

| Authors | Author Address | Title | Publication | Abstract |
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| Abbey SE. | Department of Psychiatry, Toronto Hospital, Ontario, Canada. | Somatization, illness attribution and the sociocultural psychiatry of chronic fatigue syndrome. | Ciba Found Symp 1993;173:238-52; discussion 252-61 | In addition to epidemiological and neurobiological perspectives on the relationship between chronic fatigue syndrome (CFS) and psychiatric disorders there has been increasing interest in the role of cognitive-behavioural, psychological, psychodynamic and social factors in the psychiatric aspects of this syndrome. These factors may be important in the initiation and/or maintenance of CFS and play important roles in the misdiagnosis of primary psychopathology as CFS. They may be important targets for intervention and treatment. This paper examines the relevance of the following issues for better understanding the relationship between CFS and the results of psychiatric studies: (1) the concepts of somatization and abnormal illness behaviour; (2) the role of patients' illness attributions; (3) psychological and psychodynamic constructs such as depressive vulnerability occurring in individuals dependent upon achievement for the maintenance of self-esteem and euthymic mood, perfectionism, and helplessness; (4) the role of personality characteristics and styles; (5) the potential iatrogenic role of the health care system in producing disability in individuals with a diagnosis of CFS; (6) the role of the media and other sociocultural forces in the patient's choice of the CFS label; and (7) the impact of the CFS label on the patient. The importance of differentiating between initiating and maintaining or perpetuating factors is emphasized. |
| Anon | | Inability of retroviral tests to identify persons with chronic fatigue syndrome, 1992. | MMWR Morb Mortal Wkly Rep 1993 Mar 19;42(10):183, 189-90 | Chronic fatigue syndrome (CFS) is characterized by prolonged, debilitating fatigue. Although the cause of CFS unknown, CDC and researchers in other organizations have been investigating whether infection with a previously unidentified retrovirus might be an etiologic factor. Based on reports suggesting that retroviral infection with a human T-lymphotropic virus type 2 (HTLV-II)-like retrovirus or a spumavirus might be associated with CFS, some research and commercial laboratories developed assays to test specimens from persons with CFS. Even though the hypothesized association between infection with retroviruses and CFS has not been confirmed, these tests are used commonly to evaluate patients with CFS. This report summarizes the findings of a controlled, blinded study conducted in 1992 to determine whether three retroviral tests can distinguish serologically between patients with CFS (i.e., case-patients) and healthy controls. |
| Aoki T, Miyakoshi H, Usuda Y, Herberman RB. | Department of Internal Medicine, Shinrakuen Hospital, Niigata, Japan. Review, Academic | Low NK syndrome and its relationship to chronic fatigue syndrome. | Clin Immunol Immunopathol 1993 Dec;69(3):253-65 | |
| Barnes CL, Fleming CA, Poinsett-Holmes K, Kennedy LD. | | Chronic fatigue syndrome: what are the facts? | J Pract Nurs 1993 Sep;43(3):24-31; quiz 32-4 | |
| Barnes PR, Taylor DJ, Kemp GJ, Radda GK. | MRC Biochemical and Clinical Magnetic Resonance Unit, John Radcliffe Hospital, Oxford, UK. | Skeletal muscle bioenergetics in the chronic fatigue syndrome. | J Neurol Neurosurg Psychiatry 1993 Jun;56(6):679-83 | Skeletal muscle bioenergetics and control of intracellular pH have been investigated in 46 patients with chronic fatigue syndrome by phosphorus magnetic resonance spectroscopy. The results have been compared with those from healthy controls and from a group of patients with mitochondrial cytopathies affecting skeletal muscle. No consistent abnormalities of glycolysis, mitochondrial metabolism or pH regulation were identified in the group when taken as a whole, although in 12 of the 46 patients the relationship between pH and phosphocreatine utilisation during exercise fell outside the normal range. Of these, 6 patients showed increased acidification relative to phosphocreatine depletion while 6 showed reduced acidification. These findings do not support the hypothesis that any specific metabolic abnormality underlies fatigue in this syndrome although abnormalities may be present in a minority of patients. |
| Bates DW, Schmitt W, Buchwald D, Ware NC, Lee J, Thoyer E, Kornish RJ, Komaroff AL. | Department of Medicine, Brigham and Women's Hospital, Boston, Mass. | Prevalence of fatigue and chronic fatigue syndrome in a primary care practice. | Arch Intern Med 1993 Dec 27;153(24):2759-65 | BACKGROUND: Our goals were to determine the prevalence of unusual, debilitating fatigue and the frequency with which it was associated with the chronic fatigue syndrome (CFS) or other physical or psychological illness in an outpatient clinic population. METHODS: We prospectively evaluated a cohort of 1000 consecutive patients in a primary care clinic in an urban, hospital-based general medicine practice. The study protocol included a detailed history, physical examination, and laboratory and psychiatric testing. RESULTS: Five patients who came because of CFS studies were excluded. Of the remaining 995, 323 reported fatigue, and 271 (27%) complained of at least 6 months of unusual fatigue that interfered with their daily lives. Of the 271, self-report or record review revealed a medical |

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| | | | | or psychiatric condition that could have explained the fatigue in 186 (69%). Thus, 85 (8.5%) of 995 patients had a debilitating fatigue of at least 6 months' duration, without apparent cause. Of these patients, 48 refused further evaluation, and 11 were unavailable for follow-up; 26 completed the protocol. Three of the 26 were hypothyroid, and one had a major psychiatric disorder. Of the remaining 22 patients, three met Centers for Disease Control and Prevention criteria for CFS, four met British criteria, and 10 met the Australian case definition. The point prevalences of CFS were thus 0.3% (95% confidence interval [CI], 0% to 0.6%), 0.4% (95% CI, 0% to 0.8%), and 1.0% (95% CI, 0.4% to 1.6%) using the Centers for Disease Control and Prevention, British, and Australian case definitions, respectively. These estimates were conservative, because they assumed that none of the patients who refused evaluation or were unavailable for follow-up would meet criteria for CFS. CONCLUSIONS: While chronic, debilitating fatigue is common in medical outpatients, CFS is relatively uncommon. Prevalence depends substantially on the case definition used. |
| Behan WM, Behan PO. | Department of Pathology, Western Infirmary, Glasgow, UK. | The role of viral infection in polymyositis, dermatomyositis and chronic fatigue syndrome. | Baillieres Clin Neurol 1993 Nov;2(3):637-57 | |
| Bentall RP, Wood GC, Marrinan T, Deans C, Edwards RH. | Department of Clinical Psychology, University of Liverpool, UK. | A brief mental fatigue questionnaire. | Br J Clin Psychol 1993 Sep;32 (Pt 3):375-9 | A brief mental fatigue questionnaire was administered to normal subjects and muscle-diseased, Chronic Fatigue Syndrome (CFS), recovered CFS and depressed patients. The questionnaire was found to have excellent internal consistency and discriminated effectively between CFS and depressed patients on the one hand and recovered CFS, normal and muscle-diseased patients on the other. However, the scale failed to discriminate between CFS and depressed subjects, who were found to experience qualitatively and quantitatively similar mental fatigue symptoms. |
| Bertolin JM, Bertolin V. | Centro de Salud Mental, Servicio Valenciano de Salud. Review, Academic | [Chronic fatigue syndrome: biologic and psychopathologic investigations].[article in Spanish] | Med Clin (Barc) 1993 Jun 5;101(2):67-75 | |
| Bialyszewski A. | IV Kliniki Psychiatrycznej Instytutu Psychiatrii i Neurologii, Warszawie. | [The chronic fatigue syndrome].[article in Polish] | Psychiatr Pol 1993 Nov-Dec;27(6):601-11 | The chronic fatigue syndrome (CFS) including myalgic encephalomyelitis and the postviral syndrome is a term used today to describe a not fully recognized disease characterized primarily by chronic or recurrent debilitating fatigue and various combinations of neuromuscular and neuropsychological symptoms. The term CFS has been introduced and defined by the Centers for Disease Control (CDC) in Atlanta. Fatigue is one of the most common symptoms in medicine, but CFS as defined by CDC has appeared to be quite rare in the general population. Researchers have suggested that the syndrome is a heterogenous immunologic disorder that follows viral infection, but despite numerous studies on the subject the etiologic factor of the syndrome is unknown. CFS is a controversial diagnosis. In a very high percentage of patients with the CFS depression, phobias or anxiety disorders have frequently preceded the onset of the chronic fatigue. There are many overlapping symptoms between CFS and major depression. Some clinicians suggest that it is not obvious that CFS can be distinguished from neurasthenia. |
| Blondel-Hill E, Shafran SD. | Department of Medicine, University of Alberta, University of Alberta Hospitals, Walter Mackenzie Health Sciences Centre, Edmonton, Canada. | Treatment of the chronic fatigue syndrome. A review and practical guide. | Drugs 1993 Oct;46(4):639-51 | The chronic fatigue syndrome (CFS) was formally defined in 1988 to describe a syndrome of severe and disabling fatigue of uncertain aetiology associated with a variable number of somatic and/or psychological symptoms. CFS has been reported in most industrialised countries and is most prevalent in women aged between 20 and 50 years. Despite occasional claims to the contrary, the aetiology of CFS remains elusive. Although abnormalities in tests of immune function and cerebral imaging have been described in variable numbers of CFS patients, such findings have been inconsistent and cannot be relied upon, either to establish or exclude the diagnosis. Thus, diagnosis rests on fulfillment of the Centers for Disease Control case definition which was revised in 1992. This case definition remains somewhat controversial, largely due to its subjectiveness. The mainstay of treatment is establishing the diagnosis and educating the patient about the illness. An empathetic clinician can stop further consultations elsewhere ('doctor shopping') and subsequent excessive investigations, which frequently occur in such patients. Most patients should undertake a trial of antidepressant therapy, even if major depression is not present. The choice of antidepressant drug should tailor the tolerability profile to relief of particular CFS symptoms, such as insomnia or hypersomnia. Failure to improve within 12 weeks warrants an alternative antidepressant agent of another class. Many other drugs have been |

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| | | | | reported anecdotally to be beneficial, but no therapy has been demonstrated to be reproducibly useful in double-blind, placebo-controlled clinical trials with an adequate duration of follow-up. |
| Bojic I, Mijuskovic P, Lilic D, Kuljic-Kapulica N, Mijuskovic Z, Berger S, Mitrovic D. | Vojnomedicinska akademija, Klinika za infektivne i tropske bolesti, Institut za medicinska istrazivanja. | [The chronic fatigue syndrome associated with Epstein-Barr virus infection]. [article in Serbo-Croatian (Roman)] | Vojnosanit Pregl 1993 May-Jun;50(3):304-7 | |
| Bond PA. | | A role for herpes simplex virus in the aetiology of chronic fatigue syndrome and related disorders. | Med Hypotheses 1993 May;40(5):301-8 | |
| Bowles NE, Bayston TA, Zhang HY, Doyle D, Lane RJ, Cunningham L, Archard LC. | Department of Biochemistry, Charing Cross and Westminster Medical School, London, England. | Persistence of enterovirus RNA in muscle biopsy samples suggests that some cases of chronic fatigue syndrome result from a previous, inflammatory viral myopathy. | J Med 1993;24(2-3):145-60 | Molecular hybridization using an enterovirus group specific probe detected virus RNA in muscle biopsy samples from 25 of 96 cases of inflammatory muscle disease and similarly from 41 of 158 cases of postviral fatigue syndrome (PFS). Enterovirus RNA was detected in only two of 152 samples of control muscle. The inflammatory myopathy group comprised patients with polymyositis (PM), juvenile dermatomyositis (JDM) or adult dermatomyositis (DM), and all showed the presence of an inflammatory infiltrate and fiber necrosis on histological examination of a muscle biopsy sample. In contrast, muscle samples from the PFS group were histologically normal except for non-specific changes such as occasional single fiber atrophy. By analogy with enteroviral myocarditis, which can progress to a post-inflammatory disease with persistence of virus in myocardium and disposes to the rapid development of dilated cardiomyopathy, we propose that PFS syndrome may be a sequela of a previous inflammatory viral myopathy. |
| Brook MG, Bannister BA, Weir WR. Letter | | Interferon-alpha therapy for patients with chronic fatigue syndrome. | J Infect Dis 1993 Sep;168(3):791-2 | |
| Burdge DR, O'Hanlon DP. | Department of Medicine, University of British Columbia, Vancouver, Canada. | Experience at a referral center for patients with suspected Lyme disease in an area of nonendemicity: first 65 patients. | Clin Infect Dis 1993 Apr;16(4):558-60 | A multidisciplinary referral center was established at a university hospital for prospectively assessing patients with possible Lyme disease. Borrelia burgdorferi is not known to be endemic in this region, but considerable anxiety about Lyme disease has developed among the general public. Sixty-five patients were referred for suspected Lyme borreliosis. Detailed histories were obtained and physical examinations were performed; patients were investigated aggressively in accordance with their symptom complexes. Strict diagnostic criteria consistent with published standards were applied. Only two of the 65 patients were judged to have probable Lyme disease. Definite major alternate diagnoses were made for 50 patients (77%); firm medical diagnoses (11 dermatologic, 9 rheumatologic, 9 infectious disease, 6 gastrointestinal, 4 neurological, and 2 miscellaneous) were made for 41 patients (63%); and major psychiatric diagnoses were made for 9 patients (14%). Probable diagnoses of chronic fatigue syndrome and fibromyalgia were made for 11 patients (17%). The conditions of four patients (6%) were undiagnosed. A referral center for patients with suspected Lyme disease can be useful even in an area of nonendemicity, and careful clinical assessment will reveal treatable alternate diagnoses for many patients with suspected Lyme disease. |
| Cathebras P, Bouchou K, Charmion S, Rousset H. | Service de Medecine Interne, Hopital Nord, Saint-Etienne. | [Chronic fatigue syndrome: a critical review]. [article in French] | Rev Med Interne 1993 Apr;14(4):233-42 | The term "chronic fatigue syndrome" (CFS) applies to a condition of unknown aetiology characterized clinically by an association of subjective symptoms, the most constant being an invalidating tiredness. The diagnostic criteria in current use do not permit to isolate an homogeneous subgroup among patients consulting for chronic asthenia. In the present state of research no infectious or immunological cause has been demonstrated conclusively, although a persistent enterovirus or herpesvirus type 6 infection or a state of chronic immune activation seem to play a role in some cases. Patients who fulfill the criteria of CFS present with psychiatric overmorbidity, essentially depressive, and in 50% of the cases with the mental disorders preceding CFS. The various theoretical models linking CFS to psychopathology are discussed, and finally the syndrome is regarded as a social construction reproducing or renovating the neurasthenia of the late 19th century. There is no specific treatment of CFS, but antidepressants, cognitive-behavioural therapy and perhaps certain immuno-modulators can be useful. The future lines of research should endeavour to isolate a subgroup of patients with prolonged asthenia after a recognized episode of infection and to identify the immunological, |

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| | | | | psychological and behavioral characteristics of this particular group as well as their reciprocal interactions. Review, Academic |
| Centers for Disease Control and Prevention | | From the Centers for Disease Control and Prevention. Inability of retroviral tests to identify persons with chronic fatigue syndrome, 1992. | JAMA 1993 Apr 14;269(14):1779, 1782 | |
| Chester AC. | | Hypothesis: the nasal fatigue reflex. | Integr Physiol Behav Sci 1993 Jan-Mar;28(1):76-83 | Natural selection results in adaptations. I suggest that unexplained fatigue may be an adaptive response to nasal impairment. For macroscopic animals, intact olfaction is necessary to detect predators. In such animals, any reflex (e.g., fatigue) triggered by nasal dysfunction that limited exposure would offer great survival advantage. The "fatigued" animal would remain in its protected environment, unexposed to hungry carnivores, while the nose healed. In humans, clinical syndromes associated with unexplained fatigue (chronic fatigue syndrome, tension fatigue syndrome, allergic fatigue, neurasthenia, etc.) are characterized by symptoms that, in part, are nasal in origin. The older medical literature does describe the resolution of fatigue in neurasthenia after nasal treatments. Nasal reflexes in animals do cause significant systemic effects, including an inhibition of muscle action potentials that is, perhaps, analogous to the "heavy-limbed" sensation of those with fatigue. Furthermore, reflexes similar to the one proposed do exist in humans: the diving reflex presumably served our amphibian ancestors well as an oxygen conserving technique with submersion, but serves no known useful function now. Other human nasopharyngeal reflexes with profound cardiovascular and systemic effects are well described but only occasionally studied. The proposed nasal fatigue reflex should be examined as a possible ancient adaptive response to nasal malfunction. |
| Clee MD, McLaughlin K. | | Complications of sarcoidosis. Chronic fatigue syndrome. | Sarcoidosis 1993 Sep;10(2):138 comment on: Sarcoidosis. 1993 Mar;10(1):1-3 | |
| Cox DL, Findley LJ. | | Chronic fatigue syndrome. | BMJ 1993 Jul 31;307(6899):328 comment on: BMJ. 1993 Jun 12;306(6892):1557-8 | |
| Dechene L. | Fitchburg State College, Fitchburg, Massachusetts 01420. | Chronic fatigue syndrome: influence of histamine, hormones and electrolytes. | Med Hypotheses 1993 Jan;40(1):55-60 | The chronic fatigue syndrome is poorly understood. We believe the underlying causes in many atopics and women are a persistent infection and hypersensitivity to the immune-suppressive effects of histamine and certain pathogens. We believe much to the symptomatology can be explained by all four types of hypersensitivity (Gell and Coombs classification) in reaction to a pathogen, electrolyte disturbances which include sometimes permanent changes in cell membranes' ability to pass electrolytes, sometimes permanent biochemical changes in mitochondrial function, and disturbances of insulin and T3-thyroid hormone functions. We also explain in detail what 'fatigue' means for these patients. We present evidence from the medical literature for the plausibility of our hypotheses. |
| Delage G, Salit I, Pennie R, Alary M, Duval B, Ward B. | | [The possible relation between hepatitis B vaccination and chronic fatigue syndrome]. [article in French] | Union Med Can 1993 Jul-Aug;122(4):278-9 | |
| DeLuca J, Johnson SK, Natelson BH. | Department of Physical Medicine and Rehabilitation, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark. | Information processing efficiency in chronic fatigue syndrome and multiple sclerosis. | Arch Neurol 1993 Mar;50(3):301-4 | OBJECTIVE--To compare the cognitive performance of subjects with chronic fatigue syndrome (CFS), multiple sclerosis (MS), and healthy controls. All subjects were matched for age, education, and verbal intelligence, as previous neuropsychological studies of CFS had not used appropriate control groups. DESIGN--Case-control design. All subjects were given a neuropsychological battery and the test scores were compared among the groups. SETTING--Subjects with CFS and subjects with MS were recruited from private and institutional practice and from the community. Healthy subjects were recruited from the community. PATIENTS/OTHER PARTICIPANTS--Twelve subjects (all female) with CFS participated in the study. Chronic fatigue syndrome was diagnosed in these patients in accordance with the requirements outlined by the Centers for Disease Control as modified |

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| | | | | <p>subsequently to not exclude patients with concurrent depression and/or anxiety. All subjects with CFS were referred for a neuropsychological examination to assess persistent cognitive complaints. Eleven subjects (10 female, one male) with the diagnosis of clinically stable MS were chosen from clinics and the community because of complaints of mild to moderate cognitive impairment. The subjects with MS and 11 healthy volunteers (10 female, one male) were matched to the group with CFS by age, education, and estimated verbal intelligence (based on the Vocabulary subtest of the Wechsler Adult Intelligence Scale-Revised). The subjects with MS had a mean Kurtzke Expanded Disability Status Scale score of 4.95 (SD, 1.95; range, 2.0 to 7.5). As a result of the matching procedure, there were no differences among the three groups in age ($F[2,31] = 0.32$), education ($F[2,31] = 0.80$), and verbal intelligence ($F[2,31] = 0.31$). INTERVENTIONS--None. MAIN OUTCOME MEASURES--These measures included the Beck Depression Inventory (BDI), the Paced Auditory Serial Addition Test (PASAT), Digit Span Test, and the Similarities Test of Verbal Abstract Reasoning. RESULTS--The mean number of correctly identified responses collapsed across the four PASAT trials was significantly different across groups ($F[2,31] = 4.03$; $P < .05$). While the CFS and MS groups did not differ from each other, subjects with CFS (SEM, 124.2 +/- 6.4) and subjects with MS (SEM, 112.9 +/- 10.9) scored significantly below controls (SEM, 146.4 +/- 6.4) (Fisher's Protected Least Significant Difference test; $P < .05$). There were significant differences among the three groups on mean Digit Span Test performance ($F[2,31] = 5.5$; $P < .01$). While the CFS and MS group did not differ significantly from each other, only the CFS group was significantly lower than control (Fisher's Protected Least Significant Difference test; $P < .05$). Mean performance on the Similarities test did not differ among the three groups ($F = 0.58$). In addition, there were significant differences among the three groups in mean BDI scores ($F[2,31] = 7.6$; $P < .01$). The CFS and MS groups did not differ significantly from each other, and both groups showed a statistically significantly elevated mean BDI score relative to the control group (Fisher's Protected Least Significant Difference test; $P < .05$). No significant correlations were found between BDI scores and PASAT total scores (CFS, $r = -.21$; MS, $r = .13$; control, $r = .27$), or between BDI and Digit Span Test (CFS, $r = -.32$; MS, $r = -.40$; control, $r = -.19$). Results of the PASAT and Digit Span Test were significantly correlated in the CFS group ($r = .71$; $P < .01$), but not in the MS ($r = .06$) or control groups ($r = .49$). CONCLUSIONS--These results indicate that subjects with CSF and subjects with MS show significant impairment on a test of complex concentration when compared with appropriate controls. The data suggest that subjects with CFS and subjects with MS have difficulty on tasks that require the simultaneous processing of complex cognitive information. Selective impairment in information processing efficiency may lie at the</p> |
| Denz-Penhey H, Murdoch JC. | Department of General Practice, University of Otago Medical School, Dunedin. | General practitioners acceptance of the validity of chronic fatigue syndrome as a diagnosis. | N Z Med J 1993 Apr 14;106(953):122-4 | <p>AIM. To identify whether general practitioners accept the validity of a diagnosis of chronic fatigue syndrome (CFS). METHOD. An anonymous questionnaire was sent out to 98 general practitioners in Otago. RESULTS. The clinical validity of chronic fatigue syndrome was accepted by 74 (90%); 57 believed they had sufficient knowledge about the condition to make a differential diagnosis; 72 indicated they had had patients with chronic fatigue syndrome in the past; 62 currently had patients; there is a minimum prevalence rate of 167/100,000 in the general practice population; 83 replies were received. CONCLUSION. The 90% acceptance rate of chronic fatigue syndrome as a clinically valid diagnosis suggests that amongst the Otago general practitioners the controversy had receded. The low numbers suggest that they are on the conservative end of the diagnostic spectrum.</p> |
| Denz-Penhey H, Murdoch JC. | Department of General Practice, Otago Medical School, Dunedin, New Zealand. | Service delivery for people with chronic fatigue syndrome: a pilot action research study. | Fam Pract 1993 Mar;10(1):14-8 | <p>Chronic fatigue syndrome (CFS) is a symptom complex which while mild in some cases is severely debilitating in others. Long-term ill health leads to greater use of resources but in the case of long-term CFS the anecdotal evidence suggested a low compliance with the available options and a high level of both patient and general practitioner dissatisfaction. This pilot study sought through repeated action research cycles to start to identify culturally and contextually sensitive forms of language and models for service delivery suitable for people with CFS in a general practice setting. It worked through a number of action research cycles, to initiate the identification of conceptual models acceptable to both doctors and to patients suffering from CFS, self-management options which encouraged the body's ability to heal itself and services and delivery mechanisms which met patient needs within health provider options.</p> |
| Edwards RH, Gibson H, | Department of Medicine, | Muscle histopathology and | Ciba Found Symp | <p>Chronic fatigue syndrome (CFS) is characterized by fatigue at rest which is made worse by exercise.</p> |

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| Clague JE, Helliwell T. | University of Liverpool, UK. | physiology in chronic fatigue syndrome. | 1993;173:102-17; discussion 117-31 | Previous biopsy studies on small numbers of CFS patients have shown a range of morphological changes to which have been attributed fatigue and myalgia. We have now studied 108 patients with CFS or muscle pain and 22 normal volunteers by light and electron microscopy. There was no consistent correlation between symptoms and changes in fibre type prevalence, fibre size, degenerative or regenerative features, glycogen depletion, or mitochondrial abnormalities. Physiological contractile properties of quadriceps (maximal isometric force generation, frequency: force characteristics and relaxation rate) were also examined before and for up to 48 hours after a symptom-limited incremental cycle ergometer exercise test in 12 CFS patients and 12 normal volunteers. Voluntary and stimulated force characteristics were normal at rest and during recovery. Exercise duration was similar in the two groups although CFS patients had higher perceived exertion scores in relation to heart rate during exercise, indicating a reduced effort sensation threshold. On physiological and pathological grounds it is clear that CFS is not a myopathy. Psychological/psychiatric factors appear to be of greater importance in this condition. |
| Fohlman J, Friman G. | Department of Infectious Diseases, University Hospital of Uppsala, Sweden. | Is juvenile diabetes a viral disease? | Ann Med 1993 Dec;25(6):569-74 | The purpose of this review is to discuss recent literature data concerning the etiology and pathobiology in insulin-dependent diabetes mellitus as well as present our own experience from all children up to 15 years of age in Uppsala County, Sweden presenting with juvenile (type I) diabetes since 1976. Chronic enterovirus is an emerging concept in apparently immunologically competent patients. By means of new serological and DNA-based methods, a persistent enteroviral (Coxsackie virus A, B and ECHO virus) infection can sometimes be demonstrated after an acute primary infection, which is often subclinical. There are several indications that these viruses can contribute to the development of illnesses with a pathogenesis as yet not fully understood, e.g. dilated cardiomyopathy, type I diabetes, and possibly some cases of the so-called chronic fatigue syndrome. In type I diabetes, many pieces of evidence including epidemiology, genetic analysis of the host susceptibility genes, cytokine analysis and new serological evaluation suggest an infection to be the starting point for the beta cell destruction. These etiological agents most likely belong to the enteroviral group of picornaviruses. Later events may well involve all parts of the immune system launching a selective autoimmune 'suicidal attack' on the cells necessary for glucose homeostasis. |
| Folks TM, Heneine W, Khan A, Woods T, Chapman L, Schonberger L. | Division of Viral and Rickettsial Diseases, Centers for Disease Control, Atlanta, GA 30333. | Investigation of retroviral involvement in chronic fatigue syndrome. | Ciba Found Symp 1993;173:166-6; discussion 166-75 | Within the last few years significant efforts have been made to identify objective reliable diagnostic markers from individuals with chronic fatigue syndrome (CFS). We report the absence of a previously described retroviral marker (HTLV-II gag) in a blinded study of CFS cases. Even with excellent reproducible sensitivities, this marker failed in repeated attempts to distinguish cases from controls. In addition, four other retroviruses (simian T cell leukaemia virus, human spumavirus, bovine leukaemia virus and simian retrovirus) were examined for their presence in these CFS cases and found to be absent. Our findings suggest that these agents, at least as markers, are non-distinguishing for CFS and that other factors may be confounding the resolution of an aetiology to this syndrome. |
| Fucikova T, Petanova J. | Oddeleni klinicke imunologie 1. Lekarske fakulty Univerzity Karlovy, Praha. | [Chronic fatigue syndrome].[article in Czech] | Vnitr Lek 1993 Oct;39(10):995-1002 | The authors followed up for a period of 1-14 years 52 patients with CFS who met the criteria outlined by Holmes. The group comprised 10 men and 42 women. In 15% of these patients after a mean period of 5.5 years thyroiditis was diagnosed. Complete recovery was recorded in 20%, improvement in 32% of the patients, on average after 7 years. In the course of treatment mainly immunomodulating preparations were used. Indication of these drugs was individual based on immunological examinations. The success was only partial. The clinical condition of the patients did not correlate with serological findings of IgM, IgA and IgG antibodies against VCA nor with antibodies against EA of the EBV virus. |
| Gibson H, Carroll N, Clague JE, Edwards RH. | Department of Medicine, University of Liverpool, UK. | Exercise performance and fatigability in patients with chronic fatigue syndrome. | J Neurol Neurosurg Psychiatry 1993 Sep;56(9):993-8 comment in: J Neurol Neurosurg Psychiatry. 1994 May;57(5):662-3 | To examine the role of delay in recovery of peripheral muscle function following exercise in the fatigue experienced by patients with the chronic fatigue syndrome (CFS) and to examine the influence of effort perception in limiting exercise performance in these patients, a study was carried out on a group of twelve patients with chronic fatigue syndrome and 12 sex and age-matched sedentary control subjects. Symptom limited incremental cycle exercise tests including measurements of perceived exertion were performed followed by examination of the contractile properties of the quadriceps muscle group for up to 48 hours. Muscle function was assessed by percutaneous electrical stimulation and maximum voluntary contractions. Muscle function at rest and during recovery was normal in CFS patients as assessed by maximum isometric voluntary contraction, 20:50 Hz tetanic force ratio and |

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| | | | | maximum relaxation rate. Exercise duration and the relationship between heart rate and work rate during exercise were similar in both groups. CFS patients had higher perceived exertion scores in relation to heart rate during exercise representing a reduced effort sensation threshold of 3.2 units on an unmodified Borg scale in CFS patients. Patients with chronic fatigue syndrome show normal muscle physiology before and after exercise. Raised perceived exertion scores during exercise suggest that central factors are limiting exercise capacity in these patients. |
| Goldenberg DL. | Newton-Wellesley Hospital, Massachusetts. | Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome. | Curr Opin Rheumatol 1993 Mar;5(2):199-208 | Operational diagnostic criteria for fibromyalgia were applied to most clinical studies during the past year. Similar diagnostic criteria for chronic fatigue syndrome are being revised, but criteria for myofascial pain have not been agreed on or tested. Intense research efforts focused on the role of neurohormones and the hypothalamic-pituitary-adrenal axis in fibromyalgia and chronic fatigue syndrome over the past year. |
| Goodnick PJ, Sandoval R. | Department of Psychiatry, University of Miami, FL 33136. | Psychotropic treatment of chronic fatigue syndrome and related disorders. | J Clin Psychiatry 1993 Jan;54(1):13-20 | BACKGROUND: Chronic fatigue syndrome (CFS) and fibromyalgia frequently are associated with symptoms of major depression. For this reason, antidepressants have been used in treatment of these disorders; however, little direction has been provided into this application in psychopharmacology. METHOD: First, nine studies were reviewed regarding the relationship of the symptoms of fatigue and depression. Next, 23 reports (12 double-blind studies, 7 open studies, and 4 case reports) were reviewed for the effectiveness of therapy as assessed by global response and improvement of both depression and pain. Studies were differentiated by type of controls, as well as by alleged mechanism of action of the pharmacologic agent. RESULTS: Disturbances in brain neurochemistry shared by CFS and major depression may serve as a basis for the effectiveness of some antidepressants in CFS. Response to some antidepressants in patients with CFS or fibromyalgia may occur at doses lower than those used in major depression, e.g., amitriptyline 25-75 mg/day. We further found that the more serotonergic treatments (e.g., clomipramine) were more successful in alleviating pain than depression, whereas catecholaminergic agents (e.g., maprotiline, bupropion) seemed particularly effective for symptoms of associated depression. CONCLUSION: To maximize response of the physiologic and psychological consequences of the disorder, more investigation is needed to replicate the apparent findings that relate the neurochemical impairment underlying CFS and fibromyalgia to the type of antidepressant mechanism. |
| Grafman J, Schwartz V, Dale JK, Scheffers M, Houser C, Straus SE. | Cognitive Neuroscience Section, NINDS, NIH, Bethesda, MD 20892. | Analysis of neuropsychological functioning in patients with chronic fatigue syndrome. | J Neurol Neurosurg Psychiatry 1993 Jun;56(6):684-9 | Memory impairment dominates the cognitive complaints of patients with chronic fatigue syndrome (CFS). Twenty CFS patients were available for studies with a clinical and experimental battery composed of memory and cognitive tests. The results on objective testing indicated that the CFS patients had some mild memory impairment, but only on tasks requiring conceptually driven encoding and retrieval processes. There were no associations between the nature of the precipitating illness, self ratings of fatigue, physical findings, or laboratory determination and objective memory performance or self report of memory functioning. These generally negative results indicate that memory impairment in CFS patients is typically mild and involves memory processes that participate in conceptualising information. |
| Gunn WJ, Connell DB, Randall B. | Division of Viral and Rickettsial Diseases, Centers for Disease Control, Atlanta, GA 30333. | Epidemiology of chronic fatigue syndrome: the Centers for Disease Control Study. | Ciba Found Symp 1993;173:83-93; discussion 93-101 | The US Centers for Disease Control initiated physician-based chronic fatigue syndrome (CFS) surveillance systems in four cities in September 1989 to determine the prevalence, incidence, course and impact of the illness. The participating physicians have referred to our surveillance system 590 patients who were ill during the first two years of surveillance with severe, debilitating, unexplained fatigue for at least the preceding six months. Referred patients were screened for psychiatric disorders preceding, concurrent with, and subsequent to the onset of their fatigue by specially trained nurses using a modified Diagnostic Interview Schedule. Complete health histories were obtained by interview and review of medical records and a basic panel of standard laboratory diagnostic tests were conducted. Four physicians have independently reviewed the health information of 337 of the patients for classification. Approximately 26% of patients referred to the surveillance system met the CFS case definition in all regards, 14% lacked one or more of the required eight symptom criteria, 15% were judged to have another possible or known medical illness which could account for the severe fatigue, and the remaining 45% did not meet the case definition because of histories of psychiatric disorders preceding the onset of fatigue. Minimum prevalence rates for the period 1 September 1989 to 1 September 1991 ranged from 2.0 to 7.3 per 100,000 of the general population across the four study |

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| | | | | sites and rates based on prorated data ranged from 4.6 to 11.3 per 100,000. More than 80% of the CFS cases were female, most were white, and their average age at onset was approximately 30 years. |
| Hashimoto N. | Third Department of Internal Medicine, Jikei University, School of Medicine. Review, Multicase | [Chronic fatigue syndrome].[article in Japanese] | Nippon Rinsho 1993 Jan;51 Suppl:1107-14 | |
| Heuft L, Bravenboer B, Ziekenhuis C. | | Functional hypoglycaemia postulated as cause of chronic fatigue syndrome. | BMJ 1993 Sep 18;307(6906):735 comment on: BMJ. 1993 Jun 12;306(6892):1557-8 | |
| Honda M, Kitamura K, Nakasone T, Fukushima Y, Matsuda S, Nishioka K, Matsuda J, Hashimoto N, Yamazaki S. | Laboratory of Immunology, National Institute of Health, Tokyo, Japan. | Japanese patients with chronic fatigue syndrome are negative for known retrovirus infections. | Microbiol Immunol 1993;37(10):779-84 | Although chronic fatigue syndrome (CFS) is known to be the syndrome that begins with an acute flu-like illness that may be due to the exposure to an infectious agent, there has been no convincing evidence on the causative agents. Recently, human T-lymphotropic virus type II (HTLV-II)-like virus has been reported to be associated with the CFS by using HTLV Western blot analysis and polymerase chain reaction. However, some investigators could not detect HTLV-II by indirect immunofluorescence analysis. Lately, CFS patients have been reported in Japan. We detected all 30 tested patients with CFS were seronegative for HTLV-II, HTLV-I and HIV by specific peptide ELISA and Western blot. Further, PCR analysis was negative for HTLV-II and retrovirus was not detected by coculture method with patients' PBMC. Thus, known human retrovirus infections do not cause a CFS in Japan. |
| Izquierdo Clemente C, Ibanez Estella JA, Sanchez Ibanez A, Rubio Montanes ML, Malumbres Juarros P. | | [Chronic fatigue syndrome. Diagnostic strategy in primary care].[article in Spanish] | An Med Interna 1993 Dec;10(12):622-3 | |
| Jacobson W, Saich T, Borysiewicz LK, Behan WM, Behan PO, Wreghitt TG. | University Department of Paediatrics, Addenbrooke's Hospital, Cambridge, UK. | Serum folate and chronic fatigue syndrome. | Neurology 1993 Dec;43(12):2645-7 comment in: Neurology. 1994 Nov;44(11):2214-5 | We assayed serum folate levels of 60 patients with chronic fatigue syndrome (CFS) and found that 50% had values below 3.0 micrograms/l. Some patients with CFS are deficient in folic acid. |
| James DG. | | Complications of sarcoidosis. Chronic fatigue syndrome. | Sarcoidosis 1993 Mar;10(1):1-3 comment in: Sarcoidosis. 1993 Sep;10(2):138 | Well-recognised complications are pulmonary fibrosis, cor pulmonale, glaucoma, cataract and nephrocalcinosis causing failure of lungs, heart, vision and kidneys. Less well-recognised is the post-sarcoidosis chronic fatigue syndrome. The afflicted join sarcoidosis patients' associations because of their profound symptoms of myalgia, fatigue, sleep reversal and low-spiritedness. The symptoms are out of proportion to the lack of physical signs and the absence of objective evidence of sarcoidosis. Management includes unremitting sympathy and replenishment of essential neurochemicals. |
| Jason LA, Taylor SL, Johnson S, Goldston SE, Salina D, Bishop P, Wagner L. | Department of Psychology, DePaul University, Chicago, IL 60614. | Prevalence of chronic fatigue syndrome-related symptoms among nurses. | Eval Health Prof 1993 Dec;16(4):385-99 | Chronic Fatigue Syndrome is an illness that is characterized by debilitating fatigue and a group of other related symptoms. Few epidemiological studies have been conducted, and none have focused on a nursing population. The present study is the first to assess the prevalence of Chronic Fatigue Syndrome-related symptoms in a sample of nurses. Demographic characteristics, symptoms, and possible prevalence rates are presented and discussed. When using both narrow and more inclusive criteria to define this symptom complex, higher rates of this disorder were found than in previous epidemiological studies. The implications of these findings are discussed. |
| Kent-Braun JA, Sharma KR, Weiner MW, Massie B, Miller RG. | Department of Neurology, University of California, San Francisco. | Central basis of muscle fatigue in chronic fatigue syndrome. | Neurology 1993 Jan;43(1):125-31 comment in: Neurology. 1993 Sep;43(9):1866-7 | We studied whether muscle fatigue, metabolism, or activation are abnormal in the chronic fatigue syndrome (CFS). Subjects performed both an intermittent submaximal and a sustained maximal voluntary isometric exercise protocol of the tibialis anterior muscle. The extent of fatigue, metabolic response, and changes in both M-wave amplitude and twitch tension during exercise were similar in patients and controls. The response to systemic exercise was also normal in the patients. However, voluntary activation of the tibialis was significantly lower in the patients during maximal sustained exercise. The results indicate that patients with CFS have (1) normal fatigability and metabolism at both the intracellular and systemic levels, (2) normal muscle membrane function and excitation-contraction coupling, and (3) an inability to fully activate skeletal muscle during intense, sustained exercise. This failure of activation was well in excess of that found in controls, suggesting an important |

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| | | | | central component of muscle fatigue in CFS. |
| Khan AS, Heneine WM, Chapman LE, Gary HE Jr, Woods TC, Folks TM, Schonberger LB. | Centers for Disease Control and Prevention, Atlanta, Georgia. | Assessment of a retrovirus sequence and other possible risk factors for the chronic fatigue syndrome in adults. | Ann Intern Med 1993 Feb 15;118(4):241-5 | OBJECTIVE: To assess whether the human T-lymphotropic virus type II (HTLV-II) gag gene sequence, a purportedly new laboratory marker of the chronic fatigue syndrome (CFS), and other possible risk factors for CFS, particularly those associated with retroviral transmission, are associated with well-characterized CFS. DESIGN: Two matched case-control studies. SETTING: The metropolitan Atlanta area. PATIENTS: Twenty-one patients with CFS who were identified by the Centers for Disease Control and Prevention CFS surveillance system; 21 CDC employee controls (laboratory study) and 42 neighborhood controls (risk-factor study) who were matched to patients by age, race, and gender. MEASUREMENTS: Peripheral blood lymphocytes and leukocytes were assayed for the HTLV-II gag gene sequence by polymerase chain reaction and specific Southern blot hybridization. Questionnaires elicited demographic and clinical information and a history of exposures associated with retrovirus transmission (for example, blood transfusions, sexual practices, intravenous drug use). RESULTS: All patients were white and 86% were female. The median age at illness onset was 34 years (range, 16 to 51 years). The HTLV-II gag gene sequence was not identified in the blood of any patient or control under conditions in which the appropriate assay controls were positive. No statistical differences were observed between patients and controls in frequency of blood transfusions (10% compared with 7%), median number of sex partners before illness (3 compared with 3), bisexual or homosexual behavior (14% compared with 7%), intravenous drug use (0% compared with 0%), and other factors associated with retroviral infection. CONCLUSIONS: The HTLV-II gag gene sequence was not a marker for CFS in this small study of well-defined patients, nor did other characteristics of the patients and controls support the hypothesis that a retrovirus, transmitted by usual modes, was a cause of CFS. |
| Kiener S. | Departement Innere Medizin, Universitätspoliklinik Basel. | [A case from practice (279). 1. Chronic fatigue syndrome (CFS). 2. Psychosocial problems]. [article in German] | Schweiz Rundsch Med Prax 1993 Oct 12;82(41):1142-3 | |
| Kilburn KH. | | Symptoms, syndrome, and semantics: multiple chemical sensitivity and chronic fatigue syndrome. | Arch Environ Health 1993 Sep-Oct;48(5):368-9 | |
| Kitani T. | | [Chronic fatigue syndrome]. [article in Japanese] | Nippon Naika Gakkai Zasshi 1993 Sep 10;82(9):1571-6 | |
| Komaroff AL, Bell DS, Cheney PR, Lo SC. | | Absence of antibody to Mycoplasma fermentans in patients with chronic fatigue syndrome. | Clin Infect Dis 1993 Dec;17(6):1074-5 | |
| Komaroff AL. | Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115. | Clinical presentation of chronic fatigue syndrome. | Ciba Found Symp 1993;173:43-54; discussion 54-61 | Chronic fatigue syndrome (CFS) is a chronic illness of uncertain aetiology characterized by at least six months of debilitating fatigue and associated symptoms. The symptoms of the syndrome are all non-specific and some (but not all) are also seen in psychiatric illness. The symptomatology suggesting an organic component to the illness includes its abrupt onset with an 'infectious-like' illness, intermittent unexplained fevers, arthralgias and 'gelling' (stiffness), sore throats, cough, photophobia, night sweats, and post-exertional malaise with systemic symptoms. The illness can last for years and is associated with marked impairment of functional health status. |
| Krupp LB, Jandorf L, Coyle PK, Mendelson WB. | Dept of Neurology, State University of New York, Stony Brook 11794-8121. | Sleep disturbance in chronic fatigue syndrome. | J Psychosom Res 1993 May;37(4):325-31 | Sleep and fatigue characteristics were evaluated in 72 patients who met major criteria for the chronic fatigue syndrome (CFS), 57 multiple sclerosis (MS) patients preselected for fatigue complaints, and 40 healthy controls. Using previously validated rating scales, CFS patients had significant elevations in fatigue and sleep disturbance compared to the MS and healthy control groups. To confirm these subjective measures, polysomnography was carried out in a subgroup of CFS patients who included sleep disturbance as one of their symptoms on initial clinical interview. In 10 of 16 (62.5%) polysomnography revealed clinically significant and potentially treatable sleep abnormalities. Their sleep disorders included periodic movement disorder (4), excessive daytime sleepiness (3), apnea (2), |

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| | | | | and narcolepsy (1). We conclude that subjective sleep disturbance is common in CFS and some CFS patients may have objective sleep disorders. |
| Langsjoen PH, Langsjoen PH, Folkers K. | | Isolated diastolic dysfunction of the myocardium and its response to CoQ10 treatment. | Clin Investig 1993;71(8 Suppl):S140-4 | Symptoms of fatigue and activity impairment, atypical precordial pain, and cardiac arrhythmia frequently precede by years the development of congestive heart failure. Of 115 patients with these symptoms, 60 were diagnosed as having hypertensive cardiovascular disease, 27 mitral valve prolapse syndrome, and 28 chronic fatigue syndrome. These symptoms are common with diastolic dysfunction, and diastolic function is energy dependent. All patients had blood pressure, clinical status, coenzyme Q10 (CoQ10) blood levels and echocardiographic measurement of diastolic function, systolic function, and myocardial thickness recorded before and after CoQ10 replacement. At control, 63 patients were functional class III and 54 class II; all showed diastolic dysfunction; the mean CoQ10 blood level was 0.855 micrograms/ml; 65%, 15%, and 7% showed significant myocardial hypertrophy, and 87%, 30%, and 11% had elevated blood pressure readings in hypertensive disease, mitral valve prolapse and chronic fatigue syndrome respectively. Except for higher blood pressure levels and more myocardial thickening in the hypertensive patients, there was little difference between the three groups. CoQ10 administration resulted in improvement in all; reduction in high blood pressure in 80%, and improvement in diastolic function in all patients with follow-up echocardiograms to date; a reduction in myocardial thickness in 53% of hypertensives and 36% of the combined prolapse and fatigue syndrome groups; and a reduced fractional shortening in those high at control and an increase in those initially low. (ABSTRACT TRUNCATED AT 250 WORDS) |
| Lerner AM, Lawrie C, Dworkin HS. | Wayne State University School of Medicine, Royal Oak, Mich. | Repetitively negative changing T waves at 24-h electrocardiographic monitors in patients with the chronic fatigue syndrome. Left ventricular dysfunction in a cohort. | Chest 1993 Nov;104(5):1417-21 | This study surveys the occurrence of repetitively negative to flat T waves, alternating with normal upright T waves in 24-h electrocardiographic recordings from a subspecialty infectious diseases outpatient practice during the years 1982 to 1990. Patients with normal resting electrocardiogram in the assayed leads, but with repetitively inverted to isoelectric abnormal T waves at Holter monitors, were considered to have abnormal readings. A total of 300 patients had undergone a 24-h Holter monitor. This group included 24 individuals with chronic fatigue syndrome (CFS). This population was restricted to individuals 50 years old or younger, and the patients with CFS are compared with the patients without CFS. One of the more striking differences between the two groups was the difference in abnormal Holter readings. The patients with CFS all had abnormal Holter readings, while 22.4 percent patients without CFS had abnormal readings ($p < 0.01$). We further report the occurrence of mild left ventricular dysfunction in 8 of 60 patients in continuing studies of this population with CFS, younger than 50 years old, and with no risk factors for coronary artery disease. All 60 patients with CFS showed repetitively flat to inverted T waves alternating with normal T waves. Stress multiple gated acquisitions (MUGAs) (labeled erythrocytes with stannous pyrophosphate) were abnormal in eight patients with CFS. Although resting ejection fractions (EFs) were normal (mean, 60 percent), with increasing work loads (Kilopon meters [Kpms]), gross left ventricular dysfunction occurred. The fatigue of patients with CFS may be related to subtle cardiac dysfunction occurring at work loads common to ordinary living. |
| Levine PH, Komaroff AL. | | Human herpesvirus type 6 and chronic fatigue syndrome. | Arch Intern Med 1993 Mar 8;153(5):661 comment on: Arch Intern Med. 1992 Aug;152(8):1611-6 | |
| Lloyd AR, Hickie I, Brockman A, Hickie C, Wilson A, Dwyer J, Wakefield D. | Department of Immunology, Prince Henry Hospital, Sydney, Australia. | Immunologic and psychologic therapy for patients with chronic fatigue syndrome: a double-blind, placebo-controlled trial. | Am J Med 1993 Feb;94(2):197-203 comment in: Am J Med. 1994 Nov;97(5):493-4 Am J Med. 1995 Apr;98(4):419-20; discussion 421-2 Am J Med. 1995 Apr;98(4):420-1; discussion 421-2 | PURPOSE: To evaluate the potential benefit of immunologic therapy with dialyzable leukocyte extract and psychologic treatment in the form of cognitive-behavioral therapy (CBT) in patients with chronic fatigue syndrome (CFS). PATIENTS AND METHODS: Immunologic and psychologic treatments were administered to 90 adult patients who fulfilled diagnostic criteria for CFS in a double-blind, randomized, and placebo-controlled study. A four-cell trial design allowed the assessment of benefit from immunologic and psychologic treatment individually or in combination. Outcome was evaluated by measurement of global well-being (visual analogue scales), physical capacity (standardized diaries of daily activities), functional status (Karnofsky performance scale), and psychologic morbidity (Profile of Mood States questionnaire), and cell-mediated immunity was evaluated by peripheral blood T-cell subset analysis and delayed-type hypersensitivity skin testing. RESULTS: Neither dialyzable leukocyte extract nor CBT (alone or in combination) provided greater benefit than the nonspecific |

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| | | | | treatment regimens. CONCLUSIONS: In this study, patients with CFS did not demonstrate a specific response to immunologic and/or psychologic therapy. The improvement recorded in the group as a whole may reflect both nonspecific treatment effects and a propensity to remission in the natural history of this disorder. Randomized Controlled Trial |
| Lloyd AR, Wakefield D, Hickie I. | Laboratory of Molecular Immunoregulation, National Cancer Institute, Frederick, MD 21702-1201. | Immunity and the pathophysiology of chronic fatigue syndrome. | Ciba Found Symp 1993;173:176-87; discussion 187-92 | The pathophysiology of chronic fatigue syndrome (CFS) remains unknown. The syndrome often follows a recognized or presumed infection and the disorder may therefore result from a disordered immune response to a precipitating infection or antigenic challenge. Abnormalities of both humoral and cellular immunity have been demonstrated in a substantial proportion of patients with CFS. The most consistent findings are of impaired lymphocyte responses to mitogen and reduced natural killer cell cytotoxicity. Cutaneous anergy and immunoglobulin G subclass deficiencies have also been found. Further studies are needed examining cytokine levels in serum and cerebrospinal fluid, and cytokine production in vitro in patients with CFS. Interpretation of the findings of published studies of immunity is limited by probable heterogeneity in the patient groups studied, and by the lack of standardization and reproducibility in the assays used. The pattern of abnormalities reported in immunological testing in patients with CFS is consistent with the changes seen during the resolving phases of acute viral infection. These data provide circumstantial support for the hypothesis that CFS results from a disordered immune response to an infection. Longitudinal studies of immunity in patients developing CFS after defined infectious illnesses will provide the best means of further examining this hypothesis. |
| Lusso P, Malnati MS, Garzino-Demo A, Crowley RW, Long EO, Gallo RC. | Laboratory of Tumor Cell Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892. | Infection of natural killer cells by human herpesvirus 6. | Nature 1993 Apr 1;362(6419):458-62 | Natural killer (NK) cells are a functionally defined subset of non-T, non-B lymphocytes of bone marrow origin, which induce lysis of selected target cells, including neoplastic and virus-infected cells. The NK cell function provides an important mechanism of primary defence against viruses in vivo, as demonstrated by the occurrence of multiple herpesvirus infections in patients congenitally lacking NK cells. Here we show that functionally competent CD3- NK clones can be productively infected by human herpesvirus 6 (HHV-6), a T-lymphotropic DNA virus that may play a role in the acquired immunodeficiency syndrome (AIDS) and in the chronic fatigue syndrome, two disorders associated with a defective NK cell activity. The infection is cytopathic and induces de novo expression of CD4, an antigen not expressed within the NK lineage, thereby predisposing NK cells to infection by human immunodeficiency virus type 1 (HIV-1). These results provide evidence that a herpesvirus can directly target and kill NK cells, a potential strategy to suppress the natural anti-viral immunity of the host. |
| Macintyre A, Hume MC. | | The chronic fatigue syndrome. | Postgrad Med J 1993 Feb;69(808):164 | |
| Manu P, Lane TJ, Matthews DA. | Department of Medicine, University of Connecticut School of Medicine, University of Connecticut Health Center, Farmington 06032. | Chronic fatigue and chronic fatigue syndrome: clinical epidemiology and aetiological classification. | Ciba Found Symp 1993;173:23-31; discussion 31-42 | To determine the medical and psychiatric diagnoses that have an aetiological role in chronic fatigue we conducted a prospective study of 405 (65% women) patients who presented for evaluation with this chief complaint to an academic medical centre. The average age was 38.1 years and the average duration of fatigue at entry in the study was 6.9 years. All patients were given comprehensive physical and laboratory evaluations and were administered a highly structured psychiatric interview. Psychiatric diagnoses explaining the chronic fatigue were identified in 74% of patients and physical disorders were diagnosed in 7% of patients. The most common psychiatric conditions in this series were major depression, diagnosed in 58% of patients, panic disorder, diagnosed in 14% of patients, and somatization disorder, diagnosed in 10% of patients. Primary sleep disorders, diagnosed in 2% patients, and chronic infections, confirmed in 1.6% patients, explained the majority of cases whose chronic fatigue was attributed to a physical disorder. Thirty per cent of patients met the criteria used to define the chronic fatigue syndrome (CFS). Compared with age- and gender-matched control subjects with chronic fatigue, CFS patients had a similarly high prevalence of current psychiatric disorders (78% versus 82%), but were significantly more likely to have somatization disorder (28% versus 5%) and to attribute their illness to a viral infection (70% versus 33%). We conclude that most patients with a chief complaint of chronic fatigue, including those exhibiting the features of CFS, suffer from standard mood, anxiety and/or somatoform disorders. Careful research is still needed to determine whether CFS is a distinct entity or a variant of these psychiatric illness. |
| Matsunaga K. | 1st Department of Internal Medicine, Urafune Hospital | [The "anti-Ki" syndrome: major clinical features]. [article | Rinsho Byori 1993 Aug;41(8):882-7 | OBJECTIVE. To describe the major clinical features of patients with high titers of anti-Ki antibodies. METHOD AND RESULTS. Four of 172 patients with connective tissue diseases showed high titers (> |

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| | Yokohama City University School of Medicine. | in Japanese] | | 1/256) of anti-Ki antibodies. In these four patients, (1) the common clinical findings were alopecia, disabling chronic fatigue, muscle weakness, tenosynovitis, dry mouth, and abnormal glucose tolerance test; (2) anti-Ki antibodies were positive not only in patients with sicca lupus, but also in those with nonsicca lupus. In this case, anti-insulin receptor antibody was positive and there was a regulatory insufficiency of the pituitary. (3) Symptoms of anti-Ki antibodies share many clinical and laboratory features of chronic fatigue syndrome and fibromyalgia, that is, they may share either a common etiologic agents or a common pathogenetic pathway or both. CONCLUSION. "Anti-Ki antibody" syndrome may be a subset of sicca lupus. |
| Mawle AC, Reyes M, Schmid DS. | Viral Exanthems and Herpes Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333. | Is chronic fatigue syndrome an infectious disease? | Infect Agents Dis 1993 Oct;2(5):333-41 | |
| McCluskey DR. | Department of Medicine, Queen's University of Belfast, UK. | Pharmacological approaches to the therapy of chronic fatigue syndrome. | Ciba Found Symp 1993;173:280-7; discussion 287-97 | Although a variety of pharmacological agents have been used to treat patients with chronic fatigue syndrome none has been shown to effect a complete resolution of symptoms. Data obtained from a retrospective study and from an objective assessment of the aerobic work capacity of patients with this disorder suggest that the underlying pathophysiological abnormality is a disorder of sleep regulation. This results not only in profound fatigue and lethargy but also reduced sensory threshold for pain, disordered temperature regulation, cardiovascular abnormalities, disturbed higher cerebral function and mental depression. Drugs which modulate sleep, such as tricyclic antidepressants, have a limited effect in improving the symptoms that CFS patients experience. We suggest that other agents which affect central nervous system neurotransmitters, particularly serotonin, may have potential in the management of this condition and need to be evaluated in large controlled clinical trials. |
| McDonald E, David AS, Pelosi AJ, Mann AH. | Department of Epidemiology, Institute of Psychiatry, London. | Chronic fatigue in primary care attenders. | Psychol Med 1993 Nov;23(4):987-98 | From 686 patients attending primary care physicians, 77 were identified by a screening procedure as having chronic fatigue. Of these, 65 were given a comprehensive psychological, social and physical evaluation. Seventeen cases (26%) met criteria for the chronic fatigue syndrome. Forty-seven (72%) received an ICD-9 diagnosis of whom 23 had neurotic depression, with a further 5 meeting criteria for neurasthenia. Forty-nine were 'cases' as defined by the revised Clinical Interview Schedule (CIS-R), and 42 if the fatigue item was excluded. Psychiatric morbidity was more related to levels of social stresses than was severity of fatigue. The main difference between these subjects and those examined in hospital settings is that the former are less liable to attribute their symptoms to wholly physical causes, including viruses, as opposed to social or psychological factors. Identification and management of persistent fatigue in primary care may prevent the secondary disabilities seen in patients with chronic fatigue syndromes. |
| McSherry J. | Department of Family Medicine, University of Western Ontario, London. | Chronic fatigue syndrome. A fresh look at an old problem. | Can Fam Physician 1993 Feb;39:336-40 comment in: Can Fam Physician. 1993 May;39:1022-4 | Chronic fatigue syndrome (CFS), an organic disease of unexplained origin, affects about three people in 100,000. Symptoms last approximately 2 1/2 years, and most CFS patients return to normal health. Diagnosis of CFS is by exclusion. No single remedy has yet proven consistently beneficial. Family physicians can help by providing medical validation of disability to persons who might otherwise be seen as malingerers. |
| Mechanic D. | Institute for Health, Health Care Policy and Aging Research, Rutgers University, New Brunswick, NJ 08903. | Chronic fatigue syndrome and the treatment process. | Ciba Found Symp 1993;173:318-27; discussion 327-41 | Fatigue is a common complaint in general practice and is often associated with psychiatric and psychosocial problems and demoralization. Although the Centers for Disease Control definition of chronic fatigue syndrome (CFS) excludes pre-existing psychiatric illness, common psychosocial problems short of a clinical disorder (such as irritability, difficulty in thinking, inability to concentrate, depression and sleep disturbance) overlap with the criteria for CFS. Psychological states can affect the course of CFS or become confused in the patient's and doctor's mind with the course of infection. The core dilemma in practice is how aggressively to pursue a possible basis for CFS when it persists in the absence of an identifiable external cause. Possibilities for exploration are numerous and potentially expensive. In practice, the persistence of doctors depends on the patient's illness behaviour, on financial and organizational factors, and on the culture of medical care and practice styles. It is essential to differentiate the appropriate management of CFS from scientific study where intensive |

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| | | | | investigation may be warranted. In practice doctors should proceed in a manner that conveys concern, supports function, and avoids dysfunctional illness behaviour and inadvertent legitimization and reinforcement of disability. |
| Medizinische Universitätsklinik, Bonn. | | [The chronic fatigue syndrome].[article in German] Ewig S. | Dtsch Med Wochenschr 1993 Sep 24;118(38):1373-80 | |
| Meyers DH. | | Chronic fatigue syndrome and the medical referee. | Med J Aust 1993 Sep 20;159(6):432 comment in: Med J Aust. 1994 Jan 3;160(1):47-8 | |
| Moldofsky H. | Centre for Sleep and Chronobiology, Toronto Hospital, Canada. | Fibromyalgia, sleep disorder and chronic fatigue syndrome. | Ciba Found Symp 1993;173:262-71; discussion 272-9 | Various research studies show that the amalgam of disordered sleep physiology, chronic fatigue, diffuse myalgia, and cognitive and behavioural symptoms constitutes a non-restorative sleep syndrome that may follow a febrile illness, as in the chronic fatigue syndrome. Where rheumatic complaints are prominent such a constellation of disturbed sleep physiology and symptoms also characterizes the fibromyalgia disorder. In contrast to the chronic fatigue syndrome, fibromyalgia is associated with a variety of initiating or perpetuating factors such as psychologically distressing events, primary sleep disorders (e.g. sleep apnoea, periodic limb movement disorder) and inflammatory rheumatic disease, as well as an acute febrile illness. The chronic fatigue syndrome and fibromyalgia have similar disordered sleep physiology, namely an alpha rhythm disturbance (7.5-11 Hz) in the electroencephalogram (EEG) within non-rapid eye movement (NREM) sleep that accompanies increased nocturnal vigilance and light, unrefreshing sleep. Aspects of cytokine and cellular immune functions are shown to be related to the sleep-wake system. The evidence suggests a reciprocal relationship of the immune and sleep-wake systems. Interference either with the immune system (e.g. by a viral agent or by cytokines such as alpha-interferon or interleukin 2) or with the sleeping-waking brain system (e.g. by sleep deprivation) has effects on the other system and will be accompanied by the symptoms of the chronic fatigue syndrome. |
| Morris DH, Stare FJ. | Department of Nutrition, Harvard School of Public Health, Boston, Mass. | Unproven diet therapies in the treatment of the chronic fatigue syndrome. | Arch Fam Med 1993 Feb;2(2):181-6 | This report is a review of the unproven diet therapies recommended for individuals with chronic fatigue syndrome (CFS). Diet therapies promoted for the relief of CFS symptoms by the authors of five CSF self-help books were evaluated on the basis of nutritional adequacy and scientific rationale. Unproven diet therapies for patients with CFS include megavitamin/mineral supplements; royal jelly and other dietary supplements; and elimination, avoidance, and rotation diets. Claims that these therapies relieve CFS symptoms and promote recovery are anecdotal and have not been substantiated by clinical research. The yeast-avoidance and sugar-free diets, both promoted to combat <i>Candida albicans</i> overgrowth, are of questionable value in treating patients with CFS. The rotation diet is not balanced and does not meet the current recommended dietary intake levels. Diet strategies that call for the avoidance of food additives, preservatives, sweeteners, and other ingredients are not supported by available evidence and are not practical for patients with CFS. A diet plan for patients with CFS should be based on sound nutritional principles and common sense. Until the results of studies demonstrating the benefits of particular diet therapies in the management of CFS are available, patients with CFS are advised to eat a varied diet selected from among and within the basic food groups to ensure an adequate nutrient intake and to reach and maintain a reasonable body weight. |
| Morriss R, Sharpe M, Sharpley AL, Cowen PJ, Hawton K, Morris J. | MRC Clinical Pharmacology Unit, Littlemore Hospital, Oxford. | Abnormalities of sleep in patients with the chronic fatigue syndrome. | BMJ 1993 May 1;306(6886):1161-4 | OBJECTIVE--To determine whether patients with the chronic fatigue syndrome have abnormalities of sleep which may contribute to daytime fatigue. DESIGN--A case-control study of the sleep of patients with the chronic fatigue syndrome and that of healthy volunteers. SETTING--An infectious disease outpatient clinic and subjects' homes. SUBJECTS--12 patients who met research criteria for the chronic fatigue syndrome but not for major depressive disorder and 12 healthy controls matched for age, sex, and weight. MAIN OUTCOME MEASURES--Subjective reports of sleep from patients' diaries and measurement of sleep patterns by polysomnography. Subjects' anxiety, depression, and functional impairment were assessed by interview. RESULTS--Patients with the chronic fatigue syndrome spent more time in bed than controls (544 min v 465 min, $p < 0.001$) but slept less efficiently (90% v 96%, $p < 0.05$) and spent more time awake after initially going to sleep (31.9 min v 16.6 min, $p < 0.05$). Seven patients with the chronic fatigue syndrome had a sleep disorder (four had difficulty |

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| | | | | maintaining sleep, one had difficulty getting to sleep, one had difficulty in both initiating and maintaining sleep, and one had hypersomnia) compared with none of the controls ($p = 0.003$). Those with sleep disorders showed greater functional impairment than the remaining five patients (score on general health survey 50.4% v 70.4%, $p < 0.05$), but their psychiatric scores were not significantly different. CONCLUSIONS--Most patients with the chronic fatigue syndrome had sleep disorders, which are likely to contribute to daytime fatigue. Sleep disorders may be important in the aetiology of the syndrome. |
| Morriss R. | | Insomnia in the chronic fatigue syndrome. | BMJ 1993 Jul 24;307(6898):264 | |
| Natelson BH, Cohen JM, Brassloff I, Lee HJ. | Department of Neurosciences, UMDNJ-New Jersey Medical School, Newark 07103. | A controlled study of brain magnetic resonance imaging in patients with the chronic fatigue syndrome. | J Neurol Sci 1993 Dec 15;120(2):213-7 | Two neuroradiologists compared the brain MR scans of 52 patients with the CDC criteria for the chronic fatigue syndrome (CFS) with those of 52 age and sex matched controls who had undergone imaging because of histories of head trauma or headache. CFS patients had significantly more abnormal scans than controls--27% vs 2%. Abnormalities seen were foci of increased white matter T2 signal in 9 CFS patients and one control and ventricular or sulcal enlargement in 5 CFS patients. Follow up of patients with subcortical signal hyperintensities revealed 3 who had symptoms suggestive of other known medical causes of what appeared to be CFS. The data indicate that some CFS patients have some organic problem manifesting itself on neuroimaging. But, finding MR abnormalities should warn the physician that the patient's symptoms may be secondary to some other medical illness and not simply primary CFS. |
| Nixon PG. | Charing Cross Hospital, London. | The grey area of effort syndrome and hyperventilation: from Thomas Lewis to today. | J R Coll Physicians Lond 1993 Oct;27(4):377-83 | Lewis used the diagnosis 'effort syndrome' for subjects whose ability to make and sustain effort had been reduced by homeostatic failure. A major element was depletion of the body's capacity for buffering the acids produced by exercise. In his view this systems disorder was not to be regarded as a specific organ disease, and losing sight of the metabolic element would foster the invention of fanciful, unphysiological diagnoses. His views were dismissed because normal resting plasma bicarbonate levels were considered by others in that era to exclude serious depletion of the body's total capacity for buffering the effects of exertion. Today, effort syndrome is still a useful diagnosis for a condition of exhaustion and failure of performance associated with depletion of the body's buffering systems. Other elements associated with homeostatic failure are now recognised, principally emotional hyperarousal and hyperventilation. Their physiological interrelationships are described. Effort syndrome is amenable to recovery through rehabilitation, and it may be a mistake to treat chronic fatigue syndrome and unspecific illness without including it in the differential diagnosis. |
| Norregaard J, Bulow PM, Prescott E, Jacobsen S, Danneskiold-Samsøe B. | Department of Rheumatology C, Frederiksberg Hospital, Copenhagen, Denmark. | A four-year follow-up study in fibromyalgia. Relationship to chronic fatigue syndrome. | Scand J Rheumatol 1993;22(1):35-8 | The primary objectives of this study were to examine to what extent fibromyalgia patients later on developed presumed causative somatic diseases and to examine symptoms and muscle strength some years after the diagnosis of fibromyalgia was established. A secondary objective was to describe the overlap between fibromyalgia and chronic fatigue syndrome. Only in two of 91 the muscle pain was found to be caused by another somatic disease during the median 4 year follow-up period. In one of the 83 attending subjects a somatic disease associated with muscle symptoms was established at the follow-up visit. 60 out of 83 reported increased pain, 8 reported improvement of pain. The 83 subjects showed no significant fall in muscle strength during the follow-up period. The majority reported severe fatigue but only one fifth fulfilled the proposed chronic fatigue syndrome criteria. |
| Pepper CM, Krupp LB, Friedberg F, Doscher C, Coyle PK. | Department of Psychology, State University of New York, Stony Brook 11794. | A comparison of neuropsychiatric characteristics in chronic fatigue syndrome, multiple sclerosis, and major depression. | J Neuropsychiatry Clin Neurosci 1993 Spring;5(2):200-5 | Chronic fatigue syndrome (CFS), a controversial clinical entity characterized by severe fatigue and constitutional symptoms, has been associated with a variety of psychiatric disorders. To further understand the psychiatric profile of CFS, the authors compared patients with CFS, multiple sclerosis (MS), and major depression by using diagnostic interviews and self-report measures of Axis I disorders and personality disorders. CFS patients differed from patients with major depression, with significantly less depression and fewer personality disorders. Compared with MS patients, CFS patients did not differ with regard to personality disorders. However, they did have significantly more frequent current depression than MS patients, particularly following onset of their illness. |
| Ray C, Phillips L, Weir WR. | Department of Human Sciences, Brunel University, Uxbridge, Middlesex, UK. | Quality of attention in chronic fatigue syndrome: subjective reports of everyday attention | Br J Clin Psychol 1993 Sep;32 (Pt 3):357-64 | Patients with chronic fatigue syndrome (also known as post-viral fatigue syndrome or myalgic encephalomyelitis) commonly report cognitive difficulties concerning attention, concentration and memory. In this study, patients were compared with matched controls on two questionnaires which |

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| | | and cognitive difficulty, and performance on tasks of focused attention. | | assess subjective difficulties with attention and general cognitive functioning, and on two tasks requiring focused attention. Patients reported significantly greater difficulty with attention on the Everyday Attention Questionnaire and more cognitive symptoms on the Profile of Fatigue-Related Symptoms. The objective tests did not clearly indicate a deficit in patients' focused attention; patients tended to perform less well on the Embedded Figures Test and the Stroop Colour-Word Interference Test, but these differences were not significant. There was, however, evidence of psychomotor retardation, with patients having longer response times for word reading and colour naming in the Stroop test. Difficulties in interpreting findings for both subjective and objective cognitive measures are discussed. |
| Ray C, Weir W, Stewart D, Miller P, Hyde G. | Department of Human Sciences, Brunel University, Uxbridge, Middlesex, U.K. | Ways of coping with chronic fatigue syndrome: development of an illness management questionnaire. | Soc Sci Med 1993 Aug;37(3):385-91 | Chronic fatigue syndrome (CFS) is a disorder of uncertain aetiology, and there is uncertainty also about the appropriate way in which patients should manage the illness. An illness management questionnaire (IMQ) was designed to assess coping in CFS. This was completed by 207 patients, in parallel with the COPE scales (a general measure of coping that can be applied situationally), and measures of functional impairment, anxiety and depression. The IMQ yielded four factors: maintaining activity, accommodating to the illness, focusing on symptoms and information-seeking. Scales based upon these factors together predicted 26, 27 and 22% of the variance in functional impairment, anxiety and depression, respectively, and each scale had significant relationships with relevant scales of the COPE, supporting the interpretation of the factors. It is suggested that the IMQ may be employed to relate ways of coping to outcomes in CFS, and to assess coping as a mediator of change in cognitive-behavioural interventions. |
| Robin R, Lipkin DM, Hume GW. | | Taking exception to chronic fatigue syndrome prevalence findings by Price, et al. | Public Health Rep 1993 Jan-Feb;108(1):135-7 comment on: Public Health Rep. 1992 Sep-Oct;107(5):514-22 | |
| Sharpe M. | University of Oxford Department of Psychiatry, Warneford Hospital, UK. | Non-pharmacological approaches to treatment. | Ciba Found Symp 1993;173:298-308; discussion 308-17 | Chronic fatigue syndrome (CFS) as currently defined overlaps with other syndromes including chronic pain, fibromyalgia, anxiety and depression. It also resembles historical descriptions of neurasthenia. The role of psychological (cognitive) and behavioural therapies in CFS is examined. There are both pragmatic and theoretical arguments for their application to CFS. It is pragmatic to target obvious and treatable factors including inactivity and depression. A theoretical model in which psychological, physiological and social factors interact offers a plausible rationale for such treatment but is not yet empirically proven. While there is evidence for the efficacy of this type of therapy in related syndromes, the evidence in CFS is inconclusive. A randomized controlled trial of combined cognitive and behavioural therapy currently in progress is described. Initial results suggest that most patients receiving cognitive behaviour therapy improve, especially in terms of functional impairment. It remains to be seen whether this therapy will prove to be more effective than standard general practitioner care. In the meantime cognitive behaviour therapy offers a pragmatic and rational therapy for patients with CFS. Randomized Controlled Trial Review Review, Tutorial |
| Shaw T. | | Chronic fatigue syndrome. | Aust Fam Physician 1993 Apr;22(4):635 comment on: Aust Fam Physician. 1992 Mar;21(3):278-9, 283-5 | |
| Shorter E. | History of Medicine Program, Faculty of Medicine, University of Toronto, Ontario, Canada. | Chronic fatigue in historical perspective. | Ciba Found Symp 1993;173:6-16; discussion 16-22 | Chronic fatigue as a presenting complaint, in the absence of other evident organic illness, was seldom reported historically before the second half of the 19th century. Its first eruption was the so-called 'bed cases' or 'sofa cases' among middle-class females in the period from 1860 to about 1910. 'Neurasthenia' does not necessarily represent an early forerunner of chronic fatigue. Many patients receiving that diagnosis did not complain of fatigue. Others with functional fatigue did not receive the diagnosis 'neurasthenia'. Both medical-anecdotal and quantitative sources make it clear that by the time of the First World War, chronic fatigue was a common complaint in Europe and North America. Medical concepts of chronic fatigue since the 1930s have run along four separate lines: (1) 'postinfectious neuromyasthenia', going back to an atypical 'poliomyelitis' epidemic in 1934; (2) 'chronic Epstein-Barr virus' infection, an illness attribution that increased in frequency after the discovery in 1968 that this virus caused mononucleosis; (3) 'myalgic encephalomyelitis', dating from an epidemic at the Royal |

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| | | | | Free Hospital in London in 1955; and (4) 'fibrositis', or 'fibromyalgia', used as a rheumatological description since the turn of the century. Recently, these four separate paths have tended to converge into the diagnosis of 'chronic fatigue syndrome'. |
| Simpson LO. | | Chronic fatigue syndrome. | N Z Med J 1993 May 26;106(956):211-2 | |
| Smith AP, Behan PO, Bell W, Millar K, Bakheit M. | Health Psychology Research Unit, School of Psychology, University of Wales College of Cardiff. | Behavioural problems associated with the chronic fatigue syndrome. | Br J Psychol 1993 Aug;84 (Pt 3):411-23 | Disturbances of memory, concentration and motor function are often reported by patients with the chronic fatigue syndrome (CFS). The present study objectively evaluated these behavioural problems using a computerized test battery measuring memory, attention and motor skills. Fifty-seven CFS patients were compared with 19 matched controls and all subjects completed the performance test battery and filled in questionnaires measuring psychopathology and mood. The patients reported significantly higher levels of depression, anxiety, physical symptoms and cognitive failures than the controls. Similarly, they reported more negative affect at the time of testing. The patients were slower on psychomotor tasks, showed increased visual sensitivity and impaired attention. Digit span and free recall were not impaired but retrieval from semantic memory and logical reasoning were slower. None of the performance differences between patients and controls could be attributed to differences in psychopathology. These results agree with recent findings from other laboratories, and it is now time to consider the nature of the neurological dysfunction underlying these effects. |
| Smith RD, Scott A. | | The economic impact of chronic fatigue syndrome. | Med J Aust 1993 Feb 15;158(4):286-7 comment on: Med J Aust. 1992 Nov 2;157(9):599-601 | |
| Steere AC, Taylor E, McHugh GL, Logigian EL. | Division of Rheumatology/Immunology, New England Medical Center, Boston, MA 02111. | The overdiagnosis of Lyme disease. | JAMA 1993 Apr 14;269(14):1812-6 comment in: JAMA. 1993 Dec 8;270(22):2682-3 JAMA. 1993 Dec 8;270(22):2682; discussion 2683 JAMA. 1993 Dec 8;270(22):2683 | OBJECTIVE--To analyze the diagnoses, serological test results, and treatment results of the patients evaluated in a Lyme disease clinic, both prior to referral and from current evaluation. DESIGN--Retrospective case survey of prescreened patients. SETTING--Research and diagnostic Lyme disease clinic in a university hospital. PATIENTS--All 788 patients referred to the clinic during a 4.5-year period who were thought by the referring physician or the patient to have a diagnosis of Lyme disease. MAIN OUTCOME MEASUREMENTS--Symptoms and signs of disease, immunodiagnostic tests of Lyme disease, and tests of neurological function. RESULTS--Of the 788 patients, 180 (23%) had active Lyme disease, usually arthritis, encephalopathy, or polyneuropathy. One hundred fifty-six patients (20%) had previous Lyme disease and another current illness, most commonly chronic fatigue syndrome or fibromyalgia; and in 49 patients, these symptoms began soon after objective manifestations of Lyme disease. The remaining 452 patients (57%) did not have Lyme disease. The majority of these patients also had the chronic fatigue syndrome or fibromyalgia; the others usually had rheumatic or neurological diseases. Of the patients who did not have Lyme disease, 45% had had positive serological test results for Lyme disease in other laboratories, but all were seronegative in our laboratory. Prior to referral, 409 of the 788 patients had been treated with antibiotic therapy. In 322 (79%) of these patients, the reason for lack of response was incorrect diagnosis. CONCLUSIONS--Only a minority of the patients referred to the clinic met diagnostic criteria for Lyme disease. The most common reason for lack of response to antibiotic therapy was misdiagnosis. |
| Steere AC. | Tufts University School of Medicine, Boston. | Current understanding of Lyme disease. | Hosp Pract (Off Ed) 1993 Apr 15;28(4):37-44 | It is now the most common vector-borne disease in the United States. But because of misdiagnosis, the spread of this disease may also be more apparent than real. Lack of standardized serologic tests and varying clinical presentations do create confusion. Nevertheless, it is possible to distinguish Lyme disease from look-alike disorders, such as chronic fatigue syndrome and fibromyalgia. |
| Stern K. | | Chronic fatigue syndrome: signs and symptoms. | CDS Rev 1993 Aug;86(7):26-9 | |
| Stockdale T. | | Chronic fatigue syndrome (ME) | Nutr Health 1993;9(1):59-60 | |
| Straus SE, Fritz S, Dale JK, Gould B, Strober W. | Medical Virology Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, | Lymphocyte phenotype and function in the chronic fatigue syndrome. | J Clin Immunol 1993 Jan;13(1):30-40 | Lymphocytes of 18 patients meeting the Centers for Disease Control (CDC) case definition for the chronic fatigue syndrome (CFS), 10 similar, chronically fatigued patients not fully conforming to the CDC case definition, and 17 matched, healthy individuals were studied to determine the presence of abnormalities of peripheral cell phenotype and function. Extensive phenotypic analyses of B- and T- |

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| | Bethesda, Maryland 20892. | | | cell subsets, natural killer (NK) cells, and macrophages were performed using single-, dual-, and three-color flow cytometry. Compared to controls, in CFS patients the percentage of CD4 T cells and CD4,CD45RA, or naive T cells, was reduced. The CD4,CD45RO, or memory T-cell, subset was numerically normal but expressed increased levels of adhesion markers (CD29, CD54, and CD58). CFS patient lymphocytes showed reduced proliferative responses to phytohemagglutinin, concanavalin A, and staphylococcal enterotoxin B. Lymphocytes from fatigue patients not meeting the CDC definition showed similar abnormalities. These data indicate that peripheral T cells manifest an increased state of differentiation in CFS and related conditions. This may arise as a consequence of an underlying neuropsychiatric and/or neuroendocrine disorder or because of exposure to antigens or superantigens of an infectious agent. |
| Straus SE. | Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892. | Studies of herpesvirus infection in chronic fatigue syndrome. | Ciba Found Symp 1993;173:132-9; discussion 139-45 | The relationship of herpesviruses to chronic fatigue syndrome has received considerable attention over the past decade. Data suggesting an association fall into three major categories. First, among acute precipitants of the syndrome are primary infections with some herpesviruses, most notably Epstein-Barr virus and cytomegalovirus. Second, a series of studies have detailed elevations of antibodies to most herpesviruses in selected chronic fatigue syndrome populations, with Epstein-Barr virus and human herpes type 6 being the objects of most scrutiny. Third, one recent study reported a greater ease of recovery of human herpes virus type 6 from chronic fatigue syndrome patients. This review article critically examines the cumulative data regarding an association between one or more herpesviruses and the chronic fatigue syndrome in the context of the known biology and epidemiology of these agents. In view of these, and additional considerations regarding study methodologies, the conclusion is drawn that herpesviruses are not dominant causes of the chronic fatigue syndrome and may not even be necessary to the perpetuation of the illness, but it is premature to dismiss entirely this latter possibility. |
| Symposium proceedings | | Chronic Fatigue Syndrome. Symposium proceedings. London, 12-14 May 1992. Overall | Ciba Found Symp 1993;173:1-357 | |
| Thomas PK. Historical Article | | The chronic fatigue syndrome: what do we know? | BMJ 1993 Jun 12;306(6892):1557-8 comment in: BMJ. 1993 Jul 31;307(6899):328 BMJ. 1993 Sep 18;307(6906):735 | |
| Tirelli V, Pinto A, Marotta G, Crovato M, Quaia M, De Paoli P, Galligioni E, Santini G. | | Clinical and immunologic study of 205 patients with chronic fatigue syndrome: a case series from Italy. | Arch Intern Med 1993 Jan 11;153(1):116-7, 120 | |
| Valesini G, Conti F, Priori R, Balsano F. | | Gilbert's syndrome and chronic fatigue syndrome. | Lancet 1993 May 1;341(8853):1162-3 comment on: Lancet. 1993 Mar 27;341(8848):842 | |
| Walford GA, Nelson WM, McCluskey DR. | Department of Child and Adolescent Psychiatry, Royal Belfast Hospital for Sick Children, Northern Ireland. | Fatigue, depression, and social adjustment in chronic fatigue syndrome. | Arch Dis Child 1993 Mar;68(3):384-8 | The aims of this study were to determine the characteristics and perceived levels of fatigue and the prevalence of depression in children with chronic fatigue syndrome and to assess the effects of illness on schooling and social functioning. Twelve children with chronic fatigue syndrome were compared with a matched group of children with cystic fibrosis and matched healthy controls. Levels of fatigue (fatigue questionnaire), depression (children's depression inventory), and social adjustment (semistructured interview with parents) were compared between groups. Children with chronic fatigue syndrome had significantly higher median scores for physical and mental fatigue and depressive symptomatology than either comparison group and five children scored as depressed on the children's depression inventory. Schooling and social functioning were seriously disrupted. Children with chronic fatigue syndrome reported high levels of fatigue affecting both physical and mental functioning, the association with depression found in adult studies was confirmed, and social adjustment was poor. |

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| Ware NC. | Department of Social Medicine, Harvard Medical School, Boston, MA 02115. | Society, mind and body in chronic fatigue syndrome: an anthropological view. | Ciba Found Symp 1993;173:62-73; discussion 73-82 | An anthropological view of chronic fatigue syndrome places the study of illness in social context. Data from an interview study of 50 chronically fatigued patients demonstrate the relation of local social worlds--families, workplaces, communities--to the meaning and experience of illness. Negative life events and difficulties, multiple commitments, and a hectic pace are among prominent themes in the subjects' local worlds. These themes are reflected in: (1) attributions of illness onset to social sources, (2) the symbolism of the core complaint of fatigue, and (3) an illness-induced, positively valued lifestyle transformation suggesting the rejection of culturally prescribed 'busyness'. Dichotomous definitions of the relation of mind and body are shown to be part of culture, not Nature, in the paper's second section. The 'mind-body dichotomy' and the differing values attached to physical and psychological disorders by a naturalistic scientific paradigm explain the delegitimizing experiences of sufferers, who find their illness dismissed as psychosomatic and therefore 'not real'. A conceptualization of chronic fatigue syndrome which links local social worlds to psychological distress, felt bodily sensation and biological changes is proposed. Collaborative teams of social scientists and medical researchers might fruitfully pursue aspects of social context in relation to psychiatric, immunological and viral dimensions of the illness. |
| Weiger WA. | | Chronic fatigue syndrome. | Neurology 1993 Sep;43(9):1866-7 comment on: Neurology. 1993 Jan;43(1):125-31 | |
| Wessely S. | Department of Psychological Medicine, Institute of Psychiatry, De Crespigny Park, London, UK. | The neuropsychiatry of chronic fatigue syndrome. | Ciba Found Symp 1993;173:212-29; discussion 229-37 | This paper explores the relationship between chronic fatigue syndrome (CFS) and psychiatric disorder, with special reference to neuropsychiatry. Topics reviewed include (1) epidemiological evidence of central disorder in CFS; (2) evidence from longitudinal studies of an interaction between vulnerability to CFS and psychiatric disorder; and (3) evidence from neuroimaging, neuropsychology, neurophysiology and neuroendocrinology of disordered CNS function in CFS. The most impressive evidence of CNS disturbance comes from neuroendocrinological studies, which suggest a role of hypothalamic disorder as a final common pathway for CFS. It is concluded that the equal and opposite tendencies of psychiatry to be 'brainless' and neurology to be 'mindless' have led to needless controversy over the nature of CFS. Now that the contributions of psychiatric disorder to CFS, and of neurobiological dysfunction to psychiatric disorder, are both established, it will be possible to make real advances in understanding the nature of CFS. |
| working group | | Report of the working group on the possible relationship between hepatitis B vaccination and the chronic fatigue syndrome. | CMAJ 1993 Aug 1;149(3):314-9 | |
| working group | | Report of the working group on the possible relationship between hepatitis B vaccination and the chronic fatigue syndrome. | Can Commun Dis Rep 1993 Feb 28;19(4):25-8 | |
| Young A. | | Amma therapy: a holistic approach to chronic fatigue syndrome. | J Holist Nurs 1993 Jun;11(2):172-82 | A significant number of people suffering with chronic fatigue syndrome have become more and more discouraged by the traditional medical approach, which seems to lack the proper perspective on the disease. Unfortunately, very little published information is available about specific holistic health management practices used for these patients. It is the purpose of this article to examine a specific holistic practice, called Amma Therapy, as an alternative approach for the management of this syndrome. |