cause the chronic muscle fatigue seen in patients with chronic fatigue syndrome, with acute infection directly and irreversibly impairing mitochondrial function, and persistent infection depressing muscle protein synthesis and metabolism. 2. To clarify the involvement of enterovirus infection in chronic fatigue syndrome, muscle biopsies from a group of patients with chronic fatigue syndrome were examined for the presence of enteroviral RNA by reverse transcriptase-polymerase chain reaction techniques in relation to functional studies of muscle mitochondria and the muscle RNA/DNA ratio. 3. Fifty-eight percent of patients reported an uncharacterized 'viral infection' before the onset of their illness, but none of the muscle samples from 34 patients contained detectable amounts of enteroviral RNA. Muscle tissue had a general reduction in the RNA/DNA ratio and mitochondrial enzyme activities with no specific abnormality in the activity of enzymes encoded partially on the mitochondrial genome (cytochrome-c oxidase) or nuclear genome (citrate synthase, succinate reductase). 4. These data provide no evidence of an enteroviral infection in muscle of patients with chronic fatigue syndrome, although this does not exclude a role of enterovirus in initiating the disease process. The general reduction in RNA/DNA ratio and mitochondrial enzyme activities is consistent with a general reduction in habitual activity.
<b>McCully KK, Natelson BH, Iotti S, Sisto S, Leigh JS Jr.</b>	Department of Medicine, Medical College of Pennsylvania, Philadelphia 19131, USA.	Reduced oxidative muscle metabolism in chronic fatigue syndrome.	Muscle Nerve 1996 May;19(5):621-5 comment in: Muscle Nerve. 1997 Jun;20(6):765-6	The purpose of this study was to determine if chronic fatigue syndrome (CFS) is characterized by abnormalities in oxidative muscle metabolism. Patients with CFS according to Centers for Disease Control (CDC) criteria (n = 22) were compared to normal sedentary subjects (n = 15). CFS patients were also tested before and 2 days after a maximal treadmill test. Muscle oxidative capacity was measured as the maximal rate of postexercise phosphocreatine (PCr) resynthesis using the ADP model (Vmax) in the calf muscles using 31P magnetic resonance spectroscopy. Vmax was significantly reduced in CFS patients (39.6 +/- 2.8 mmol/L/min, mean +/- SE) compared to controls (53.8 +/- 2.8 mmol/L/min). Two days postexercise there was no change in resting inorganic phosphate (Pi)/PCr or Vmax in the CFS patients (n = 14). In conclusion, oxidative metabolism is reduced in CFS patients

				compared to sedentary controls. In addition, a single bout of strenuous exercise did not cause a further reduction in oxidative metabolism, or alter resting Pi/PCr ratios.
<b>McCully KK, Sisto SA, Natelson BH.</b>	Department of Medicine, Medical College of Pennsylvania, USA.	Use of exercise for treatment of chronic fatigue syndrome.	Sports Med 1996 Jan;21(1):35-48	Chronic fatigue syndrome (CFS) is a condition that results in moderate to severe disability, the primary feature of which is fatigue of unknown origin. There is a lot of interest in classifying, characterising and treating patients with CFS. Currently, the two major theories of a medical cause of CFS are viral infection and immune dysregulation. Patients report critical reductions in levels of physical activity, and many experience 'relapses' of severe symptoms following even moderate levels of exertion. Despite this, most studies report CFS patients to have normal muscle strength and either normal or slightly reduced muscle endurance. Histological and metabolic studies report mixed results: CFS patients have either no impairment or mild impairment of mitochondria and oxidative metabolism compared with sedentary controls. Current treatments for CFS are symptom-based, with psychological, pharmacological and rehabilitation treatments providing some relief but no cure. Immunological and nutritional treatments have been tried but have not provided reproducible benefits. Exercise training programmes are thought to be beneficial (if 'relapses' can be avoided), although few controlled studies have been performed. CFS is a long-lasting disorder that can slowly improve with time, but often does not. Further studies are needed to better understand the multiple factors that can cause chronic fatigue illness, as well as the effect that exercise training has on the symptoms of CFS.
<b>McGregor NR, Dunstan RH, Zerbes M, Butt HL, Roberts TK, Klineberg IJ.</b>	Collaborative Pain Research Unit, University of Sydney, Westmead Hospital, NSW, Australia.	Preliminary determination of a molecular basis of chronic fatigue syndrome.	Biochem Mol Med 1996 Apr;57(2):73-80	Chronic fatigue syndrome (CFS/ME) is a debilitating fatigue illness that has an unknown etiology. We studied 20 chronic fatigue syndrome (CFS) patients, who complied with the Oxford and American CDC definitions, and 45 non-CFS subjects. Participants completed questionnaires, were clinically examined, and had first morning urine specimens collected, which were screened by gas chromatography-mass spectrometry for changes in metabolite excretion. Multivariate analysis of the urinary metabolite profiles differed significantly in the CFS patients compared to the non-CFS patients ( $P < 0.004$ ). The CFS patients had increases in aminohydroxy-N-methylpyrrolidine ( $P < 0.00003$ , referred to as chronic fatigue symptom urinary marker 1, or CFSUM1), tyrosine ( $P < 0.02$ ), beta-alanine ( $P < 0.02$ ), aconitic acid ( $P < 0.05$ ), and succinic acid ( $P < 0.05$ ) and reductions in an unidentified urinary metabolite, CFSUM2 ( $P < 0.0007$ ), alanine ( $P < 0.005$ ), and glutamic acid ( $P < 0.02$ ). CFSUM1, beta-alanine, and CFSUM2 were found by discriminant function analysis to be the first, second, and third most important metabolites, respectively for discriminating between CFS and non-CFS subjects. The abundances of CFSUM1 and beta-alanine were positively correlated with symptom incidence ( $P < 0.01$ and $P < 0.001$ , respectively), symptom severity, core CFS symptoms, and SCL-90-R somatization ( $P < 0.00001$ ), suggesting a molecular basis for CFS.
<b>McGregor NR, Dunstan RH, Zerbes M, Butt HL, Roberts TK, Klineberg IJ.</b>	Collaborative Pain Research Unit, University of Sydney, Australia.	Preliminary determination of the association between symptom expression and urinary metabolites in subjects with chronic fatigue syndrome.	Biochem Mol Med 1996 Jun;58(1):85-92	Chronic fatigue syndrome (CFS) patients have a urinary metabolite labeled CFSUM1 with increased incidence ( $P < 0.004$ ) and relative abundance ( $P < 0.00003$ ). The relative abundances of urinary CFSUM1 and beta-alanine were associated with alterations in metabolite excretion and symptom incidence. In 20 CFS patients and 45 non-CFS subjects, symptom/metabolite associations were investigated by assessing symptom sensitivity and specificity, and symptom indices of total symptom incidence, CFS core symptoms, cognitive, neurological, musculoskeletal, gastrointestinal, infection-related and genitourinary symptom indices, as well as a visual analogue pain scale of average pain intensity. Thirty-three symptoms had significant ( $P < 0.005$ ) sensitivity and specificity in the CFS patients compared to that in the non-CFS controls. Severe fatigue was the only symptom with 100% sensitivity and specificity and CFSUM1 excretion was the primary metabolite for expression of this symptom. All nine symptom indices had elevated responses in the CFS patients (all $P < 0.0000001$ ). Multiple regression analyses indicated that all the symptom indices had significant correlations (R) with changes in the urinary excretion of metabolites ( $P < 0.0001$ ). CFSUM1 and beta-alanine were the first and second metabolites correlated with the CFS core symptom index and CFSUM1 was primarily associated with infection-related and musculoskeletal indices whereas beta-alanine was primarily associated with gastrointestinal and genitourinary indices. The strong associations of CFSUM1 and beta-alanine with CFS symptom expression provide a molecular basis for developing an objective test for CFS.
<b>Mesch U, Lowenthal RM, Coleman D.</b>		Lead poisoning masquerading as chronic fatigue syndrome.	Lancet 1996 Apr 27;347(9009):1193	

<b>Michiels V, Cluydts R, Fischler B, Hoffmann G, Le Bon O, De Meirleir K.</b>	Department of Psychology, Free University of Brussels (VUB), Belgium.	Cognitive functioning in patients with chronic fatigue syndrome.	J Clin Exp Neuropsychol 1996 Oct;18(5):666-77	A comprehensive battery of neuropsychological tests was administered to 35 outpatients suffering from Chronic Fatigue Syndrome (CFS). They were compared to 33 normal controls matched for age, gender, intelligence, and education. The patients displayed psychomotor slowing and impaired attention. The learning rate of verbal and visual material for patients with CFS was slower, and delayed recall of verbal and visual information was impaired. Because there was a high variability in cognitive impairment within the CFS group, it would be inappropriate to generalize results to the entire CFS population. Two neuropsychological variables indicating aspects of psychomotor performance and verbal memory were found to discriminate best between patients and controls.
<b>Minowa M, Jiamo M.</b>	Department of Epidemiology, National Institute of Public Health, Tokyo, Japan.	Descriptive epidemiology of chronic fatigue syndrome based on a nationwide survey in Japan.	J Epidemiol 1996 Jun;6(2):75-80	In order to clarify the epidemiological features of chronic fatigue syndrome (CFS), a nationwide survey was conducted using the Japanese version of the CDC Criteria prepared by the CFS Research Group of Japan. All clinical departments of internal medicine, pediatrics, psychiatry and neurology at university hospitals and at ordinary hospitals with 200 or more beds were surveyed. Major results were as follows: (1) Period prevalence adjusted for response rate was 0.85 (0.63 for males and 1.02 for females) per 100,000 population during the year 1992; (2) Based on the first and final dates of hospital visits, the prevalences on January 1 of 1992 and 1993 were 0.40 and 0.60 per 100,000 population, respectively, suggesting an increasing trend; (3) Reported new cases during 1992 were 301, and the response adjusted-incidence was estimated to be 0.46 per 100,000 person-years; (4) The proportion of post-infectious CFS cases was 14.8% for both sexes, and tended to be slightly higher among females than males, but was not related to age. Three clusterings of two cases were reported.
<b>Moss-Morris R, Petrie KJ, Large RG, Kydd RR.</b>		Neuropsychological deficits in chronic fatigue syndrome: artifact or reality?	J Neurol Neurosurg Psychiatry 1996 May;60(5):474-7	
<b>Mulube M.</b>		Myths dispelled about chronic fatigue syndrome.	BMJ 1996 Oct 5;313(7061):839	
<b>Nakaya T, Takahashi H, Nakamura Y, Asahi S, Tobiume M, Kuratsune H, Kitani T, Yamanishi K, Ikuta K.</b>	Section of Serology, Hokkaido University, Sapporo, Japan.	Demonstration of Borna disease virus RNA in peripheral blood mononuclear cells derived from Japanese patients with chronic fatigue syndrome.	FEBS Lett 1996 Jan 8;378(2):145-9	CFS, a recently named heterogeneous disorder, is an illness of unknown etiology. The association of CFS with viral infections has been suggested. A common association between CFS and several viruses examined has not been confirmed. Here, we centered on the possible link between CFS and BDV infection. By nested RT-PCR followed by hybridization, BDV RNA was demonstrated as a clear signal in PBMCs in 3 out of 25 CFS patients. The amplified cDNA fragments were cloned and sequenced. A total of 16 clones were studied. Intra-patients divergencies of the p24 were 2-9%, 3-20%, and 3-11% in the deduced amino acids. Inter-patient divergencies among the 16 clones were 3-24%. Antibodies to recombinant BDV p24 protein were detected in 6 CFS patients including one carrying BDV RNA. Overall, these gave the prevalence of 32% (8/25) in Japanese CFS patients, suggesting that Japanese CFS is highly associated with active infection of BDV, or a related agent.
<b>Natelson BH, Cheu J, Pareja J, Ellis SP, Policastro T, Findley TW.</b>	CFS Center, New Jersey Medical School, East Orange 07018, USA.	Randomized, double blind, controlled placebo-phase in trial of low dose phenelzine in the chronic fatigue syndrome.	Psychopharmacology (Berl) 1996 Apr;124(3):226-30	Because of the striking similarity of the clinical manifestations produced by use of the drug reserpine and seen in patients with the chronic fatigue syndrome (CFS), we theorized that CFS was a disorder of reduced central sympathetic drive. Because of the pharmacology of control of this central sympathetic system, we further postulated that CFS symptoms would respond quickly to low dose treatment with a monamine oxidase inhibitor. To test these hypotheses, we designed a randomized, double blind placebo controlled study using phenelzine. No patient in the trial had a diagnosis of lifetime or current psychiatric disorder and none had depressed mood in the range of clinically depressed patients on a paper and pencil test of depression. Patients in the placebo group received placebo for 6 weeks while those in the drug treatment group were treated in three 2-week segments-placebo, 15 mg phenelzine every other day, and then 15 mg daily. This treatment regimen produced a significant pattern of improvement compared to worsening in 20 self report vehicles of CFS symptoms, illness severity, mood or functional status. Thus the data support our hypothesis of reduced sympathetic drive, although an alternative hypothesis of pain alleviation is also possible. The study design also allowed us to evaluate patients for a placebo effect: no evidence for this was found, suggesting that CFS is not an illness due to patients' being overly suggestible. Randomized Controlled Trial
<b>Neri G, Bianchedi M, Croce A, Moretti A.</b>	Clinica Otorinolaringoiatrica, Universita G. d'Annunzio di Chieti.	["Prolonged" decay test and auditory brainstem responses in the clinical diagnosis of the	Acta Otorhinolaryngol Ital 1996 Aug;16(4):317-23	The chronic fatigue syndrome (CFS) was formally defined to describe disabling fatigue of unknown etiology with immunologic disfunctions. In most cases occur abnormalities of neurophysiological tests. In this paper the Authors use the low (11 pps) and high (51-71 pps) frequency ABR for detecting

		chronic fatigue syndrome]. [article in Italian]		the electrophysiological function of auditory brainstem responses and propose the "Prolonged Decay Test", a modified impedenzometric technique that explores any alterations of the stapedial contraction, as a new diagnostic test for CFS. Twenty-one patients with suspected CFS, with an age between 17 and 50 years, were examined and the instrumental data were correlated with the clinical findings. The results of the ABR study showed in the examined subjects no many abnormalities in the 11 pps frequency test. The high frequency stimulation trials (with 51 and 71 pps) proved many alterations in 10 patients (absence of the first wave in 6 cases, in 5 many wave latency delay and in 1 patient absence of the first wave and many wave latency delay). The high frequency trials showed no abnormalities in the 11 remaining patients. The clinical-audiological correlation showed a 61.9% of comparison with 33.3% of false negatives and 4.8% of false positives. The Prolonged Decay Test showed a 71.4% of clinical-audiological comparison with 23.8% of false negatives and 4.8% of false positives. The Prolonged Decay Test together with the ABR showed a 81.8% of clinical-audiological comparison with 18.2% of false negatives and 0% of false positives. These preliminary data show that the stapedial reflex together with the ABR test could be useful for the diagnosis of CFS.
<b>Nishikai M, Akiya K, Tojo T, Onoda N, Tani M, Shimizu K.</b>	Department of Internal Medicine, Second Tokyo National Hospital, Japan.	'Seronegative' Sjogren's syndrome manifested as a subset of chronic fatigue syndrome.	Br J Rheumatol 1996 May;35(5):471-4	We determined the extent to which chronic fatigue syndrome (CFS) patients with sicca symptoms fulfil the diagnostic criteria for Sjogren's syndrome (SS). Three sets of diagnostic criteria for SS, formulated by the Japanese, Europeans and Fox, were used. One-third of the CFS patients with sicca symptoms fulfilled the diagnostic criteria for SS. However, they were 'seronegative', differing from the ordinary primary SS.
<b>Oberg K.</b>	Uppsala University, Sweden.	Interferon-alpha versus somatostatin or the combination of both in gastroenteropancreatic tumours.	Digestion 1996;57 Suppl 1:81-3	Interferon-alpha (IFN-alpha) has a direct anti-tumour effect and is an immunomodulator. Somatostatin analogues, by contrast, when used to treat neuroendocrine tumours, control the secretion and peripheral effects of hormones, although at high doses they induce apoptosis. We have used IFN-alpha to treat > 350 patients with neuroendocrine tumours, and combining our and published data gives a median 44% biochemical response rate and 11% tumour response rate. Side-effects are mainly flu-like symptoms, then low-grade chronic fatigue syndrome. 15% may develop autoimmune reactions. The side-effects profile of somatostatin analogues is better but patients must take frequent injections and may have bile problems. We combined IFN-alpha and octreotide treatment in 24 patients with malignant carcinoid tumours who did not respond biochemically to high-dose (300 micrograms/day) octreotide alone. Biochemical response occurred in 77% but no significant anti-tumour effect was noted besides disease stabilisation in 4 cases. The combination therapy had an effect on clinical symptoms rather than tumour mass. Interferon was better tolerated when in the combination.
<b>Oughton RA.</b>		Chronic fatigue syndrome (CFS) in Army general practice.	J R Army Med Corps 1996 Jun;142(2):85 comment on: J R Army Med Corps. 1994 Jun;140(2):59-60	
<b>Patarca R, Nancy Klimas Dmitry Sandler, Maria N. Garcia , Mary Ann Fletcher</b>		Interindividual Immune Status Variation Patterns in Patients with Chronic Fatigue Syndrome Association with Gender and the Tumor Necrosis Factor System	Journal of Chronic Fatigue Syndrome 1996: 2(1): 13 - 39	Changes in soluble immune mediator levels in association with the chronic fatigue syndrome (CFS) usually occur within normal ranges and are apparent mainly as changes in the skewness of population distributions. The latter finding undermines the usefulness of cytokine levels as clinical tools at the individual level as has been seen in sepsis syndrome where a similar overlap occurs. Nonetheless, changes in cytokine levels at the population level can contribute to an understanding of the disease process. For example, we reported previously that significant proportions of CFS patients showed elevated serum levels of either soluble tumor necrosis factor-receptor I (sTNF-RI, sCD120a) or TNF-a as compared to controls. The latter results could reflect different disease processes or extremes of a common disease process. Using sera collected over a five-year period, we have now studied an extended cohort of 108 CFS patients and our results are consistent with a common graded disease process. When we assessed the effect of gender on the distributions of serum levels of immune mediators, levels of sTNF-RI, sTNF-RII (sCD 120b), sIL-6R (sCD126), and sICAM-1 were found to be consistently higher among males than females and among CFS patients as compared to controls regardless of gender. Moreover, differences in soluble immune mediator levels between CFS and control individuals were more clearly defined when restricting the analysis to the female gender. These observations are consistent with endocrine influences on immunological changes.
<b>Pearce J.</b>		Cognitive behaviour therapy	BMJ 1996 Apr	

		for the chronic fatigue syndrome. Cognitive behavior therapy should be compared with placebo treatments.	27;312(7038):1097; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
<b>Pearn J</b>		Chronic Ciguatera One Organic Cause of the Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1996: 2(2/3): 29 - 34	Ciguatera is a distressing form of fish poisoning, caused by the ingestion of one or more of a series of ciguatoxins. These poisons, some of the most potent mammalian neurotoxins known, are manufactured in reef-dwelling dinoflagellates and concentrated up the piscine food chain. Human victims, not uncommon in the Pacific, Atlantic and Indian Ocean tropical and subtropical littorals, become poisoned by eating risk species of fish. The acute intoxication is clinically dramatic, resulting in paraesthesiae, dysaesthesiae, prostration, myalgia and arthralgia. In some 20 percent of cases, symptoms of fatigue, reduced exercise tolerance and non-specific aches and pains persist for months and, in a small percentage of cases, for years. Such cases would, in the absence of the prior episode of acute poisoning, satisfy the diagnostic criteria for the chronic fatigue syndrome (CFS). Occasionally, patients are encountered who have been diagnosed as having CFS because of lack of awareness of the ciguatera syndrome, but in whom in retrospect the episode of acute fish poisoning can be established. The fact that at least one potent mammalian toxin can cause a chronic syndrome indistinguishable from CFS opens the way for further research into this enigmatic condition.
<b>Reiffenberger DH, Amundson LH.</b>	Brown Clinic, Watertown, South Dakota, USA.	Fibromyalgia syndrome: a review.	Am Fam Physician 1996 Apr;53(5):1698-712	Fibromyalgia syndrome includes symptoms of widespread, chronic musculoskeletal aching and stiffness and soft tissue tender points. It is frequently accompanied by fatigue and sleep disturbance. Fibromyalgia is more common in women than in men, and it occurs at a mean age of 49 years. Differential diagnosis includes myofascial pain syndrome and chronic fatigue syndrome. Fibromyalgia is a multifactorial problem and no universal treatment guidelines apply to all cases. Pharmacologic therapy may include tricyclic antidepressants. In addition to commonly used pharmacologic therapies, patient education, reassurance and an exercise program can each play an important role in relieving the symptoms associated with this common musculoskeletal syndrome.
<b>Reyes M, James G. Dobbins , Alison C. Mawle , Lea Steele , Howard E. Gary , Hina Malani , Scott Schmid , Keiji Fukuda John Stewart Rosane Nisenbaum , William C. Reeves</b>		Risk Factors for Chronic Fatigue Syndrome A Case-Control Study	Journal of Chronic Fatigue Syndrome 1996: 2(4): 17 - 33	Objective: To study various risk factors previously reported to be associated with chronic fatigue syndrome (CFS). Design: Case-control study. Setting: Metropolitan Atlanta CFS surveillance registry consisting of physicians and clinics that evaluate patients with fatiguing illness. Patients: Twenty-five CFS patients identified from the Centers for Disease Control and Prevention, Atlanta CFS study site, were matched by race, sex, and age to two randomly selected controls. Cases were further subgrouped by type of illness onset-sudden, occurring within a few days, or gradual, occurring over a longer time period. Main outcome measures: A broad panel of risk factors previously associated with CFS. Results: CFS patients were significantly more likely than controls to report a history of stress, persistent nasal symptoms, ear infections, and ingestion of B-complex vitamins during the year prior to the case's onset of illness. In addition, women patients were significantly more likely to have had a hysterectomy. The subset of patients (n = 17) who reported a gradual onset were significantly more likely than patients reporting a sudden onset of illness or controls to report stressful events in the year prior to onset, certain dental procedures, sinusitis, exposures to herbicides, pesticides, or insecticides, and a history of hysterectomy. We could not confirm previously reported associations of CFS with a history of asthma or eczema; exposure to sick animals; exposure to solvents, paint, or other chemicals; ingestion of raw-milk, or travel, occupation, or recreational activity. Conclusions: While no risk factors were identified that effectively distinguish CFS cases from controls, the data do suggest that gradual and sudden onset CFS constitute distinct subclasses of the syndrome. Future studies should subgroup patients based on type of illness onset and further evaluate risk factors of interest, focusing on the role
<b>Ross E.</b>		The history and treatment of chronic fatigue syndrome.	Nurs Times 1996 Oct 30-Nov 5;92(44):34-6	This article looks at chronic fatigue syndrome, a common condition affecting 1-2.5% of the population. The criteria for diagnosis are described and the nurse's role in treatment is discussed.
<b>Rouillon F, Delhommeau L, Vinceneux P.</b>	Service de Psychiatrie, Hopital Louis Mourier, Colombes.	[Chronic fatigue syndrome]. [article in French]	Presse Med 1996 Dec 21;25(40):2031-6	Fatigue is one of the most common medical complaints. Sometimes, fatigue is chronic, unexplained and induces significant distress or impairment in social, occupational or other important areas of functioning. This condition was described as neurasthenia by Beard at the end of the 19th Century; more recently the United States Centers for Disease Control and Prevention (CDC) suggested to call it "Chronic Fatigue Syndrome" (SFC). Both are considered as physical diseases and share certain

				therapeutic measures. Pathophysiology is still unknown and may involve viral agents, immunological processes or psychiatric disorders. Similarly most of the treatments which have been properly evaluated seem to be more or less inefficacious.
<b>Salit IE.</b>	Division of Infection Diseases, The Toronto Hospital, Canada.	The chronic fatigue syndrome: a position paper.	J Rheumatol 1996 Mar;23(3):540-4	
<b>Samii A, Wassermann EM, Ikoma K, Mercuri B, George MS, O'Fallon A, Dale JK, Straus SE, Hallett M.</b>	Human Motor Control Section, National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892-1428, USA.	Decreased postexercise facilitation of motor evoked potentials in patients with chronic fatigue syndrome or depression.	Neurology 1996 Dec;47(6):1410-4	We studied the effects of exercise on motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation (TMS) in 18 normal (control) subjects, 12 patients with chronic fatigue syndrome, and 10 depressed patients. Subjects performed repeated sets of isometric exercise of the extensor carpi radialis muscle until they were unable to maintain half maximal force. MEPs were recorded before and after each exercise set and for up to 30 minutes after the last set. The mean amplitude of MEPs recorded from the resting muscle immediately after each exercise set was 218% of the mean pre-exercise MEP amplitude in normal subjects, 126% in chronic fatigue patients, and 155% in depressed patients, indicating postexercise MEP facilitation in all three groups. The increases in the patient groups, however, were significantly lower than normal. The mean amplitudes of MEPs recorded within the first few minutes after the last exercise sets in all three groups were approximately half their mean pre-exercise MEP amplitudes. This postexercise MEP depression was similar in all groups. We conclude that postexercise cortical excitability is significantly reduced in patients with chronic fatigue syndrome and in depressed patients compared with that of normal subjects.
<b>Scheurlen M.</b>	Medizinische Poliklinik, Universitat, Wurzburg.	[Pathogenicity of fungi in the intestines--current status of the discussion].[article in German]	Fortschr Med 1996 Sep 20;114(26):319-21	The hypothesis that colonization of the intestinal tract by yeasts (e.g. Candida albicans) can lead to disease in immunocompromised individuals is currently being discussed controversially. Proponents assume that toxins produced by the fungi can trigger such complaints as irritable bowel syndrome of the chronic fatigue syndrome, and that such chronic or recurrent infections may be caused by an intestinal reservoir of yeasts. Opponents of the hypothesis, however, point out that no hard data on the pathogenetic significance of an intestinal reservoir of yeasts are available, controlled studies have failed to demonstrate the effectiveness of antifungal treatment. Discussions are however, hampered by a lack of objective data. The postulated pathomechanisms therefore need to be clarified, diagnostic criteria developed, and the efficacy of the proposed therapeutic measures shown by controlled studies. Until this has been done, assumption about the pathogenicity of yeasts in the bowel, cannot be taken as a basis for binding therapeutic recommendations.
<b>Schmaling KB, Jones JF.</b>	Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle 98105, USA.	MMPI profiles of patients with chronic fatigue syndrome.	J Psychosom Res 1996 Jan;40(1):67-74	Fifty-three patients with chronic fatigue syndrome (CFS) and 43 healthy nonpatient controls completed the Minnesota Multiphasic Personality Inventory (MMPI). All subjects varied in their degree of seropositivity to active Epstein-Barr virus (EBV) as measured by their anti-early antigen titers. EBV titers were higher among CFS patients and were associated with being more symptomatic. Differences in patient status were associated with statistically significant elevations on 8 of 9 clinical scales, 4 of which also showed clinically significant elevations (T scores > or = 70): scales 1, 2, 3, and 8. These results are discussed in terms of their implications for intervention strategies associated with MMPI-based CFS subtypes.
<b>Schnitzer TJ, Penmetcha M.</b>	Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL 60612, USA.	Viral arthritis.	Curr Opin Rheumatol 1996 Jul;8(4):341-5	Viral infections can present with different patterns of joint and soft tissue involvement, and the etiologic role of viruses in various rheumatic diseases is a subject of continued great interest. Recently, new immunoenzymatic assays have brought a better understanding of the relationship between hepatitis C virus serotypes and their immunologic manifestations. Our knowledge of the consequences of parvovirus B19 infection has broadened to include the variable clinical spectrum the role of inflammatory cytokine production in parvovirus-induced arthritis, a postulated causative role for B19 in rheumatoid arthritis, and a negative association between parvovirus and Still's disease as well as chronic fatigue syndrome. New, specific antibodies to nonstructural protein NS-1 in parvovirus B19-associated arthritis have been detected. Arthritis related to hepatitis B virus vaccination or measles and mumps vaccination was also reported. The papers reviewed here demonstrate the continuing efforts in defining the etiopathogenesis of virus-induced rheumatic diseases.
<b>Scott LV, T. G. Dinan</b>		The Neuroendocrinology of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1996: 2(4): 49 - 59	Since the introduction of operationalized criteria, there has been considerable interest in the pathophysiology of chronic fatigue syndrome (CFS). There is an increasing volume of evidence to support the view that patients with this syndrome have unique neuroendocrinology patterns. Central to this endocrine dysfunction is altered hypothalamic-pituitary-adrenal axis (HPA) activity. The cardinal

				findings include attenuated adrenocorticotrophic hormone (ACTH) responses to corticotropin-releasing hormone (CRH) and low 24-hour urinary cortisol. These are compatible with a mild central adrenal insufficiency. Adrenal steroids have widespread impact in the brain, and of particular importance is their dense concentration on serotonergic and noradrenergic neurotransmitter pathways. Using a variety of different challenge drugs, a supersensitivity of the serotonergic 5-HT 1A receptor has been demonstrated although the results have not been entirely consistent. A blunting of dexamethasone-induced growth hormone release has been described and may reflect a relative subsensitivity of the steroid receptor. It is proposed that the disruption of the HPA, which may be triggered by a number of stressors including infections, may represent a primary phenomenon, and that the neurotransmitter abnormalities described are in fact secondarily heralded by prolonged HPA dysregulation.
<b>See DM, Tilles JG.</b>	Department of Medicine School of Medicine, University of California at Irvine Orange 92668, USA.	alpha-Interferon treatment of patients with chronic fatigue syndrome.	Immunol Invest 1996 Jan- Mar;25(1-2):153-64	Thirty patients who fulfilled clinical criteria defined by the CDC for Chronic Fatigue Syndrome were treated with alfa 2a interferon or placebo in a double-blind crossover study. Outcome was evaluated by Natural Killer (NK) cell function, lymphocyte proliferation to mitogens and soluble antigens, CD4/CD8 counts and a 10 item Quality of Life (QOL) survey. Although mean NK function rose from 87.8 +/- 19.6 to 129.3 +/- 20.7 lytic units (LU; p < .05) with 12 weeks of interferon therapy, there was no significant change in the other immunologic parameters or QOL scores. When the 26 patients who completed the study were stratified according to their baseline NK function and lymphocyte proliferation, 4 groups were identified: 3 patients had normal NK cell function and lymphocyte proliferation when compared to normal, healthy controls, 9 had isolated deficiency in lymphocyte proliferation, 7 had diminished NK function only, and 7 had abnormalities for both parameters. QOL scores were not significantly different for the four groups at baseline. After 12 weeks of interferon therapy, QOL score significantly improved in each of the seven patients with isolated NK cell dysfunction (mean score, 16.3 +/- 7.9) compared to baseline (39.7 +/- 12.1; p < .05). In these patients the mean NK function increased from 35.1 +/- 11.7 to 91.5 +/- 22.7 LU (p < .01). Significant improvement was not recorded for QOL in the other three groups. Thus, therapy with alpha interferon has a significant effect on the QOL of that subgroup of patients with CFS manifesting an isolated decrease in NK function. Randomized Controlled Trial
<b>Selden SM, Cameron AS.</b>	Communicable Disease Control Unit, South Australian Health Commission, Adelaide, SA.	Changing epidemiology of Ross River virus disease in South Australia.	Med J Aust 1996 Sep 16;165(6):313-7 comment in: Med J Aust. 1997 Aug 18;167(4):229-30 Med J Aust. 1997 Mar 17;166(6):333; discussion 334 Med J Aust. 1997 Mar 17;166(6):334	OBJECTIVE: To investigate changes in epidemiology and symptoms of Ross River virus (RRV) disease in South Australia. DESIGN: Longitudinal questionnaire-based survey of notified cases from one to 36 months after infection. SUBJECTS: All patients with recent serologically confirmed RRV infection notified to the Communicable Disease Control Unit, South Australian Health Commission, between 1 October 1992 and 30 June 1993. OUTCOME MEASURES: Sociodemographic data, source of infection, symptoms and ability to carry out daily activities (at onset of illness and at time of questionnaire, up to 36 months after infection), symptom duration, economic impact of the illness, cases recovery time, factors predictive of delayed recovery. RESULTS: Information was obtained on the acute illness from 698 of the 821 subjects and at 15 months after infection from 436. At 15 months, 51% of respondents still had joint pain and 45% had persistent tiredness and lethargy. Other common symptoms included myalgia (34%), lymphadenopathy (25%), headache (23%) and depression (22%). These symptoms were still common 30 months after infection. Increasing age was the only statistically significant predictor of delayed recovery. Infections were acquired across the State, away from previously recognised RRV-endemic areas. CONCLUSIONS: For many people, RRV disease is debilitating, with long term symptoms similar to those of chronic fatigue syndrome. The geographic range of the infection has expanded in SA.
<b>Sharma A, Kendall MJ, Oyebode F, Jones D.</b>		Fluoxetine and chronic fatigue syndrome.	Lancet 1996 Jun 22;347(9017):1770-1; discussion 1771-2	
<b>Sharpe M, Clements A, Hawton K, Young AH, Sargent P, Cowen PJ.</b>	University Department of Psychiatry, Warneford and Littlemore Hospitals, Oxford, UK.	Increased prolactin response to buspirone in chronic fatigue syndrome.	J Affect Disord 1996 Nov 4;41(1):71-6	We studied the endocrine and subjective responses that followed acute administration of the 5-HT1A receptor agonist buspirone (0.5 mg/kg orally) in 11 male patients with chronic fatigue syndrome (CFS) and a group of matched healthy controls. Patients with CFS had significantly higher plasma prolactin concentrations and experienced more nausea in response to buspirone than did controls. However, the growth hormone response to buspirone did not distinguish CFS patients from controls. Our data

				question whether the enhancement of buspirone-induced prolactin release in CFS is a consequence of increased sensitivity of post-synaptic 5-HT1A receptors. It is possible that the increased prolactin response to buspirone in CFS could reflect changes in dopamine function.
<b>Sharpe M, Hawton K, Simkin S, Surawy C, Hackmann A, Klimes I, Peto T, Warrell D, Seagroatt V.</b>	University Department of Psychiatry, Warneford Hospital, Oxford.	Cognitive behaviour therapy for the chronic fatigue syndrome: a randomized controlled trial.	BMJ 1996 Jan 6;312(7022):22-6 comment in: ACP J Club. 1996 May-Jun;124(3):71 BMJ. 1996 Apr 27;312(7038):1096-7; discussion 1098 BMJ. 1996 Apr 27;312(7038):1096; discussion 1098 BMJ. 1996 Apr 27;312(7038):1097-8 BMJ. 1996 Apr 27;312(7038):1097; discussion 1098	OBJECTIVE--To evaluate the acceptability and efficacy of adding cognitive behaviour therapy to the medical care of patients presenting with the chronic fatigue syndrome. DESIGN--Randomised controlled trial with final assessment at 12 months. SETTING--An infectious diseases outpatient clinic. SUBJECTS--60 consecutively referred patients meeting consensus criteria for the chronic fatigue syndrome. INTERVENTIONS--Medical care comprised assessment, advice, and follow up in general practice. Patients who received cognitive behaviour therapy were offered 16 individual weekly sessions in addition to their medical care. MAIN OUTCOME MEASURES--The proportions of patients (a) who achieved normal daily functioning (Karnofsky score 80 or more) and (b) who achieved a clinically significant improvement in functioning (change in Karnofsky score 10 points or more) by 12 months after randomisation. RESULTS--Only two eligible patients refused to participate. All randomised patients completed treatment. An intention to treat analysis showed that 73% (22/30) of recipients of cognitive behaviour therapy achieved a satisfactory outcome as compared with 27% (8/30) of patients who were given only medical care (difference 47 percentage points; 95% confidence interval 24 to 69). Similar differences were observed in subsidiary outcome measures. The improvement in disability among patients given cognitive behaviour therapy continued after completion of therapy. Illness beliefs and coping behaviour previously associated with a poor outcome changed more with cognitive behaviour therapy than with medical care alone. CONCLUSION--Adding cognitive behaviour therapy to the medical care of patients with the chronic fatigue syndrome is acceptable to patients and leads to a sustained reduction in functional impairment. Randomized Controlled Trial
<b>Sharpe M.</b>	Department of Psychiatry, University of Oxford, United Kingdom.	Chronic fatigue syndrome.	Psychiatr Clin North Am 1996 Sep;19(3):549-73	Chronic fatigue syndrome (CFS) is a medically unexplained illness characterized by chronic, disabling fatigue, impaired concentration, muscle pain, and other somatic symptoms. The conceptual difficulties associated with all medically unexplained illnesses contribute to the controversy surrounding CFS, which has centered around whether it is best regarded as a medical or as a psychiatric condition. Clinically, such an approach is not helpful, and current research suggests that both pathophysiologic changes and psychosocial factors are important. Pragmatic management based on a detailed assessment of the individual is outlined.
<b>Shepherd C.</b>		Cognitive behaviour therapy for the chronic fatigue syndrome. Good general care may offer as much benefit as cognitive behaviour therapy.	BMJ 1996 Apr 27;312(7038):1096; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
<b>Sisto SA, LaManca J, Cordero DL, Bergen MT, Ellis SP, Drastal S, Boda WL, Tapp WN, Natelson BH.</b>	Department of Neurosciences, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, USA.	Metabolic and cardiovascular effects of a progressive exercise test in patients with chronic fatigue syndrome.	Am J Med 1996 Jun;100(6):634-40 comment in: Am J Med. 1997 Jul;103(1):83-4 Am J Med. 1997 Jul;103(1):84-6	PURPOSE: To evaluate the aerobic power (as maximum volume of oxygen consumed [VO2 max]) of women with chronic fatigue syndrome (CFS). PATIENTS AND METHODS: Twenty-one women with CFS and 22 sedentary healthy controls (CON) were studied at the CFS Cooperative Research Center Exercise Laboratory at the VA Medical Center, East Orange, New Jersey. Performance was measured on an incremental treadmill protocol walking to exhaustion. Expired gases were analyzed by a metabolic system, heart rate was recorded continuously, and ratings of perceived exertion (RPE) were taken at each workload. The groups were divided into those who achieved VO2 max (CFS-MAX and CON-MAX) and those who stopped at a submaximal level (CFS-NOMAX and CON-NOMAX) by using standard criteria. RESULTS: Seventeen CON and 10 CFS subjects achieved VO2 max. The VO2 max (mL/kg/min) of the CFS-MAX (28.1 +/- 5.1) was lower than that of the CON-MAX (32.1 +/- 4.3, P = 0.05). The CFS-MAX achieved 98 +/- 11% of predicted VO2 max. The CFS group had a higher RPE at the same absolute workloads as controls (P < 0.01) but not the same relative workloads. CONCLUSION: Compared with normal controls, women with CFS have an aerobic power indicating a low normal fitness level with no indication of cardiopulmonary abnormality. Our CFS group could withstand a maximal treadmill exercise test without a major exacerbation in either fatigue or other symptoms of their illness.
<b>Snorrason E, Arni Geirsson,</b>		Trial of a Selective	Journal of Chronic Fatigue	The purpose of the study was to search for a means of diminishing the plight of patients with chronic

<b>Kari Stefansson</b>		Acetylcholinesterase Inhibitor, Galanthamine Hydrobromide, in the Treatment of Chronic Fatigue Syndrome	Syndrome 1996; 2(2/3): 35 - 54	fatigue syndrome (CFS) and to test the hypothesis that central to the pathogenesis of CFS is a cholinergic defect. Forty-nine patients who fulfilled consensus criteria for CFS were treated with the acetylcholinesterase inhibitor, galanthamine hydrobromide. Thirty-nine patients finished the study according to the protocol with 43% reporting 50% improvement in fatigue, myalgia and sleep and 70% reporting 30% improvement whereas patients in the placebo group reported only 10% improvement in the same parameters of CFS. The improvement of patients on galanthamine was in most cases gradual and reached significance for the group only after four to eight weeks. The improvement was stable, and no patients who reported over 50% improvement on galanthamine relapsed to a pretrial level of any symptom. One of the most surprising effects was the dramatic improvement of sleep disturbances that occurred in most patients on this medication: more than 60% of the patients who finished the study reported over 70% improvement in sleep deficit. If the subjective report by patients can be proved by objective means, this would be the first demonstration of a drug that can be used to correct a sleep disturbance that also influences a specific stage in normal sleep. The most common adverse effect of galanthamine, as given in this study, was nausea that was dose-dependent and reversible. Galanthamine hydrobromide is relatively safe and appears to be an effective medication against many symptoms of CFS. But the positive results of this study have to be interpreted cautiously because of methodological limitations of this trial. First, this study was originally organized as a double-blind, placebo-controlled trial but was changed to an optional crossover after two weeks of treatment. Also, the adverse effects of the active drug in 30% of patients could compromise the double-blind. With these limitations in mind, it is nevertheless tempting to conclude that this study lends an indirect support to our hypothesis that a cholinergic deficit may play a role in the pathogenesis of the syndrome.
<b>St George IM.</b>	Wellington School of Medicine, New Zealand.	Did Cook's sailors have Tapanui 'flu? --chronic fatigue syndrome on the Resolution.	N Z Med J 1996 Jan 26;109(1014):15-7	The 1982 publication of the Resolution journal of Johann George Reinhold Forster provided justification for his recognition as a scientist, and gave a remarkable insight into his character. It also included an account of an illness suffered by many of the sloop's crew, including Forster, after a period ashore at Queen Charlotte Sound. The symptoms of the illness were remarkably similar to those now clustered as the chronic fatigue syndrome.
<b>Steinberg P, McNutt BE, Marshall P, Schenck C, Lurie N, Pheley A, Peterson PK.</b>	Department of Medicine, Hennepin County Medical Center, Minneapolis, MN 55415, USA.	Double-blind placebo-controlled study of the efficacy of oral terfenadine in the treatment of chronic fatigue syndrome.	J Allergy Clin Immunol 1996 Jan;97(1 Pt 1):119-26	<b>BACKGROUND:</b> There is no established treatment for chronic fatigue syndrome (CFS), an illness characterized by disabling fatigue exacerbated by physical activity. A variety of immunologic abnormalities have been reported, including a high incidence of atopy and hypoergy or anergy. <b>OBJECTIVE:</b> Because of anecdotal reports and uncontrolled trials showing antihistamine efficacy in CFS, we evaluated the clinical efficacy of the antihistamine terfenadine (60 mg twice daily) in a placebo-controlled study. <b>METHODS:</b> Thirty patients with CFS were enrolled in a 2-month, double-blind, placebo-controlled trial of terfenadine. Participants underwent a battery of both immediate- and delayed-type hypersensitivity skin tests and completed a self-assessment questionnaire used to measure severity of symptoms, physical and social functioning, health perceptions, and mental health before each of six biweekly visits. <b>RESULTS:</b> Twenty-eight patients completed the trial. History of atopy and positive immediate skin test results were prevalent, 73% and 53%, respectively. No evidence for hypoergy or anergy after delayed-type hypersensitivity skin testing was found. No therapeutic benefit from terfenadine could be detected in terms of symptom amelioration, improved physical or social functioning, health perceptions, or mental health. A high incidence of atopy in patients with CFS was confirmed. <b>CONCLUSION:</b> Although this trial involved a small number of patients, the results suggest that terfenadine is unlikely to be of clinical benefit in treating CFS symptoms. Randomized Controlled Trial
<b>Steinberg P, Pheley A, Peterson PK.</b>	Division of Allergy and Clinical Immunology, Hennepin County Medical Center, Minneapolis 55415, USA.	Influence of immediate hypersensitivity skin reactions on delayed reactions in patients with chronic fatigue syndrome.	J Allergy Clin Immunol 1996 Dec;98(6 Pt 1):1126-8	
<b>Sterzl I, Zamrazil V.</b>	Endokrinologicky ustav, Praha.	[Endocrinopathy in the differential diagnosis of chronic fatigue	Vnitr Lek 1996 Sep;42(9):624-6	Fatigue is a frequent and sometimes dominant symptom of some endocrinopathies. It may be associated with other symptoms which are included among the criteria of the chronic fatigue syndrome. These units are not always quite distinct and frequently endocrine diseases and chronic

		syndrome].[article in Czech]		fatigue syndrome (CFS) overlap. From this ensue differential diagnostic problems and ideas on possible causal relations. The authors concentrate in articular on autoimmune endocrinopathies and the polyglandular autoimmune syndrome (APS) with emphasis on the necessity of an accurate endocrinological diagnosis, where is some patients with suspected CFS a defined endocrinopathy was revealed. Attention will be also paid to recent views on the possible participation of disorders of the hypothalamus-pituitary-adrenal axis in the etiopathogenesis of CFS where endocrine and immune regulation overlap and condition each other.
<b>Straus SE.</b>		Chronic fatigue syndrome.	BMJ 1996 Oct 5;313(7061):831-2	
<b>Studd J, Panay N.</b>		Chronic fatigue syndrome.	Lancet 1996 Nov 16;348(9038):1384 comment on: Lancet. 1996 Oct 12;348(9033):971	
<b>Swanink CM, Vercoulen JH, Galama JM, Roos MT, Meyaard L, van der Ven-Jongekrijg J, de Nijs R, Bleijenberg G, Fennis JF, Miedema F, van der Meer JW.</b>	Department of General Internal Medicine, University Hospital Nijmegen, Netherlands.	Lymphocyte subsets, apoptosis, and cytokines in patients with chronic fatigue syndrome.	J Infect Dis 1996 Feb;173(2):460-3	Whether immunologic abnormalities correlate with fatigue severity and functional impairment in chronic fatigue syndrome (CFS) was investigated. Blood mononuclear cells were immunophenotyped and circulating ex vivo-produced cytokines were measured in 76 CFS patients and 69 healthy matched controls. Expression of CD11b on CD8 cells was significantly decreased in CFS patients. However, the previously reported increased expression of CD38 and HLA-DR was not confirmed. There was no obvious difference in apoptosis in leukocyte cultures, circulating cytokines, and ex vivo production of interleukin (IL)-1 alpha and IL-1 receptor antagonist. Endotoxin-stimulated ex vivo production of tumor necrosis factor-alpha and IL-beta was significantly lower in CFS. The immunologic test results did not correlate with fatigue severity or psychologic well-being was measured by Checklist Individual Strength, Beck Depression Inventory, and Sickness Impact Profile. Thus, these immunologic tests cannot be used as diagnostic tools in individual CFS patients.
<b>Tripathy BK, Agarwal AK, Sangla KS, Singh CP, Chandra S.</b>	Department of Medicine, Safdarjang Hospital, New Delhi.	Infectious agents and immunological disturbances in relation to chronic fatigue syndrome.	J Assoc Physicians India 1996 May;44(5):335-8	
<b>van Waveren EK.</b>		The rise and fall of the chronic fatigue syndrome as defined by Holmes et al.	Med Hypotheses 1996 Feb;46(2):63-6	This paper is a sequel to my monograph on neurocirculatory asthenia and chronic fatigue syndrome. It pays special attention to the nature of chronic fatigue syndrome, to the forms of neurocirculatory asthenia, and above all to the 6th form in which profound fatigue is the dominant symptom. All forms including the 6th are characterized by the presence of concomitant symptoms due to dysfunction of the autonomic nervous system. Chronic fatigue syndrome as defined by Holmes et al is devoid of these symptoms. Up till the present day no case histories of it have been published. It is argued that chronic fatigue syndrome sensu Holmes et al does not exist, the 6th form of neurocirculatory asthenia having to take up its place.
<b>Vecchiet L, Montanari G, Pizzigallo E, Iezzi S, de Bigontina P, Dragani L, Vecchiet J, Giamberardino MA.</b>	Institute of Medical Pathophysiology, 'G. D'Annunzio' University of Chieti, Italy.	Sensory characterization of somatic parietal tissues in humans with chronic fatigue syndrome.	Neurosci Lett 1996 Apr 19;208(2):117-20	Patients with chronic fatigue syndrome (CFS) mainly complain of symptoms in the musculoskeletal domain (myalgias, fatigue). In 21 CFS patients the deep (muscle) versus superficial (skin, subcutis) sensitivity to pain was explored by measuring pain thresholds to electrical stimulation unilaterally in the deltoid, trapezius and quadriceps and overlying skin and subcutis in comparison with normal subjects. Thresholds in patients were normal in skin and subcutis but significantly lower than normal (hyperalgesia) in muscles ( $P < 0.001$ ) in all sites. The selective muscle hypersensitivity corresponded also to fiber abnormalities at muscle biopsy (quadriceps) performed in nine patients which were absent in normal subjects (four cases): morphostructural alterations of the sarcomere, fatty degeneration and fibrous regeneration, inversion of the cytochrome oxidase/succinate dehydrogenase ratio, pleio/polymorphism and monstrosity of mitochondria, reduction of some mitochondrial enzymatic activities and increments of common deletion of 4977 bp of mitochondrial DNA 150-3000 times the normal values. By showing both sensory (diffuse hyperalgesia) and anatomical (degenerative picture) changes at muscle level, the results suggest a role played by peripheral mechanisms in the genesis of CFS symptoms. They would exclude the heightened perception of physiological signals from all districts hypothesized by some authors, especially as the hyperalgesia is absent in skin/subcutis.
<b>Vercoulen JH, Hommes OR,</b>	Department of Medical	The measurement of fatigue in	Arch Neurol 1996	OBJECTIVE: To provide a multidimensional characterization of fatigue in patients with multiple

<p><b>Swanink CM, Jongen PJ, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G.</b></p>	<p>Psychology, University Hospital Nijmegen, The Netherlands.</p>	<p>patients with multiple sclerosis. A multidimensional comparison with patients with chronic fatigue syndrome and healthy subjects.</p>	<p>Jul;53(7):642-9</p>	<p>sclerosis (MS). DESIGN: Cross-sectional design. Fifty patients with clinically definite MS were compared on the dimensions of fatigue with 51 patients with chronic fatigue syndrome (CFS) and 53 healthy subjects. RESULTS: Forty-six percent of the patients with MS reported fatigue to be present at least once a week. Patients with MS and patients with CFS had significantly higher subjective fatigue severity scores than healthy subjects. Patients with MS and patients with CFS had significantly higher scores on measures of psychological well-being than healthy subjects. Patients with MS had scores similar to those of patients with CFS, except that patients with CFS had significantly higher somatization scores. High somatization scores reflect strong focusing on bodily sensations. Both groups of patients were significantly less active than the healthy subjects. The Kurtzke Expanded Disability Status Scale (EDSS) and the Beck Depression Inventory scores were not related to subjective fatigue severity. In patients with MS and in patients with CFS, subjective fatigue severity was related to impairment in daily life, low sense of control over symptoms, and strong focusing on bodily sensations. In CFS, but not in MS, evidence was found for a relationship between low levels of physical activity and attributing symptoms to a physical cause and between subjective fatigue severity and physical activity. CONCLUSIONS: Patients with MS experienced significant fatigue, which had a significant impact on daily functioning and was not related to depression on Expanded Disability Status Scale score. Psychological factors, such as focusing on bodily sensations and low sense of control play a role in the experience of fatigue in MS and CFS.</p>
<p><b>Vercoulen JH, Swanink CM, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G.</b></p>	<p>Department of Medical Psychology, University Hospital Nijmegen, The Netherlands.</p>	<p>Prognosis in chronic fatigue syndrome: a prospective study on the natural course.</p>	<p>J Neurol Neurosurg Psychiatry 1996 May;60(5):489-94</p>	<p>OBJECTIVE--To determine spontaneous improvement after a follow up interval of 18 months in patients with chronic fatigue syndrome and to identify factors that predict improvement. METHODS--A longitudinal study was used. Of 298 initially assessed self referred patients fulfilling criteria for chronic fatigue syndrome, 246 patients completed self report questionnaires at follow up (response rate 83%). A multidimensional assessment method was used, measuring behavioural, emotional, cognitive, and social functioning. Comparison data from 53 healthy subjects matched for age, sex, and educational level were available. RESULTS--Three per cent of patients reported complete recovery and 17% reported improvement. At follow up, there were considerable problems at work and consumption of medication was high. Subjective improvement was confirmed by dimensional change: at follow up recovered patients had similar scores to healthy subjects and improved patients showed significant improvement on four out of seven outcome measures and had higher scores than healthy subjects in all dimensions. Sociodemographic variables or treatment by specialists and alternative practitioners did not predict improvement. Predictors of improvement were: subjective sense of control over symptoms, less fatigue, shorter duration of complaints, and a relative absence of physical attributions. CONCLUSION--The improvement rate in patients with a relatively long duration of complaints is small. Psychological factors are related to improvement, especially cognitive factors.</p>
<p><b>Vercoulen JH, Swanink CM, Zitman FG, Vreden SG, Hoofs MP, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G.</b></p>	<p>Department of Medical Psychology, University Hospital, Nijmegen, The Netherlands.</p>	<p>Randomised, double-blind, placebo-controlled study of fluoxetine in chronic fatigue syndrome.</p>	<p>Lancet 1996 Mar 30;347(9005):858-61</p>	<p>BACKGROUND: No somatic treatment has been found to be effective for chronic fatigue syndrome (CFS). Antidepressant therapy is commonly used. Fluoxetine is recommended in preference to tricyclic agents because it has fewer sedative and autonomic nervous system effects. However, there have been no randomised, placebo-controlled, double-blind studies showing the effectiveness of antidepressant therapy in CFS. We have carried out such a study to assess the effect of fluoxetine in depressed and non-depressed CFS patients. METHODS: In this randomised, double-blind study, we recruited 44 patients to the depressed CFS group, and 52 to the non-depressed CFS group. In each group participants were randomly assigned to receive either fluoxetine (20 mg once daily) or placebo for 8 weeks. The effect of fluoxetine was assessed by questionnaires, self-observation lists, standard neuropsychological tests, and a motion-sensing device (Actometer), which were applied on the day treatment started and on the last day. FINDINGS: The two groups were well matched in terms of age, sex distribution, employment and marital status, and duration of CFS. There were no significant differences between the placebo and fluoxetine-treated groups in the change during the 8-week treatment period for any dimension of CFS. There was no change in subjective assessments of fatigue, severity of depression, functional impairment, sleep disturbances, neuropsychological function, cognitions, or physical activity in the depressed or the non-depressed subgroup. INTERPRETATION: Fluoxetine in a 20 mg daily dose does not have a beneficial effect on any characteristic of CFS. The lack of effect of fluoxetine on depressive symptoms in CFS suggests that processes underlying the</p>

				presentation of depressive symptoms in CFS may differ from those in patients with major depressive disorder. Randomized Controlled Trial
<b>Wagner M, Gerhard R. F. Krueger, Dharam V. Ablashi, James E. Whitman</b>		Chronic Fatigue Syndrome (CFS): A Critical Evaluation of Testing for Active Human Herpesvirus-6 (HHV-6) Infection Review of Data of 107 Cases	Journal of Chronic Fatigue Syndrome 1996; 2(4): 3 - 16	Aim: To conduct a virologic study in patients with chronic fatigue syndrome (CFS, ICD-10: G 93.3) for identification of reactivated human herpesvirus-6 (HHV-6) infection. Patients and Method: One hundred seven patients (60 women, 47 men, f/m ratio: 1.27/1; age: between 7 and 76 years, medium 41.8 years) with clinical CFS were studied with follow-up periods from 10 months to 7.5 years. Patients were recruited for the study by answering a standard questionnaire and by matching the Holmes' criteria for CFS. This was followed by physical examination, conventional hematological and chemistry testing, lymphocyte phenotyping, and control of other immunologic parameters. Testing for HHV-6 infection included indirect immunofluorescence assays (IFA), antigen capture enzyme linked immunosorbent assay (antigen capture ELISA, ACE), nested polymerase chain reaction (nPCR) on peripheral blood cells, and virus isolation. Results: HHV-6 seroprevalence in CFS patients was 97%. Seventy-two percent of the CFS patients had elevated serum anti-HHV-6 IgG titers, but active HHV-6 infection was detected in only 38.6% of the cases as identified by ACE, nPCR, and virus isolation. In absence of anti-HHV-6-IgM, anti-HHV-6-IgG titers were less reliable for monitoring virus activity. Among other infections EBV was seen in 19.6% of the cases and, less frequently, HSV, Chlamydia, Campylobacter, coxsackie, CMV, Yersinia or Candida. In 46% of the patients there were evident signs of immune deficiency. In additional 20% evidence was less clear (e.g., decreased lymphocyte stimulation: PHA/ConA 46%; low NK cell levels: 35%; and low CD4/CD8 cell ratio: 21%). Conclusion: Active HHV-6 infection was prevalent in one third of our CFS patients, much less than expected. Additional testing besides routine IFA is necessary for confirminig virus activity.
<b>Ward MH, DeLisle H, Shores JH, Slocum PC, Foresman BH.</b>	Department of Medicine, University of North Texas Health Science Center, Fort Worth, USA.	Chronic fatigue complaints in primary care: incidence and diagnostic patterns.	J Am Osteopath Assoc 1996 Jan;96(1):34-46, 41	The complaint of chronic fatigue is ubiquitous in the primary care setting. Because of the nonspecific nature of chronic fatigue, practitioners do not focus on this complaint. Furthermore, most physicians use a problem-based approach. Such a prematurely narrowed focus could overlook the chronic fatigue complaint. Omissions in the data collection process would prove this oversight. Therefore, we postulated that a retrospective review of evaluations for chronic fatigue would demonstrate significant categorical deficiencies. These deficiencies would indicate a problem focus different than the chronic fatigue complaint itself. The authors reviewed the current literature to establish historical, physical, and laboratory findings pertinent to the evaluation of chronic fatigue. Six major categories and the associated data elements were identified for use in analyzing patient records. The patient records from the preceding 6 months were reviewed to find those containing a complaint of chronic fatigue. These records were analyzed to determine if a complete data set had been sought and if an associated diagnosis was made. A total of 425 consecutive charts from an academic family practice clinic were retrospectively reviewed; 9.9% (42) mentioned chronic fatigue. Physicians were lax in performing the mental status and physical examinations; taking the patient's psychiatric and sleep history, as well as the history of chief complaint; and ordering laboratory evaluations. The physician diagnoses included: depression (40.4%), nonspecific fatigue (35.7%), general medical disorders (16.6%), chronic fatigue syndrome (2.4%), fibromyalgia (2.4%), and sleep apnea (2.4%). From these data, the investigators conclude that the workup for chronic fatigue is often incomplete or lacks documentation. This oversight is likely due to a problem focus not directed at the chronic fatigue complaints. Also complicating the evaluation process are the multiple associated disorders, the prevalence of the complaint, and cost/benefit issues facing the primary care physician.
<b>Wearden AJ, Appleby L.</b>	Department of Psychiatry, University Hospital of South Manchester, UK. awearden@psy.man.ac.uk	Research on cognitive complaints and cognitive functioning in patients with chronic fatigue syndrome (CFS): What conclusions can we draw?	J Psychosom Res 1996 Sep;41(3):197-211	People with chronic fatigue syndrome (CFS) complain of difficulties with concentration and memory yet studies suggest that they do not suffer gross deficits in cognitive functioning. Depressed patients make similar cognitive complaints, and there is symptomatic overlap between CFS and depression. Cognitive complaints and depressed mood are positively correlated in CFS patients but, except on tasks which are particularly sensitive to depression, cognitive performance and depression are not. The inconsistency between cognitive complaints and results of tests of cognitive functioning resembles that found in other subject groups and may be due in part to the inappropriate use of laboratory memory tests for assessing "everyday" cognitive functioning. Even when cognitive capacity is intact, cognitive performance may be affected by factors such as arousal, mood, and strategy. In CFS patients, everyday cognitive tasks may require excessive processing resources leaving patients with diminished spare

<b>Wessely S, Chalder T, Hirsch S, Wallace P, Wright D.</b>	Department of Psychological Medicine, King's College School of Medicine and Dentistry, London.	Psychological symptoms, somatic symptoms, and psychiatric disorder in chronic fatigue and chronic fatigue syndrome: a prospective study in the primary care setting.	Am J Psychiatry 1996 Aug;153(8):1050-9	attentional capacity or flexibility. OBJECTIVE: This study assessed relationships among psychological symptoms, past and current psychiatric disorder, functional impairment, somatic symptoms, chronic fatigue, and chronic fatigue syndrome. METHOD: A prospective cohort study was followed by a nested case-control study. The subjects, aged 18-45 years, had been in primary care for either clinical viral infections or a range of other problems. Questionnaire measures of fatigue and psychological symptoms were completed by 1,985 subjects 6 months later; 214 subjects with chronic fatigue were then compared with 214 matched subjects without fatigue. Assessments were made with questionnaires, interviews, and medical records of fatigue, somatic symptoms, psychiatric disorder, and functional impairment. RESULTS: Subjects with chronic fatigue were at greater risk than those without chronic fatigue for current psychiatric disorder assessed by standardized interview (60% versus 19%) or by questionnaire (71% versus 31%). Chronic fatigue subjects were more likely to have received psychotropic medication or experienced psychiatric disorder in the past. There was a trend for previous psychiatric disorder to be associated with comorbid rather than noncomorbid chronic fatigue. Most subjects with chronic fatigue syndrome also had current psychiatric disorder when assessed by interview (75%) or questionnaire (78%). Both the prevalence and incidence of chronic fatigue syndrome were associated with measures of previous psychiatric disorder. The number of symptoms suggested as characteristics of chronic fatigue syndrome was closely related to the total number of somatic symptoms and to measures of psychiatric disorder. Only postexertion malaise, muscle weakness, and myalgia were significantly more likely to be observed in chronic fatigue syndrome than in chronic fatigue. CONCLUSIONS: Most subjects with chronic fatigue or chronic fatigue syndrome in primary care also meet criteria for a current psychiatric disorder. Both chronic fatigue and chronic fatigue syndrome are associated with previous psychiatric disorder, partly explained by high rates of current psychiatric disorder. The symptoms thought to represent a specific process in chronic fatigue syndrome may be related to the joint experience of somatic and psychological distress.
<b>Wessely S.</b>	King's College School of Medicine and Dentistry, London.	Chronic fatigue syndrome. Summary of a report of a joint committee of the Royal Colleges of Physicians, Psychiatrists and General Practitioners.	J R Coll Physicians Lond 1996 Nov-Dec;30(6):497-504	Chronic Fatigue Syndrome (CFS) is not a single diagnostic entity. It is a symptom complex which can be reached by many different routes. The conceptual model of CFS needs to be changed from one determined by a single cause/agent to one in which dysfunction is the end stage of a multifactorial process. Although it is important to recognise the role of factors that precipitate the condition, greater understanding is required of factors that predispose individuals to develop the illness, and those that perpetuate disability.
<b>Wiebe E.</b>	Department of Family Practice, University of British Columbia, Vancouver.	N of 1 trials. Managing patients with chronic fatigue syndrome: two case reports.	Can Fam Physician 1996 Nov;42:2214-7	Chronic fatigue syndrome is a heterogeneous condition with as proves effective treatment. I present two case reports in which N of 1 trials helped me make management decisions. High-dose vitamin B12 injections were ineffective in one case; nimodipine was very effective in the other case.
<b>Wilhelmsen I, Bodtker J.</b>		[Chronic fatigue syndrome and cognitive therapy].[article in Norwegian]	Tidsskr Nor Laegeforen 1996 May 20;116(13):1615 comment on: Tidsskr Nor Laegeforen. 1996 Mar 10;116(7):861-4 Tidsskr Nor Laegeforen. 1996 May 10;116(12):1503	
<b>Williams DC.</b>	Virginia-Carolina Sleep Disorders Center in Danville, USA.	Periodic limb movements of sleep and the restless legs syndrome.	Va Med Q 1996 Fall;123(4):260-5	Periodic limb movements of sleep and the restless legs syndrome are not diagnoses but rather an indication that there is some CNS disturbance and are associated with an ever-growing number of conditions. They are very common, exist in many forms and are often overlooked by physicians. It is the author's opinion that they are parts of what has been called an akathisia syndrome in the most severe situations and may include the same mechanisms that underlie attention disorders, chronic fatigue syndrome and "sun-downing." They are likely parts of a syndrome caused by dysfunction in a complex brainstem center. This center's normal function is to maintain a smooth electrical template on which discrete neuronal impulses sculpture the rich repertoire we recognize as sensory and motor function awake and to effect a smooth "switching" mechanism allowing sleep to occur without motor and sensory input invading consciousness (awakening). While the DA-ergic CNS pathways have been thought to be the primary neurotransmitter involved, the opioids secondary, there is mounting

				evidence that the situation is far more complicated, that many neurotransmitter, including stimulating and inhibiting amino acids, play a part. These patients agonize with their indisposition but can be helped by various treatments. Treatment alleviates not only the distress caused by the symptoms but also the devastating insomnia and excessive daytime sleepiness associated with it.
<b>Williams G, Pirmohamed J, Minors D, Waterhouse J, Buchan I, Arendt J, Edwards RH.</b>	Department of Medicine, University of Liverpool, UK.	Dissociation of body-temperature and melatonin secretion circadian rhythms in patients with chronic fatigue syndrome.	Clin Physiol 1996 Jul;16(4):327-37	Many patients with chronic fatigue syndrome (CFS) display features of hypothalamic dysfunction. We have investigated aspects of circadian rhythmicity, an important hypothalamic function, in 20 CFS patients and in 17 age- and sex-matched healthy control subjects. There were no differences between the two groups in the amplitude, mesor (mean value) or timing of the peak (acrophase) of the circadian rhythm of core temperature, or in the timing of the onset of melatonin secretion. However, the CFS patients showed no significant correlation between the timing of the temperature acrophase and the melatonin onset ( $P < 0.5$ ), whereas the normal significant correlation was observed in the controls ( $P < 0.05$ ). Dissociation of circadian rhythms could be due to the sleep deprivation and social disruption, and/or the reduction in physical activity which typically accompany CFS. By analogy with jet-lag and shift-working, circadian dysrhythmia could be an important factor in initiating and perpetuating the cardinal symptoms of CFS, notably tiredness, impaired concentration and intellectual impairment.
<b>Zorzenon M, Gull Rukh, Giuseppe A. Botta, Roberto Colle, Laura A. Barsanti, Luca Ceccherini-Nelli</b>		Active HHV-6 Infection in Chronic Fatigue Syndrome Patients from Italy New Data	Journal of Chronic Fatigue Syndrome 1996: 2(1): 3 - 12	Primary Human Herpesvirus-6 (HHV-6) infection has been related to different clinical pictures and, notably, to Chronic Fatigue Syndrome (CFS). We studied 52 patients fulfilling the criteria of Centers for Disease Control (CDC) for CFS and a control group of 51 matched healthy blood donors. HHV-6 was recovered by culture and confirmed by immunofluorescence assay (IFA) and by PCR in 30/52 patients (57.7%) and in 6/51 (11.7%) of blood donors.