

Authors	Author Address	Title	Publication	Abstract
Abbey SE, Garfinkel PE.	Toronto Hospital, Toronto General Division, Ontario.	Chronic fatigue syndrome and the psychiatrist.	Can J Psychiatry 1990 Oct;35(7):625-33	The number of patients who are identified as having chronic fatigue syndrome (CFS) has increased, and as a result, chronic fatigue syndrome has received widespread attention. Research has demonstrated that cognitive, affective and behavioural symptoms are prominent in CFS. Psychiatrists are therefore being asked to participate in the assessment and management of patients with this syndrome. This paper will provide an overview of the clinical characteristics of CFS and the current empirical findings related to its pathology, and will conclude with a discussion of the management of these patients. Publication Types: Review Review, Tutorial
Ablashi DV, Josephs SF, Buchbinder A, Hellman K, Nakamura S, Llana T, Lusso P, Kaplan M, Dahlberg J, Memon S, et al.	Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, MD.	Human B-lymphotropic virus (human herpesvirus-6).	J Virol Methods 1988 Sep;21(1-4):29-48	Human B-lymphotropic virus (HBLV), also known as human herpesvirus-6 (HHV-6) was first isolated in 1986 from AIDS patients and patients with other lymphoproliferative disorders. HBLV is distinct from known human herpesviruses, biologically, immunologically and by molecular analysis. HBLV can infect and replicate in fresh and established lines of hemopoietic cells and cells of neural origin, suggesting wide tropism. The prevalence of HBLV antibody in the normal population was 26% though clear differences between different populations were observed. The prevalence of HBLV antibody an elevated antibody titer was higher in sera from certain malignancies, Sjogren's syndrome and sarcoidosis. Antibody to HBLV was also elevated in AIDS patients and patients with chronic fatigue syndrome. HBLV-DNA was detected in some B-cell lymphomas. The broad in vitro tropism, combined with immunological and molecular evidence of HBLV infection in individuals raise the question of the pathogenicity of this virus in some diseases. Because in vitro co-infection of CD4 cells by HBLV and HIV leads to enhanced degeneration, this raises the possibility that infection in AIDS patients by both viruses can aggravate the HIV-induced immunodeficiency. Specific reagents and immunological and molecular assays are currently being investigated, which will aid in virus detection in cells from patients, and in elucidating the possible pathogenesis of HBLV.
Ablashi DV, Lusso P, Hung CL, Salahuddin SZ, Josephs SF, Llana T, Kramarsky B, Biberfeld P, Markham PD, Gallo RC.	Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, MD 20892.	Utilization of human hematopoietic cell lines for the propagation and characterization of HBLV (human herpesvirus 6).	Int J Cancer 1988 Nov 15;42(5):787-91	Details of the productive infection of established human cell lines of diverse origin by HBLV (also designated Human Herpesvirus 6) are described in this report. The infection and replication of HBLV in several T and B lymphoid and other cell lines was observed by electron microscopic examination, by the detection of viral antigen expression by indirect immunofluorescence assay (IFA) and by the presence of HBLV DNA by Southern blot hybridization. Several of these cell lines produced large amounts of virus. For this reason and because of the absence of other human herpesviruses, these lines have provided a valuable resource for the preparation of reagents and the development of assays for the detection and characterization of HBLV. The isolation and characterization of new HBLV isolates from patients with chronic fatigue syndrome were also facilitated by using some of the cell lines reported here. The host range of HBLV in established cell lines, therefore, does not appear to be limited to the B lymphocytes, as initially suggested by in vivo studies. The infection of T and B lymphocytes, megakaryocytes and neuronal cells in vitro suggests a need for the evaluation of diverse hematological and neurological disorders to shed light on a possible HBLV involvement.
Adolphe AB.		Chronic fatigue syndrome: possible effective treatment with nifedipine.	Am J Med 1988 Dec;85(6):892	
Altay HT, Toner BB, Brooker H, Abbey SE, Salit IE, Garfinkel PE.	Department of Psychology, York University, Ontario, Canada.	The neuropsychological dimensions of postinfectious neuromyasthenia (chronic fatigue syndrome): a preliminary report.	Int J Psychiatry Med 1990;20(2):141-9	Postinfectious neuromyasthenia (PIN) is a clinical syndrome of protracted and incomplete recovery after an apparent viral-like illness. Medical investigation yields few abnormalities which might account for the symptomatology. A substantial number of PIN patients complain of cognitive changes. Specific complaints include impaired attention, concentration and abstraction skills. This study was designed to systematically investigate whether the aforementioned subjective complaints could be quantified objectively using standard neuropsychological instruments. Results indicated that on all tests but one, the subjects' performances were significantly higher than those of their age matched groups in the normative data. Specifically, PIN patients scored significantly better than their age matched norms on tests of concentration, attention and abstraction. What is most striking is the discrepancy between the subjective complaints of cognitive impairment and the objective results of the subjects' performances on all tests. These findings suggest that psychological factors may play an important role in the cognitive functioning of individuals diagnosed with postinfectious neuromyasthenia.

Anon		Immunological abnormalities in the chronic fatigue syndrome.	Med J Aust 1990 Jan 1;152(1):50-2 comment on: Med J Aust. 1989 Aug 7;151(3):122-4	
Anon		Life insurance MDs sceptical when chronic fatigue syndrome diagnosed.	CMAJ 1990 Dec 15;143(12):1283-6 comment on: Can Med Assoc J. 1990 Sep 1;143(5):413-5	
Anon		Chronic fatigue syndrome.	Br J Psychiatry 1990 Sep;157:447-50 comment on: Br J Psychiatry. 1990 Apr;156:534-40	
Anon		[Chronic infection caused by Epstein-Barr virus and chronic fatigue syndrome]. [article in Spanish]	Med Clin (Barc) 1990 Mar 3;94(8):315-6 comment on: Med Clin (Barc). 1989 Apr 29;92(16):619-22	
Anon		Acyclovir treatment of the chronic fatigue syndrome.	N Engl J Med 1989 Jul 20;321(3):187-9 Erratum in: N Engl J Med 1989 Oct 12;321(15):1057 comment on: N Engl J Med. 1988 Dec 29;319(26):1726-8	
Anon		Chronic fatigue syndrome [correction]	CMAJ 1989 Apr 15;140(8):897	
Anon		The Epstein-Barr virus and chronic fatigue syndrome.	JAMA 1989 Mar 3;261(9):1277-8 comment on: JAMA. 1988 Aug 19;260(7):971-3	
Anon		Chronic fatigue syndrome.	CMAJ 1989 Feb 15;140(4):361, 364 Erratum in: Can Med Assoc J 1989 Apr 15;140(8):897	
Anon		"The chronic fatigue syndrome".	Ann Intern Med 1988 Jul 15;109(2):166-7	
Bennett RM.	Division of Arthritis and Rheumatic Diseases, Oregon Health Sciences University, Portland 97201.	Confounding features of the fibromyalgia syndrome: a current perspective of differential diagnosis.	J Rheumatol Suppl 1989 Nov;19:58-61	Patients eventually diagnosed as having the fibromyalgia syndrome often have symptoms which suggest alternate diagnoses such as peripheral neuropathy, spondylitis, metabolic myopathy, polymyalgia, early rheumatoid arthritis, early systemic lupus erythematosus or a chronic fatigue syndrome. Delay in diagnosis of fibromyalgia often proves costly and frustrating to the patient and may lead to inappropriate therapy.
Berends GM, Peeters MF, Lepoutre JM, van Liebergen FJ, Kurstjens RM, Koolen MI.		[Chronic fatigue syndrome; is there a connection with the Epstein-Barr virus]? [article in Dutch]	Ned Tijdschr Geneesk 1988 May 7;132(19):874-8	
Bosse D, Ades EW.	Biological Products Branch, Centers for Disease Control, Atlanta, GA 30333.	Immunotherapy and enhanced antibody-dependent cell-mediated cytotoxicity using virally-infected target cells.	J Clin Lab Immunol 1989 Jul;29(3):109-10	We examined the ability of in vitro addition of Interleukin-2 (IL-2) to differentially enhance antibody-dependent cell mediated cytotoxicity (ADCC) utilizing cultured Epstein-Barr virus infected cells and gammaglobulin (Sandoglobulin). We found significant enhancement of ADCC when IL-2 was added. Chronic Epstein-Barr virus or Chronic Fatigue Syndrome patients in a therapeutic gammaglobulin program may benefit from IL-2 given in vivo.
Bradley CA.		Psychiatric diagnoses and chronic fatigue syndrome.	J Clin Psychiatry 1990 Feb;51(2):86 comment on: J Clin Psychiatry. 1989	

			Feb;50(2):53-6	
Buchwald D, Sullivan JL, Leddy S, Komaroff AL.	Department of Medicine, Brigham and Women's Hospital, Boston 02115.	"Chronic Epstein-Barr virus infection" syndrome and polymyalgia rheumatica.	J Rheumatol 1988 Mar;15(3):479-82 comment in: J Rheumatol. 1989 Mar;16(3):414-5	Twenty-three patients with polymyalgia rheumatica (PMR) followed in an academic rheumatology practice frequently reported symptoms commonly found in the recently described "chronic fatigue syndrome" or "chronic Epstein-Barr infection syndrome." These symptoms persisted for months after treatment had reduced the severity of the myalgias and lowered the sedimentation rate: periodically disabling fatigue (33%), recurrent pharyngitis (30%), sleep disorder (65%) and arthralgias (70%). However, antibody titers to Epstein-Barr virus in the patients with PMR were not significantly different from those in age and sex matched control subjects.
Camps Bansell J, Prieto Valtuena J.		[Chronic fatigue syndrome]. [article in Spanish]	An Med Interna 1990 Oct;7(10):497-9	
Cassel W, Archer-Duste H.		The new epidemic: chronic fatigue syndrome.	1631: Calif Nurse 1989 Apr;85(4):6-7	
Chao CC, Gallagher M, Phair J, Peterson PK.		Serum neopterin and interleukin-6 levels in chronic fatigue syndrome.	J Infect Dis 1990 Dec;162(6):1412-3	
Cheney PR, Dorman SE, Bell DS.		Interleukin-2 and the chronic fatigue syndrome.	Ann Intern Med 1989 Feb 15;110(4):321	
Coulter P.		Chronic fatigue syndrome: an old virus with a new diagnosis.	J Community Health Nurs 1988;5(2):87-95	
Cunningham L, Bowles NE, Lane RJ, Dubowitz V, Archard LC.	Department of Biochemistry, Charing Cross and Westminster Medical School, London, U.K.	Persistence of enteroviral RNA in chronic fatigue syndrome is associated with the abnormal production of equal amounts of positive and negative strands of enteroviral RNA.	J Gen Virol 1990 Jun;71 (Pt 6):1399-402	A subgenomic restriction fragment from cDNA prepared from Coxsackie B2 virus (CVB2) RNA was subcloned into a riboprobe vector allowing the production of enteroviral group-specific RNA probes complementary to either the positive (genomic) or negative (template) strand of enteroviral RNA. These riboprobes were used to follow productive infection of cultured cells by CVB2; as expected, positive strand RNA was synthesized in approximately 100-fold excess over negative strand. RNA was extracted from muscle biopsy samples from patients with chronic fatigue syndrome and probed for the presence of enteroviral RNA. In cases where enteroviral RNA was detected the amounts of positive and negative strands of enteroviral RNA were approximately equal, in contrast to the situation in lytic infection of cultured cells. This suggests that enterovirus persistence in muscle is due to a defect in control of viral RNA synthesis.
Dale JK, Straus SE, Ablashi DV, Salahuddin ZS, Gallo RC, Nishibe Y, Inoue YK.		The Inoue-Melnick virus, human herpesvirus type 6, and the chronic fatigue syndrome.	Ann Intern Med 1989 Jan 1;110(1):92-3	
David A, Pelosi A, McDonald E, Stephens D, Ledger D, Rathbone R, Mann A.	Section of Epidemiology and General Practice, Institute of Psychiatry, London.	Tired, weak, or in need of rest: fatigue among general practice attenders.	BMJ 1990 Nov 24;301(6762):1199-202 comment in: BMJ. 1991 Jan 19;302(6769):181 BMJ. 1991 Jan 5;302(6767):50	OBJECTIVES--To determine the prevalence and associations of symptoms of fatigue. DESIGN--Questionnaire survey. SETTING--London general practice. PARTICIPANTS--611 General practice attenders. MAIN OUTCOME MEASURES--Scores on a fatigue questionnaire and reasons given for fatigue. RESULTS--10.2% Of men (17/167) and 10.6% of women (47/444) had substantial fatigue for one month or more. Age, occupation, and marital status exerted minor effects. Subjects attributed fatigue equally to physical and non-physical causes. Physical ill health, including viral infection, was associated with more severe fatigue. Women rather than men blamed family responsibilities for their fatigue. The profile of persistent fatigue did not differ from that of short duration. Only one person met criteria for the chronic fatigue syndrome. CONCLUSIONS--Fatigue is a common complaint among general practice attenders and can be severe. Patients may attribute this to physical, psychological, and social stress.
Denman AM.	Division of Immunological Medicine, Northwick Park Hospital, Harrow, Middlesex, UK.	The chronic fatigue syndrome: a return to common sense.	Postgrad Med J 1990 Jul;66(777):499-501	
Ewig S, Dengler HJ.	Medizinische Klinik der Universitat Bonn.	[Chronic fatigue syndrome]. [article in German]	Klin Wochenschr 1990 Aug 17;68(16):789-96	Reports on conditions of chronic fatigue associated with other somatopsychic symptoms after acute viral infections have led to the hypothesis of a "chronic fatigue syndrome" (CFS). Historical disease descriptions, like e.g. "myalgic encephalomyelitis", were updated by means of modern virological diagnostic techniques and data analysis. Several viral agents like enteroviruses, Epstein-Barr virus,

				Human-Herpesvirus 6 and other herpesviruses have been implicated for possible underlying infections. A preliminary disease definition by the Center for Disease Control (CDC) seeks to provide a rational basis for further etiological studies. In fact, there is growing consensus that the syndrome comprises various separate disease entities and causative agents. Today we can tentatively differentiate a "chronic mononucleosis" after infection with Epstein-Barr virus, an etiologically undetermined "postviral fatigue syndrome" and a fatigue syndrome of the myalgic type after Coxsackie-B virus infection. Furthermore, a valid diagnosis of CFS must be based on the exclusion of defined other diseases and the awareness of dealing with a hypothetical concept. As a result, current knowledge does not yet allow specific therapeutic recommendations.
Gantz NM, Holmes GP.	University of Massachusetts Medical Center, Worcester.	Treatment of patients with chronic fatigue syndrome.	Drugs 1989 Dec;38(6):855-62	
Gin W, Christiansen FT, Peter JB.	Department of Clinical Immunology, Queen Elizabeth II Medical Centre, Nedlands.	Immune function and the chronic fatigue syndrome.	Med J Aust 1989 Aug 7;151(3):117-8	
Goldenberg DL, Simms RW, Geiger A, Komaroff AL.	Arthritis-Fibrositis Center, Newton-Wellesley Hospital, MA 02162.	High frequency of fibromyalgia in patients with chronic fatigue seen in a primary care practice.	Arthritis Rheum 1990 Mar;33(3):381-7	We administered a standardized history questionnaire and performed a tender point examination on 27 patients with debilitating fatigue of at least 6 months duration, seen in a primary care practice, as well as on 20 patients with fibromyalgia. Sixteen of the 27 patients with chronic fatigue met the full criteria for the working case definition of chronic fatigue syndrome (CFS). Eight patients with chronic fatigue denied having any current persistent, diffuse musculoskeletal pain, and their tender point scores were similar to those in 10 normal control subjects. In contrast, 19 patients with chronic fatigue (70%) had persistent, diffuse musculoskeletal pain. The results of their tender point examinations were similar to those of the patients with fibromyalgia. Thus, the majority of these patients with debilitating chronic fatigue, including those who met criteria for CFS, met the historical and tender point diagnostic criteria for fibromyalgia. The presence of current musculoskeletal pain will identify those CFS patients who have fibromyalgia.
Goldenberg DL.	Newton-Wellesley Hospital, Department of Medicine, Tufts University School of Medicine, MA 02162.	Fibromyalgia and its relation to chronic fatigue syndrome, viral illness and immune abnormalities.	J Rheumatol Suppl 1989 Nov;19:91-3	Fibromyalgia and chronic fatigue syndrome have similar clinical and demographic features. We found that most patients with chronic fatigue syndrome have a tender point examination similar to patients with fibromyalgia. Similar pathophysiologic mechanisms are also being explored in each syndrome, including a potential role for viral induced immune dysfunction.
Goodnick PJ.		Bupropion in chronic fatigue syndrome.	Am J Psychiatry 1990 Aug;147(8):1091	
Goodwin SD, Sproat TT, Russell WL.	College of Pharmacy, University of Florida, Gainesville.	Management of Lyme disease.	Clin Pharm 1990 Mar;9(3):192-205	The microbiology, transmission, epidemiology, pathogenesis, clinical manifestations, diagnosis, and treatment of Lyme disease are reviewed. Lyme disease, a tick-borne syndrome, was first described in 1975. The etiologic agent of Lyme disease is <i>Borrelia burgdorferi</i> , a slow-growing spirochete. Lyme disease is the most prevalent tick-borne disease in this country; endemic areas in the United States include the northeastern, north central, and western regions. Both infectious and immunologic mechanisms are important factors in the pathogenesis of Lyme disease. The primary mechanism, however, is thought to be infectious. Three stages of Lyme disease have been described; stage I, characterized by erythema chronicum migrans and flu-like symptoms; stage II, characterized by dermatologic, ophthalmologic, neurologic, and cardiac disorders; and stage III, characterized by arthritis, a multiple sclerosis-like syndrome, psychiatric disorders, and a chronic fatigue syndrome. Therapy with penicillin or tetracycline hastens the resolution of stage I symptoms. Treatment duration normally ranges between 10 days and three weeks. Tetracycline or doxycycline appears to be more effective than penicillin in preventing the development of late Lyme disease. Although intravenous penicillin G and ceftriaxone are both effective for the treatment of late Lyme disease, many clinicians consider ceftriaxone to be the agent of choice. Whether exposed patients from endemic areas should receive antimicrobial prophylaxis is controversial. Further clinical studies are needed to determine optimal therapy for the various stages of Lyme disease, particularly Lyme arthritis.
Greenberg DB.	Department of Psychiatry, Massachusetts General Hospital Cancer Center,	Neurasthenia in the 1980s: chronic mononucleosis, chronic fatigue syndrome, and	Psychosomatics 1990 Spring;31(2):129-37	In the 1980s, patients suffering from unexplained fatigue and what seemed like a prolonged attack of acute mononucleosis were given the diagnosis of chronic mononucleosis or chronic infection with the Epstein-Barr virus. Although the diagnosis has great appeal, the Epstein-Barr virus does not cause the

	Boston.	anxiety and depressive disorders.		syndrome (CFS) of chronic fatigue, which has been renamed and redefined chronic fatigue syndrome to remove the inference that the virus is its cause. From a historical perspective, both syndromes represent the 1980s equivalent of neurasthenia, a disease of fatigue that influenced the development of psychiatric nosology. Because patients with depression and anxiety also have chronic fatigue and because most patients with CFS have an affective disorder, the assessment of organic causes of this syndrome requires careful psychiatric diagnosis and treatment. Defining chronic fatigue syndrome as a medical disorder may deprive patients of competent treatment of their affective disorder.
Hellinger WC, Smith TF, Van Scoy RE, Spitzer PG, Forgacs P, Edson RS.	Division of Infectious Diseases and Internal Medicine, Mayo Clinic, Rochester, MN 55905.	Chronic fatigue syndrome and the diagnostic utility of antibody to Epstein-Barr virus early antigen.	JAMA 1988 Aug 19;260(7):971-3 comment in: JAMA. 1989 Mar 3;261(9):1277-8	Antibody to Epstein-Barr virus (EBV) early antigen has been said to be the most specific indicator of symptomatic chronic EBV infection. We studied the clinical utility of this serologic test in the evaluation of patients with chronic fatigue. Thirty patients with chronic fatigue and highly elevated titers of antibody to early antigen (greater than or equal to 1:160) were compared with 30 age- and sex-matched controls with no antibody to early antigen. There were no significant differences noted between patients and controls at the initial evaluation (symptoms, physical examination, laboratory data). Follow-up information, available for 15 matched pairs, showed no differences in outcome between patients and controls. We conclude that the antibody to EBV early antigen is not helpful in the clinical evaluation of patients with chronic fatigue.
Hickie I, Lloyd A, Wakefield D, Parker G.	Division of Psychiatry, Prince Henry Hospital, Sydney, Australia.	The psychiatric status of patients with the chronic fatigue syndrome.	Br J Psychiatry 1990 Apr;156:534-40 comment in: Br J Psychiatry. 1990 Sep;157:447-50 Br J Psychiatry. 1991 May;158:717	The prevalence of psychiatric disorder in 48 patients with chronic fatigue syndrome (CFS) was determined. Twenty-two had had a major depressive (non-endogenous) episode during the course of their illness, while seven had a current major (non-endogenous) depression. The pre-morbid prevalence of major depression (12.5%) and of total psychiatric disorder (24.5%) was no higher than general community estimates. The pattern of psychiatric symptoms in the CFS patients was significantly different to that of 48 patients with non-endogenous depression, but was comparable with that observed in other medical disorders. Patients with CFS were not excessively hypochondriacal. We conclude that psychological disturbance is likely to be a consequence of, rather than an antecedent risk factor to the syndrome.
Holland R.		Chronic fatigue syndrome.	CMAJ 1989 Sep 1;141(5):375 comment on: Can Med Assoc J. 1989 Jul 1;141(1):11-2	
Holland R.		Chronic fatigue syndrome.	CMAJ 1989 May 1;140(9):1016	
Holmes GP, Kaplan JE, Gantz NM, Komaroff AL, Schonberger LB, Straus SE, Jones JF, Dubois RE, Cunningham-Rundles C, Pahwa S, et al.	Division of Viral Diseases, Centers for Disease Control, Atlanta, Georgia.	Chronic fatigue syndrome: a working case definition.	Ann Intern Med 1988 Mar;108(3):387-9	The chronic Epstein-Barr virus syndrome is a poorly defined symptom complex characterized primarily by chronic or recurrent debilitating fatigue and various combinations of other symptoms, including sore throat, lymph node pain and tenderness, headache, myalgia, and arthralgias. Although the syndrome has received recent attention, and has been diagnosed in many patients, the chronic Epstein-Barr virus syndrome has not been defined consistently. Despite the name of the syndrome, both the diagnostic value of Epstein-Barr virus serologic tests and the proposed causal relationship between Epstein-Barr virus infection and patients who have been diagnosed with the chronic Epstein-Barr virus syndrome remain doubtful. We propose a new name for the chronic Epstein-Barr virus syndrome--the chronic fatigue syndrome--that more accurately describes this symptom complex as a syndrome of unknown cause characterized primarily by chronic fatigue. We also present a working definition for the chronic fatigue syndrome designed to improve the comparability and reproducibility of clinical research and epidemiologic studies, and to provide a rational basis for evaluating patients who have chronic fatigue of undetermined cause.
Holy J.		[Chronic fatigue syndrome].[article in Czech]	Cas Lek Cesk 1989 Apr 14;128(16):501	
Jones JF, Williams M, Schooley RT, Robinson C, Glaser R.	Department of Pediatrics National Jewish Center for Immunology and Respiratory Medicine, Denver, CO 80206.	Antibodies to Epstein-Barr virus-specific DNase and DNA polymerase in the chronic fatigue syndrome.	Arch Intern Med 1988 Sep;148(9):1957-60	In an attempt to examine further the association between active Epstein-Barr virus (EBV) infection and the chronic fatigue syndrome (chronic EBV syndrome, or chronic or atypical mononucleosis), antibodies acting against EBV-specific DNase and DNA polymerase, which are expressed only during virus replication, were assayed. Serum samples from 25 healthy EBV-seropositive individuals neutralized 3.5 +/- 5.1 U (mean +/- SD) of DNase activity and 14.7 +/- 8.5 U of DNA polymerase activity. From these values were selected upper limits of anti-EBV enzyme activity of 17.9 and 31.3 U

				neutralized in normal individuals, respectively (representing the 95% confidence limit). Serum samples from six groups of subjects representing a variety of EBV-related illnesses were then studied. Only patients with notably elevated anti-EBV antibody titers to viral capsid antigen (VCA) (greater than 10,000) had elevated levels of anti-EBV DNase (38 to 56 U neutralized) and anti-EBV DNA polymerase (72 to 106 U neutralized). Three additional patients and two geriatric controls with average anti-EBV early antigen/VCA titers had slightly elevated levels of antibody to EBV DNA polymerase. IgA anti-VCA, anti-early antigen antibodies, or both, were also detected in the same patients who had high EBV DNase and polymerase antibody levels. These antibody profiles are similar to those in patients with nasopharyngeal carcinoma. Since three of the six patients with elevated anti-EBV enzyme antibody levels developed fatal lymphomas, patients with chronic EBV and this antibody profile might be in another illness category at risk for malignant disease.
Jones JF.	Department of Paediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206.	Epstein-Barr virus and the chronic fatigue syndrome: a short review.	Microbiol Sci 1988 Dec;5(12):366-9	Chronic Fatigue Syndrome (CFS), previously known as neuroasthenia is often considered to be due to psychiatric causes. Evidence for a possible role for the Epstein-Barr virus in CFS is summarized. A plea is made for physicians to accept CFS as a non-psychiatric chronic illness to encourage further research into a clear definition of the syndrome.
Kaslow JE, Rucker L, Onishi R.	Division of Basic and Clinical Immunology, University of California Irvine Medical Center, Orange 92668.	Liver extract-folic acid-cyanocobalamin vs placebo for chronic fatigue syndrome.	Arch Intern Med 1989 Nov;149(11):2501-3	Chronic fatigue syndrome is a recently defined entity for which clinical criteria were proposed by the Centers for Disease Control, Atlanta, Ga. A frequently advocated treatment in Southern California is an injectable solution of bovine liver extract containing folic acid and cyanocobalamin (LEFAC). We conducted a double-blind, placebo-controlled, crossover trial of intramuscular LEFAC in 15 patients who met the Centers for Disease Control criteria for chronic fatigue syndrome. Although patients responded to placebo and LEFAC by several criteria of functional status, no significant difference was apparent between response to placebo and that to LEFAC. The placebo response appeared to be strong. Randomized Controlled Trial
Katz BZ, Andiman WA.	Department of Pediatrics, Yale University School of Medicine, New Haven, CT 06510.	Chronic fatigue syndrome.	J Pediatr 1988 Nov;113(5):944-7	
Klimas NG, Salvato FR, Morgan R, Fletcher MA.	Miami Veterans Administration Medical Center, Florida.	Immunologic abnormalities in chronic fatigue syndrome.	J Clin Microbiol 1990 Jun;28(6):1403-10	The chronic fatigue syndrome (CFS), formerly known as chronic Epstein-Barr virus syndrome, is a clinical state of some complexity and uncertain etiology. In order to characterize in a comprehensive manner the status of laboratory markers associated with cellular immune function in patients with this syndrome, 30 patients with clinically defined CFS were studied. All of the subjects were found to have multiple abnormalities in these markers. The most consistent immunological abnormality detected among these patients, when compared with normal controls, was low natural killer (NK) cell cytotoxicity. The number of NK cells, as defined by reactivity with monoclonal antibody NKH.1 (CD56), was elevated, but the killing of K562 tumor cells per CD56 cell was significantly diminished. Lymphoproliferative responses after stimulation with phytohemagglutinin and pokeweed mitogen were decreased in most patients when compared with those in normal controls, as was the production of gamma interferon following mitogen stimulation. Lymphocyte phenotypic marker analysis of peripheral blood lymphocytes showed that there were significant differences between patients with CFS and controls. There was an increase in the percentage of suppressor-cytotoxic T lymphocytes, CD8, and a proportionally larger increase in the number of CD8 cells expressing the class II activation marker. Most patients had an elevated number of CD2 cells which expressed the activation marker CDw26. The numbers of CD4 cells and the helper subset of CD4+CD29+ cells in patients with CFS were not different from those in controls. There was, however, a significant decrease in the suppressor inducer subset of CD4+ CD45RA+ cells.(ABSTRACT TRUNCATED AT 250 WORDS)
Komaroff AL, Geiger AM, Wormsely S.		IgG subclass deficiencies in chronic fatigue syndrome.	Lancet 1988 Jun 4;1(8597):1288-9	
Komaroff AL, Goldenberg D.	Department of Medicine, Brigham and Women's Hospital, Harvard Medical	The chronic fatigue syndrome: definition, current studies and lessons for fibromyalgia	J Rheumatol Suppl 1989 Nov;19:23-7	Chronic fatigue syndrome (CFS) is characterized by chronic, debilitating fatigue lasting greater than 6 months. Frequent chronic and recurrent findings include fever, pharyngitis, myalgias, adenopathy, arthralgias, difficulties in cognition and disorders of mood. In the majority of patients, the illness starts

	School, Boston, MA 02115.	research.		suddenly with an acute, "flu-like" illness. The following laboratory abnormalities are seen with some frequency, although none are seen in all patients: lymphocytosis, atypical lymphocytosis, monocytosis, elevation of hepatocellular enzymes, low levels of antinuclear antibodies, varying levels of antithyroid antibodies, partial hypergammaglobulinemia, elevated CD4:CD8 ratio, decreased cytolytic activity of natural killer cells, and low levels of immune complexes. Clinical and serologic studies suggest an association of CFS with all of the human herpesviruses, particularly Epstein-Barr virus (EBV) and the recently discovered human B lymphotropic virus (HBLV) or human herpesvirus 6; neither EBV nor HBLV has yet been shown to play a causal role in the illness. Preliminary evidence suggests that many of these features of CFS also are seen in patients with fibromyalgia.
Komaroff AL, Straus SE, Gantz NM, Jones JF.		The chronic fatigue syndrome.	Ann Intern Med 1989 Mar 1;110(5):407-8	
Komaroff AL.	Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.	Chronic fatigue syndromes: relationship to chronic viral infections.	J Virol Methods 1988 Sep;21(1-4):3-10	Chronic fatigue syndrome (CFS) is a newly-recognized clinical entity characterized by chronic, debilitating fatigue lasting longer than six months. Common associated findings are chronic and recurrent fever, pharyngitis, myalgias, adenopathy, arthralgias, difficulties in cognition and disorders of mood. In the majority of patients, the illness starts suddenly with an acute, 'flu-like' illness. The following abnormalities are seen with some frequency although none are seen in all patients: lymphocytosis, atypical lymphocytosis, monocytosis, elevation of hepatocellular enzymes, low levels of antinuclear antibodies, low levels of immune complexes. Clinical and serologic studies suggest an association of CFS with all of the human herpesviruses, particularly Epstein-Barr virus (EBV) and the recently-discovered human B-lymphotropic virus (HBLV) or human herpesvirus-6; neither EBV nor HBLV has yet been shown to play a causal role in the illness.
Koo D.		Chronic fatigue syndrome. A critical appraisal of the role of Epstein-Barr virus.	West J Med 1989 May;150(5):590-6	The symptom complex currently designated the chronic fatigue syndrome was previously termed the chronic or chronic active Epstein-Barr virus syndrome or the chronic mononucleosis syndrome, prematurely assuming an etiologic role for the Epstein-Barr virus (EBV). This presumption derived from the fact that some patients with the chronic fatigue syndrome have very high or very low titers of certain antibodies to EBV. A review of seroepidemiologic patterns of response to EBV and of studies of patients with the chronic fatigue syndrome shows that these antibody titers overlap considerably both with those of controls or other healthy persons and with those of patients with other illnesses. Given the high prevalence of exposure to EBV, it would be difficult to determine whether the virus caused the syndrome or whether the antibody elevations resulted from the illness, even if distinct differences in titers existed. Other methodologic issues of control selection, laboratory test comparability, and differing case definitions pose problems in studying this syndrome. The recently published working case definition should facilitate the continuing search for causes.
Krueger GR, Sander C.	Institute of Pathology, University of Cologne, FRG.	What's new in human herpesvirus-6? Clinical immunopathology of the HHV-6 infection.	Pathol Res Pract 1989 Dec;185(6):915-29	Human herpesvirus-6 (HHV-6), formerly known as human B-lymphotropic virus (HBLV), was first isolated in 1986 from patients with lymphoproliferative disorders and AIDS. Antibody prevalence against HHV-6 varies between about 60-80% indicating a widespread latent infection. Although HHV-6 infects in vivo primarily T-lymphocytes, it is associated with similar diseases as in infection with Epstein-Barr virus (EBV), a clearly B-lymphotropic virus. Reactivation of latent HHV-6 infection in patients with subnormal host defense may cause persistent active infection with so-called postinfectious chronic fatigue syndrome (PICFS) or may contribute to other pathologies such as immune deficiency itself, autoimmune disorders or progressive lymphoproliferation. Coinfection of CD4 cells by HHV-6 and human immunodeficiency virus (HIV 1) in AIDS patients can aggravate HIV-induced acquired immune deficiency. These characteristics of the only recently detected new virus justify further intense investigation. Review Literature
Kruesi MJ, Dale J, Straus SE.	National Institute of Mental Health, Child Psychiatry Branch, Bethesda, Md 20892.	Psychiatric diagnoses in patients who have chronic fatigue syndrome.	J Clin Psychiatry 1989 Feb;50(2):53-6 Erratum in: J Clin Psychiatry 1989 Apr;50(4):148 comment in: J Clin Psychiatry. 1990 Apr;51(4):169 J Clin Psychiatry. 1990 Feb;51(2):86	Patients with persistent fatigue are often suspected of having psychiatric illnesses, particularly depression. The authors used the Diagnostic Interview Schedule to assess the lifetime prevalence of psychiatric disorders in 28 patients who met Centers for Disease Control case definition criteria for chronic fatigue syndrome. Compared with studies of the general population and studies of chronically medically ill patients who received the same structured interview, the rates of psychiatric illness in patients with the chronic fatigue syndrome appeared high. An examination of the medical histories of the 28 patients indicated that psychiatric disorders more often preceded the chronic fatigue than followed it.

Lechky O.		Life insurance MDs sceptical when chronic fatigue syndrome diagnosed.	CMAJ 1990 Sep 1;143(5):413-5 comment in: Can Med Assoc J. 1990 Dec 15;143(12):1283-6	
Levine PH, Krueger GR, Straus SE.	Environmental Epidemiology Branch, National Cancer Institute, NIH, Bethesda, MD 20892.	A postviral chronic fatigue syndrome: a round table.	J Infect Dis 1989 Oct;160(4):722-4	
Linde A, Hammarstrom L, Smith CI.		IgG subclass deficiency and chronic fatigue syndrome.	Lancet 1988 Apr 16;1(8590):885-6	
Linde A.		[Chronic fatigue syndrome--a diagnosis to be seriously considered]?[article in Swedish]	Lakartidningen 1989 May 3;86(18):1687-90	
Lloyd A, Hickie I, Wakefield D, Boughton C, Dwyer J.	Department of Infectious Diseases, Prince Henry Hospital, Sydney, Australia.	A double-blind, placebo-controlled trial of intravenous immunoglobulin therapy in patients with chronic fatigue syndrome.	Am J Med 1990 Nov;89(5):561-8 comment in: Am J Med. 1990 Nov;89(5):551-3 Am J Med. 1991 Jun;90(6):768 Am J Med. 1991 Oct;91(4):443-4 Am J Med. 1991 Sep;91(3):320-1	PURPOSE: The chronic fatigue syndrome (CFS) is characterized by profound fatigue, neuropsychiatric dysfunction, and frequent abnormalities in cell-mediated immunity. No effective therapy is known. PATIENTS AND METHODS: Forty-nine patients (40 with abnormal cell-mediated immunity) participated in a randomized, double-blind, placebo-controlled trial to determine the effectiveness of high-dose intravenously administered immunoglobulin G. The patients received three intravenous infusions of a placebo solution or immunoglobulin at a dose of 2 g/kg/month. Assessment of the severity of symptoms and associated disability, both before and after treatment, was completed at detailed interviews by a physician and psychiatrist, who were unaware of the treatment status. In addition, any change in physical symptoms and functional capacity was recorded using visual analogue scales, while changes in psychologic morbidity were assessed using patient-rated indices of depression. Cell-mediated immunity was evaluated by T-cell subset analysis, delayed-type hypersensitivity skin testing, and lymphocyte transformation with phytohemagglutinin. RESULTS: At the interview conducted by the physician 3 months after the final infusion, 10 of 23 (43%) immunoglobulin recipients and three of the 26 (12%) placebo recipients were assessed as having responded with a substantial reduction in their symptoms and recommencement of work, leisure, and social activities. The patients designated as having responded had improvement in physical, psychologic, and immunologic measures (p less than 0.01 for each). CONCLUSION: Immunomodulatory treatment with immunoglobulin is effective in a significant number of patients with CFS, a finding that supports the concept that an immunologic disturbance may be important in the pathogenesis of this disorder. Randomized Controlled Trial
Lloyd A, Wakefield D, Smith L, Isbister J, McGrath M, Collings A, Bajenov N.		Red blood cell morphology in chronic fatigue syndrome.	Lancet 1989 Jul 22;2(8656):217 comment in: Lancet. 1989 Sep 30;2(8666):805 comment on: Lancet. 1987 Aug 8;2(8554):328-9	
Lloyd AR, Hickie I, Boughton CR, Spencer O, Wakefield D.	Department of Immunology, Prince Henry Hospital, Little Bay, NSW.	Prevalence of chronic fatigue syndrome in an Australian population.	Med J Aust 1990 Nov 5;153(9):522-8	An epidemiological study was undertaken to provide the first reported estimate of the point prevalence of chronic fatigue syndrome in an Australian community. After a pilot study in a separate location, the population of the Richmond Valley, New South Wales, was sampled using a structured case-finding technique, which included notification from local medical practitioners, the use of a screening questionnaire and standardised interviews conducted by a physician and psychiatrist. In addition, investigations were performed to exclude alternative diagnoses and to assess cell-mediated immunity. Forty-two patients with chronic fatigue syndrome, with a female:male ratio of 1.3:1.0, were detected in a population of 114,000. The mean age at onset of symptoms was 28.6 years (SD, 12.3 years), and the median duration of symptoms from onset to sampling date was 30 months. The social status of the patients was distributed in accordance with that of the remainder of the population sampled, with no bias towards the middle or upper social classes. The disorder was causing considerable incapacity, with

				43% of patients unable to attend school or work. The conservative estimate from this study suggests a prevalence on June 30 1988 of 37.1 cases per 100,000 (95% confidence interval [CI], 26.8-50.2). Chronic fatigue syndrome is an important disorder in this Australian community that affects young individuals from all social classes and causes considerable ill health and disability.
Lloyd AR, Wakefield D, Boughton CR, Dwyer JM.	Department of Immunology, Prince Henry Hospital, Little Bay, NSW.	Immunological abnormalities in the chronic fatigue syndrome.	Med J Aust 1989 Aug 7;151(3):122-4 comment in: Med J Aust. 1990 Jan 1;152(1):50-2	The chronic fatigue syndrome is a disorder of unknown aetiology which is characterized by debilitating fatigue. Recent evidence has suggested that viruses may persist in the tissues of patients with chronic fatigue syndrome. A concurrent immunological disturbance is likely to be associated with the persistence of viral antigens. Therefore, the humoral and cellular immunity of 100 patients who were suffering from chronic fatigue syndrome and that of 100 healthy, age- and sex-matched control subjects were compared. This study documents the frequent occurrence of abnormalities within the cellular and humoral immune systems of patients with well-defined chronic fatigue syndrome. Disordered immunity may be central to the pathogenesis of chronic fatigue syndrome. In patients with chronic fatigue syndrome, a significant (P less than 0.01) reduction was found in the absolute number of peripheral blood lymphocytes in the total T-cell (CD2), the helper/inducer T-cell (CD4) and the suppressor/cytotoxic T-cell (CD8) subsets. A significant (P less than 0.001) reduction also was found in T-cell function, which was measured: in vivo by delayed-type hypersensitivity skin-testing (reduced responses were recorded in 50 [88%] of 57 patients); and in vitro by phytohaemagglutinin stimulation. Reduced immunoglobulin (Ig) levels were common (56% of patients), with the levels of serum IgG3- and IgG1-subclasses particularly (P less than 0.05) affected.
Lloyd AR.	Department of Infectious Diseases, Prince Henry Hospital, Little Bay, NSW.	Muscle versus brain: chronic fatigue syndrome.	Med J Aust 1990 Nov 5;153(9):530-4 comment in: Med J Aust. 1991 Feb 4;154(3):220	
Luka J, Okano M, Thiele G.	Department of Pathology and Microbiology, University of Nebraska Medical Center, Omaha.	Isolation of human herpesvirus-6 from clinical specimens using human fibroblast cultures.	J Clin Lab Anal 1990;4(6):483-6	The isolation and characterization of human herpesvirus-6 (HHV-6) has been hindered by the lack of cell lines useful for its rapid propagation. Recently, we have reported that the MRC-5 cell line (human diploid lung fibroblasts) was susceptible for HHV-6 infection. In this study, we report on the isolation of HHV-6 from the peripheral blood or buffy coat of three chronic fatigue syndrome patients, one post-liver transplant patient, and one severe chronic active Epstein-Barr virus syndrome patient using the MRC-5 cell line. Additionally, it was observed by Southern blot hybridization studies that four of five isolates had different restriction enzyme fragment patterns than the isolate obtained from the National Institutes of Health with Eco RI. These data suggest the usefulness of the MRC-5 cell line in the isolation and characterization of HHV-6 from various patients.
Manu P, Lane TJ, Matthews DA.	University of Connecticut School of Medicine, Farmington.	The frequency of the chronic fatigue syndrome in patients with symptoms of persistent fatigue.	Ann Intern Med 1988 Oct 1;109(7):554-6 Erratum in: Ann Intern Med 1988 Dec 15;109(12):997	STUDY OBJECTIVE: To determine the frequency of the chronic fatigue syndrome among patients with symptoms of fatigue. DESIGN: Prospective, cohort study. SETTING: Referral clinic, based in a primary care general internal medicine faculty practice of a university medical center. PATIENTS: Consecutive sample of 135 patients (53 men, 82 women) with 6 months or more of debilitating fatigue. INTERVENTIONS: All patients had a complete history taken, had a physical examination and a comprehensive battery of blood tests, and were given the Diagnostic Interview Schedule of the National Institute of Mental Health, a highly-structured 260-item instrument designed to enable accurate psychiatric diagnoses. Other diagnostic studies (for example, sleep studies and electroencephalography) were ordered if necessary for individual patients. MEASUREMENTS AND MAIN RESULTS: Six of the one hundred thirty-five patients met criteria for chronic fatigue syndrome (95% CI, 0 to 10). Ninety-one (67%) patients (CI, 56 to 78) had clinically active psychiatric disorders and 4 (3%) patients (CI, 0 to 8) had medical disorders that were considered a major cause of their fatigue. Thirty-four (25%) patients (CI, 14 to 36) had insufficient symptoms or objective findings of the chronic fatigue syndrome. CONCLUSION: The chronic fatigue syndrome is rare among patients with symptoms of persistent fatigue. Most of these patients have psychiatric disorders.
Martin-Du-Pan R.		[Chronic fatigue syndrome, fibromyalgia and depression].[article in French]	Rev Med Suisse Romande 1990 Oct;110(10):923-8	
Matthews DA, Lane TJ,		Definition of the chronic	Ann Intern Med 1988 Sep	

Manu P.		fatigue syndrome.	15;109(6):511-2	
Moldofsky H, Saskin P, Lue FA.	Department of Psychiatry, University of Toronto, ON, Canada.	Sleep and symptoms in fibrositis syndrome after a febrile illness.	J Rheumatol 1988 Nov;15(11):1701-4	Sleep physiology and symptoms of 9 patients with fibrositis syndrome secondary to a febrile illness were compared to 9 patients with fibrositis syndrome who did not attribute their symptoms to a febrile illness and to 10 healthy controls. Both patient groups showed an alpha EEG (7.5 to 11 Hz) nonrapid eye movement sleep anomaly, had similar observed tender points, and self-ratings of musculoskeletal pain. These findings suggest that patients with postfebrile fibrositis have a nonrestorative sleep disorder characteristic of patients with fibrositis syndrome and share similar symptoms with patients who have a "chronic fatigue syndrome."
Montague TJ, Marrie TJ, Klassen GA, Bewick DJ, Horacek BM.	Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada.	Cardiac function at rest and with exercise in the chronic fatigue syndrome.	Chest 1989 Apr;95(4):779-84	To evaluate a possible cardiac pathophysiology of the chronic fatigue syndrome, we compared the resting cardiac function and exercise performance of 41 patients to those of an age-matched and sex-matched normal control group. Persistent fatigue following an acute apparently viral illness was the major complaint of all patients; none had specific cardiac symptoms nor abnormal physical findings. Electrocardiographic spatial patterns were normal in the patients, and there were no differences in the body surface sum of positive T-wave integrals between the patients (240 microV.x 10(2) +/- 107 microV.s x 10(2)) and control (244 microV.x 10(2) +/- 108 microV.s x 10(2) subjects. Twenty-four hour ambulatory ECGs revealed no differences in sinus rates and incidences of ventricular dysrhythmias in the two populations. Left ventricular dimensions and systolic fractional shortening values were also similar in both groups; moreover none of the patients had segmental wall motion abnormalities. On graded exercise testing, 20 of 32 normal subjects achieved target (85 percent of age-maximum) heart rates, compared to four of 31 patients (p less than 0.001). The duration of exercise averaged 12 +/- 4 minutes for the normal subjects and 9 +/- 4 minutes for the patients (p less than 0.01). The temporal profile of exercise heart rates was dissimilar in the two groups, with patients' rates consistently and progressively less than those of normal subjects. Peak heart rate averaged 152 +/- 16 beats per minute for the normal group vs 124 +/- 19 beats per minute for the patients (p less than 0.0001); in age-related terms, respectively, 82 +/- 6 percent of the maximum heart rate vs 66 +/- 10 percent (p less than 0.0001). Thus, patients with chronic fatigue syndrome have normal resting cardiac function but a markedly abbreviated exercise capacity characterized by slow acceleration of heart rate and fatigue of exercising muscles long before peak heart rate is achieved.(ABSTRACT TRUNCATED AT 250 WORDS)
Morte S, Castilla A, Civeira MP, Serrano M, Prieto J.		Production of interleukin-1 by peripheral blood mononuclear cells in patients with chronic fatigue syndrome.	J Infect Dis 1989 Feb;159(2):362	
Morte S, Castilla A, Civeira MP, Serrano M, Prieto J.		Gamma-interferon and chronic fatigue syndrome.	Lancet 1988 Sep 10;2(8611):623-4	
Nix WA.	Klinik und Poliklinik fur Neurologie, Johannes Gutenberg-Universitat, Mainz.	[Chronic fatigue syndrome--a new disease picture]?[article in German]	Nervenarzt 1990 Jul;61(7):390-6	The chronic fatigue syndrome has recently been more frequently diagnosed. Yet it is unknown if this syndrome represents a disease entity of its own or merely a diagnostic label for a miscellaneous group of disorders. Further investigations are needed to find out if the syndrome has an organic or psychosomatic aetiology, or a mixture of both. In the meantime it is the responsibility of the clinician to make this decision in each individual case.
Parras F, Salva F, Reina J, Gil J, Portela D, Alomar P.		[Chronic fatigue syndrome associated with Epstein-Barr virus infection].[article in Spanish]	Med Clin (Barc) 1989 Apr 29;92(16):619-22 comment in: Med Clin (Barc). 1990 Mar 3;94(8):315-6	Epstein-Barr virus (EBV) infection is ubiquitous and may result in multiple and widely different clinical features; the most common of these is infectious mononucleosis (IM). Recently, a group of patients has been included in the chronic EBV infection syndrome (EBVIS), with a sustained nonspecific syndrome consisting of asthenia, anorexia, low grade fever and changes in mood, associated with a viral infection not necessarily caused by EBV; this has been called chronic fatigue syndrome (CFS). We report a patient who fulfilled the criteria for CFS associated with EBV after an acute, well documented EBV infection. We discuss its etiological and pathophysiological implications, emphasizing the need for extreme caution in the diagnosis of CFS. A merely clinical diagnosis may hide severe mistakes.
Payne CB Jr, Sloan HE.		Pulmonary function and the chronic fatigue syndrome.	Ann Intern Med 1989 Nov 15;111(10):860	

Peterson PK, Shepard J, Macres M, Schenck C, Crosson J, Rechtman D, Lurie N.	Department of Medicine, Hennepin County Medical Center, Minneapolis, Minnesota 55415.	A controlled trial of intravenous immunoglobulin G in chronic fatigue syndrome.	Am J Med 1990 Nov;89(5):554-60 comment in: Am J Med. 1990 Nov;89(5):551-3	PURPOSE: Currently, there is no established therapy for chronic fatigue syndrome (CFS), a recently defined illness that has been associated with a variety of immunologic abnormalities. Based on the hypothesis that a chronic viral infection or an immunoregulatory defect is involved in the pathogenesis of CFS, the therapeutic benefit of intravenous immunoglobulin G (IV IgG) was evaluated in a group of patients with CFS. Additionally, serum immunoglobulin concentrations and peripheral blood lymphocyte subset numbers were measured at the outset of the study, and the effect of IV IgG therapy on IgG subclass levels was determined. PATIENTS AND METHODS: Thirty patients with CFS were enrolled in a double-blind, placebo-controlled trial of IV IgG. The treatment regimen consisted of IV IgG (1 g/kg) or intravenous placebo (1% albumin solution) administered every 30 days for 6 months. Participants completed a self-assessment form prior to each of the six treatments, which was used to measure severity of symptoms, functional status, and health perceptions. Patients were also asked to report adverse experiences defined as worsening of symptoms occurring within 48 hours of each treatment. RESULTS: Twenty-eight patients completed the trial. At baseline, all 28 patients complained of moderate to severe fatigue, and measures of social functioning and health perceptions showed marked impairment. Low levels of IgG1 were found in 12 (42.9%), and 18 (64.3%) had low levels of IgG3. At the end of the study, no significant therapeutic benefit could be detected in terms of symptom amelioration or improvement in functional status, despite restoration of IgG1 levels to a normal range. Major adverse experiences were observed in 20% of both the IV IgG and placebo groups. CONCLUSION: The results of this study indicate that IV IgG is unlikely to be of clinical benefit in CFS. In addition to the ongoing need for placebo-controlled trials of candidate therapies for CFS, an expanded research effort is needed to define the etiology and pathogenesis of this disorder.
Phillips H.		Chronic fatigue syndrome.	Med J Aust 1989 Mar 20;150(6):351-2	
Pinardi G, Scarlato G.	Istituto di Clinica neurologica, Universita, Ospedale maggiore Policlinico, Milano.	[The chronic fatigue syndrome. A multifactorial approach and the treatment possibilities].[article in Italian]	Recenti Prog Med 1990 Dec;81(12):773-7	The chronic fatigue syndrome is a poorly defined symptoms complex characterized primarily by chronic or recurrent debilitating fatigue and various combinations of other symptoms, including psychological symptoms, sore throat, lymph node pain, headache, myalgia, arthralgias. Psychological disturbances, ranging from mild depression or anxiety to severe behavioral abnormalities, are always present. Chronic fatigue syndrome is the name that more accurately describes this symptom complex of unknown cause. A viral aetiology has long been hypothesized: many viruses are potential candidates, including any of the 23 Coxsackie A or 6 Coxsackie B viruses, herpes viruses, particularly Epstein-Barr virus and varicella. These studies, though interesting, remain unconvincing because of methodological flaws such as a poor case definition and inadequate control groups. This syndrome may represent an infection by a yet unidentified virus. It is more likely due to an abnormal immune response toward different intracellular pathogens. There is no treatment to ameliorate the chronic fatigue syndrome. Epidemiological studies are essential with explicit operational case definition before progress can be made in the management of this distressing disorder.
Portwood M.		More information on chronic fatigue syndrome.	Nurse Pract 1988 Sep;13(9):8	
Portwood MF.		Chronic fatigue syndrome--a diagnosis for consideration.	Nurse Pract 1988 Feb;13(2):11-2, 15-8, 23	Chronic fatigue syndrome (CFS) is an illness which may be mild or completely disabling. Clients who return with recurring non-related symptoms and no specific diagnosis may suffer from CFS. The symptoms of CFS are numerous and varied, including fatigue, malaise, myalgias, difficulty concentrating, headaches and sore throat. Patient complaints seem out of proportion to the physical findings, which may be normal. There is no cure for this chronic disease. Therapy is primarily symptomatic. The role of the health care provider is to recognize this confusing disorder and help the patient and family cope with its many effects.
Powell MA.		Epstein-Barr antibody titer and chronic fatigue syndrome.	J Am Acad Nurse Pract 1990 Jan-Mar;2(1):33-4	
Powell R, Dolan R, Wessely S.	National Hospital For Nervous Diseases, Queen Square, London, U.K.	Attributions and self-esteem in depression and chronic fatigue syndromes.	J Psychosom Res 1990;34(6):665-73	There is considerable overlap in symptomatology between chronic fatigue syndrome (CFS) and affective disorder. We report a comparison of depressive phenomenology and attributional style between a group of CFS subjects seen in a specialized medical setting, which included a high proportion with depression diagnosed by Research Diagnostic Criteria (RDC), and depressed controls

				seen in a specialized psychiatric setting. Significant symptomatic differences between the depressed CFS group and depressed controls were observed for features such as self-esteem and guilt as well as attribution of illness. All the CFS groups tended to attribute their symptoms to external causes whereas the depressed controls experienced inward attribution. This may have resulted from differences in the severity of mood disorder between the samples, but it is also suggested that an outward style of attribution protects the depressed CFS patients from cognitive changes associated with low mood but at the expense of greater vulnerability towards somatic symptoms such as fatigue.
Prieto J, Subira ML, Castilla A, Serrano M.	Department of Internal Medicine, University Clinic, School of Medicine, Pamplona, Spain.	Naloxone-reversible monocyte dysfunction in patients with chronic fatigue syndrome.	Scand J Immunol 1989 Jul;30(1):13-20	We studied monocyte function in 35 consecutive patients with chronic fatigue syndrome (CFS) and 25 healthy controls. Eighty-five per cent of the patients showed monocyte dysfunction characterized by marked reduction in the number of monocytes displaying immunoreactive cytoskeletal vimentin filaments, a low phagocytosis index, and a reduced expression of HLA-DR antigens. These values increased dramatically after incubation of the patients' monocytes with the opioid antagonist naloxone. Other immunological abnormalities also noted in the patients were low lymphocyte blastogenesis and diminished numbers of monocytes displaying receptors for Fc of IgG (FcR) and C3b (CR1). These findings suggest that an increased opioid activity acting through a classical receptor mechanism is active on monocytes from a high proportion of patients with CFS and that this represents a novel example of immunomodulation by opioid peptides in human disease. We suggest that endogenous opioids are involved in the pathogenesis of the chronic fatigue syndrome.
Pritchard C.		Fibrositis and the chronic fatigue syndrome.	Ann Intern Med 1988 Jun;108(6):906	
Read R, Spickett G, Harvey J, Edwards AJ, Larson HE.		IgG1 subclass deficiency in patients with chronic fatigue syndrome.	Lancet 1988 Jan 30;1(8579):241-2	
Reilly PA, Littlejohn GO.	Prince Henry's Hospital, Melbourne, Australia.	Fibromyalgia and chronic fatigue syndrome.	Curr Opin Rheumatol 1990 Apr;2(2):282-90	
Reiss GR.		Chronic fatigue syndrome.	J Clin Psychiatry 1990 Apr;51(4):169 comment on: J Clin Psychiatry. 1989 Feb;50(2):53-6	
Richards AJ.		Epstein-Barr virus and chronic fatigue syndrome.	J Rheumatol 1988 Oct;15(10):1595	
Riley MS, O'Brien CJ, McCluskey DR, Bell NP, Nicholls DP.	Department of Medicine, Royal Victoria Hospital, Belfast.	Aerobic work capacity in patients with chronic fatigue syndrome.	BMJ 1990 Oct 27;301(6758):953-6 comment in: BMJ. 1990 Nov 24;301(6762):1217 BMJ. 1991 Jan 5;302(6767):50	OBJECTIVE--To determine the aerobic work capacity of patients with the chronic fatigue syndrome and compare it with that of two control groups, and to assess the patients' perception of their level of activity before and during illness. DESIGN--A symptom limited exercise treadmill test with on line gas analysis and blood sampling was used. Subjects were assessed by one investigator, who was blind to the group which they were in. SETTING--Department of medicine, Royal Victoria Hospital, Belfast. SUBJECTS--13 Patients (10 women, three men) who fulfilled the diagnostic criteria for chronic fatigue syndrome. Two control groups of similar age, sex, and body weight: 13 normal subjects (10 women, three men) and seven patients (five women, two men) with the irritable bowel syndrome. MAIN OUTCOME MEASURES--Aerobic work capacity as assessed by several variables such as length of time on treadmill, heart rate, and biochemical measurements; Borg score; and visual analogue scores of perceived level of physical activity. RESULTS--The patients with the chronic fatigue syndrome had a reduced exercise capacity compared with that of the other subjects, spending a significantly shorter time on the treadmill. They had a significantly higher heart rate at submaximal levels of exertion and at stage III exertion had significantly higher blood lactate concentrations. Using a Borg score, they showed a significantly altered perception of their degree of physical exertion with a mean score of 8.2 compared with 6.6 and 5.3 for the normal subjects and patients with the irritable bowel syndrome respectively. Using a visual analogue scale they indicated that they had a greater capacity for activity before illness than had the patients with the irritable bowel syndrome, but the scores were not significantly different between the two groups. Both groups of patients indicated reduced activity at the time of testing. Normal controls and patients with the irritable bowel syndrome

				aspired to a greater level of activity than their current level, but the patients with the chronic fatigue syndrome aspired to a level similar to that which they had had before their illness. CONCLUSIONS-- Patients with the chronic fatigue syndrome have reduced aerobic work capacity compared with normal subjects and patients with the irritable bowel syndrome. They also have an altered perception of their degree of exertion and their premorbid level of physical activity.
Roath S.		Blood cell morphology in chronic fatigue syndrome.	Lancet 1989 Sep 30;2(8666):805 comment on: Lancet. 1989 Jul 22;2(8656):217	
Rosen SD, King JC, Wilkinson JB, Nixon PG.	Department of Cardiology, Charing Cross Hospital, London.	Is chronic fatigue syndrome synonymous with effort syndrome?	J R Soc Med 1990 Dec;83(12):761-4	Chronic fatigue syndrome (CFS), including myalgic encephalomyelitis (ME) and postviral syndrome (PVS), is a term used today to describe a condition of incapacity for making and sustaining effort, associated with a wide range of symptoms. None of the reviews of CFS has provided a proper consideration of the effort syndrome caused by chronic habitual hyperventilation. In 100 consecutive patients, whose CFS had been attributed to ME or PVS, the time course of their illness and the respiratory psychophysiological studies were characteristic of chronic habitual hyperventilation in 93. It is suggested that the labels 'CFS', 'ME' or 'PVS' should be withheld until chronic habitual hyperventilation - for which conventional rehabilitation is available - has been definitively excluded.
Rosen SD, King JC, Wilkinson JB, Nixon PG.		Aerobic work capacity in chronic fatigue syndrome.	BMJ 1990 Nov 24;301(6762):1217 comment on: BMJ. 1990 Oct 27;301(6758):953-6	
Ross GH, Rea WJ, Johnson AR.		Chronic fatigue syndrome.	CMAJ 1989 Jul 1;141(1):11-2 comment in: Can Med Assoc J. 1989 Sep 1;141(5):375	
Sawyer MH, Webb DE, Balow JE, Straus SE.	Medical Virology Section, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland.	Acyclovir-induced renal failure. Clinical course and histology.	Am J Med 1988 Jun;84(6):1067-71	Four patients with a chronic fatigue syndrome experienced five episodes of acute renal insufficiency associated with high-dose (500 mg/m ²) intravenous acyclovir administered intravenously as one-hour infusions. Nephrotoxicity developed despite precautions to avoid volume contraction. Examination of the urinary sediment of three patients by polarizing microscopy showed birefringent needle-shaped crystals within leukocytes. In the most severely affected patient, a serum creatinine concentration of 8.6 mg/dl developed and the patient underwent percutaneous renal biopsy that revealed foci of interstitial inflammation without tubular necrosis. Urine, blood, and renal tissue levels of acyclovir were high. One patient was rechallenged with low-dose intravenous acyclovir and the four patients later received oral acyclovir, all without adverse effect. The combined data from these patients support crystalluria and obstructive nephropathy as a mechanism of acyclovir-induced renal failure in humans. This experience emphasizes the importance of maintaining adequate hydration during high-dose acyclovir therapy.
Schooley RT. Review, Academic		Chronic fatigue syndrome: a manifestation of Epstein-Barr virus infection?	Curr Clin Top Infect Dis 1988;9:126-46	
Shahar E, Lederer J.	Department of Family Medicine, Sackler School of Medicine, Tel-Aviv University, Israel.	Asthenic symptoms in a rural family practice. Epidemiologic characteristics and a proposed classification.	J Fam Pract 1990 Sep;31(3):257-61; discussion 261-2 comment in: J Fam Pract. 1991 Jan;32(1):14	Asthenic symptoms (eg, fatigue, lassitude, weakness) are of major concern in family practice setting, yet relatively little research has addressed this issue. A retrospective chart review over a 10-year period was conducted to better characterize these symptoms in a rural family practice providing health care to 508 adult patients. Asthenic complaints were recorded at least once in the medical charts of 164 patients (32%) with a preponderance of female patients. Peak prevalence occurred in the third decade of age and during the summer months. Associated symptoms, mainly pain and dizziness, were reported in 75% of the cases. A cause or diagnosis was not identified by the practicing physician in nearly 50% of the encounters; nevertheless, most episodes resolved spontaneously. Patients could be subclassified into three categories according to the recurrence pattern of their asthenic symptoms during the study period. The largest category (64%) included patients who had a single or two episodes and was thus termed "episodic asthenia." Forty-five patients (27%) with recurrent episodes (mean 4.4, range 3 to 10) were classified as having "recurrent episodic asthenia." A third small group (14 patients, 9%) with

				persistent complaints over the years but no evidence of the chronic fatigue syndrome were classified as having "chronic persistent asthenia." The proposed classification may help future research of asthenic symptoms in the family practice setting.
Simpson LO.		Are ME and chronic fatigue syndrome the same disease?	N Z Med J 1990 Jun 27;103(892):305 comment in: N Z Med J. 1990 Aug 8;103(895):378	
Spracklen FH.	Department of Medicine, University of Cape Town.	The chronic fatigue syndrome (myalgic encephalomyelitis)--myth or mystery?	S Afr Med J 1988 Nov 5;74(9):448-52	The chronic fatigue syndrome (CFS) or myalgic encephalomyelitis has caused great confusion, misunderstanding and perhaps even mismanagement of many persons presenting with a variety of combinations of ill-defined complaints. The history, possible pathogenesis and clinical features, of what is probably in most instances a post-viral infection syndrome, are reviewed. The recent Centers for Disease Control case definition is summarised and simplified. The need for such uniformity of definition, acceptable to most workers in the field, is emphasised in order to facilitate further studies into the cause, diagnosis, course and treatment of CFS. The difficulty in treating this condition and the currently recommended management are described. Double-blind controlled studies are essential in assessing any proposed new treatment.
Straus SE, Dale JK, Peter JB, Dinarello CA.		Circulating lymphokine levels in the chronic fatigue syndrome.	J Infect Dis 1989 Dec;160(6):1085-6	
Straus SE, Dale JK, Tobi M, Lawley T, Preble O, Blaese RM, Hallahan C, Henle W.	Medical Virology Section, National Institute of Allergy and Infectious Diseases, Bethesda, Md 20892.	Acyclovir treatment of the chronic fatigue syndrome. Lack of efficacy in a placebo-controlled trial.	N Engl J Med 1988 Dec 29;319(26):1692-8	Twenty-seven adults with a diagnosis of the chronic fatigue syndrome were enrolled in a double-blind, placebo-controlled study of acyclovir therapy. The patients had had debilitating fatigue for an average of 6.8 years, accompanied by persisting antibodies to Epstein-Barr virus early antigens (titers greater than or equal to 1:40) or undetectable levels of antibodies to Epstein-Barr virus nuclear antigens (titers less than 1:2) or both. Each course of treatment consisted of intravenous placebo or acyclovir (500 mg per square meter of body-surface area) administered every eight hours for seven days. The same drug was then given orally for 30 days (acyclovir, 800 mg four times daily). There were six-week observation periods before, between, and after the treatments. Three patients had acyclovir-induced nephrotoxicity and were withdrawn from the study. Of the 24 patients who completed the trial, similar numbers improved with acyclovir therapy and with placebo (11 and 10, respectively). Neither acyclovir treatment nor clinical improvement correlated with alterations in laboratory findings, including titers of antibody to Epstein-Barr virus or levels of circulating immune complexes or of leukocyte 2',5'-oligoadenylate synthetase. Subjective improvement correlated with various measures of mood. We conclude that acyclovir, as used in this study, does not ameliorate the chronic fatigue syndrome. We believe that the clinical improvement observed in most patients reflected either spontaneous remission of the syndrome or a placebo effect.
Straus SE, Dale JK, Wright R, Metcalfe DD.	Medical Virology Section, National Institute of Allergy and Infectious Diseases, Bethesda, MD 20892.	Allergy and the chronic fatigue syndrome.	J Allergy Clin Immunol 1988 May;81(5 Pt 1):791-5	The chronic fatigue syndrome is a heterogeneous disorder characterized by easy fatigability, feverishness, diffuse pains, and depression. Many patients also report inhalant, food, or drug allergies. This article reviews the clinical features of the syndrome and hypotheses of its pathogenesis, especially those regarding the Epstein-Barr virus and cellular immune mechanisms. Also summarized are recent studies of the validity of atopic complaints in the syndrome. The results of epicutaneous skin testing demonstrated a high correlation with history in 24 patients. Atopy coexists with the chronic fatigue syndrome in greater than 50% of patients.
Straus SE. Editorial		Intravenous immunoglobulin treatment for the chronic fatigue syndrome.	Am J Med 1990 Nov;89(5):551-3 comment in: Am J Med. 1991 Sep;91(3):320-1 comment on: Am J Med. 1990 Nov;89(5):554-60 Am J Med. 1990 Nov;89(5):561-8	
Subira ML, Castilla A, Civeira MP, Prieto J.		Deficient display of CD3 on lymphocytes of patients with	J Infect Dis 1989 Jul;160(1):165-6	

		chronic fatigue syndrome.		
Swartz MN.		The chronic fatigue syndrome-one entity or many?	N Engl J Med 1988 Dec 29;319(26):1726-8 comment in: N Engl J Med. 1989 Jul 20;321(3):187-9	
Valdini A.	Department of Family Medicine, State University of New York, Stony Brook 11794.	Selections from current literature: chronic fatigue syndrome.	Fam Pract 1990 Jun;7(2):152-5	
Wakefield D, Lloyd A, Brockman A.	Department of Immunopathology and Infectious Diseases, Prince Henry Hospital, Sydney, Australia.	Immunoglobulin subclass abnormalities in patients with chronic fatigue syndrome.	Pediatr Infect Dis J 1990 Aug;9(8 Suppl):S50-3	
Wessely S, David A, Butler S, Chalder T.		Management of chronic (post-viral) fatigue syndrome.	J R Coll Gen Pract 1989 Jan;39(318):26-9 comment in: J R Coll Gen Pract. 1989 Apr;39(321):171-3 J R Coll Gen Pract. 1989 May;39(322):213-4	Simple rehabilitative strategies are proposed to help patients with the chronic fatigue syndrome. A model is outlined of an acute illness giving way to a chronic fatigue state in which symptoms are perpetuated by a cycle of inactivity, deterioration in exercise tolerance and further symptoms. This is compounded by the depressive illness that is often part of the syndrome. The result is a self-perpetuating cycle of exercise avoidance. Effective treatment depends upon an understanding of the interaction between physical and psychological factors. Cognitive behavioural therapy is suggested. Cognitive therapy helps the patient understand how genuine symptoms arise from the frequent combination of physical inactivity and depression, rather than continuing infection, while a behavioural approach enables the treatment of avoidance behaviour and a gradual return to normal physical activity.
Wigley RD.		Chronic fatigue syndrome, ME and fibromyalgia.	N Z Med J 1990 Aug 8;103(895):378 comment on: N Z Med J. 1990 Jun 27;103(892):305	