

| Authors | Author Address | Title | Publication | Abstract |
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| Abbot NC, Spence VA, Lowe JG, Potts RC, Hassan AH, Belch JJ, Beck JS. | | Chronic fatigue syndrome. Immunological findings vary between populations. | BMJ 1994 May 14;308(6939):1299 comment on: BMJ. 1994 Mar 19;308(6931):756-9 | |
| Ablashi DV, Berneman ZN, Kramarsky B, Asano Y, Choudhury S, Pearson GR. | Georgetown University School of Medicine, Washington, DC 20007. | Human herpesvirus-7 (HHV-7). | In Vivo 1994 Jul-Aug;8(4):549-54 | HHV-7 first isolated in 1990 from a healthy individual, is a ubiquitous agent. The second independent isolation of HHV-7 from a chronic fatigue syndrome patient was reported in 1992. The seroepidemiology of HHV-7 suggested that its prevalence rate in the U.S.A. population is > 85%; however, in Japan a low prevalence rate has been reported. HHV-7 can be more readily isolated from the saliva than HHV-6. The primary infection of HHV-7 appears later in life than HHV-6. No disease has been reported that is etiologically linked to HHV-7. HHV-7 is more closely related to HHV-6 and the human cytomegalovirus than other members of the human herpesvirus family. |
| Ablashi DV. | National Cancer Institute, Bethesda, Maryland. | Viral studies of chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S130-3 | |
| Agut H, Aubin JT. | Laboratoire de virologie, CNRS EP 57, CERVI, hopital Pitie-Salpetriere, Paris. | [A new virus: the human herpesvirus 6].[article in French] | Rev Prat 1994 Apr 1;44(7):871-4 | Human herpesvirus 6 (HHV-6) was discovered in 1986. This novel virus is genetically related to cytomegalovirus. HHV-6 mainly infects T lymphocytes but its tropism appears to be much wider and probably involves some epithelial cells. Two HHV-6 variants, designated as A and B, can be distinguished by genetical and immunological analysis. HHV-6 infection is ubiquitous and widespread; it occurs most often during infancy and it is life-long. During primary infection, HHV-6 is the causative agent of exanthem subitum and fever episodes without rash in infants. HHV-6 is suspected to be the causative agent of opportunistic infections such as pneumonitis and retinitis in immunocompromised subjects. Its role in human immunodeficiency virus infection, lymphomas and chronic fatigue syndrome is controversial. In vitro, HHV-6 is sensitive to ganciclovir and foscarnet. |
| Altura BT, Burack JL, Cracco RQ, Galland L, Handwerker SM, Markell MS, Mauskop A, Memon ZS, Resnick LM, Zisbrod Z, et al. | Department of Physiology, State University of New York, Health Science Center at Brooklyn 11203. | Clinical studies with the NOVA ISE for IMg2+. | Scand J Clin Lab Invest Suppl 1994;217:53-67 | The Nova ISE for IMg2+ was utilized to examine IMg2+ in plasma and serum of patients with a variety of pathophysiologic and disease syndromes (e.g., long-term renal transplants [LTRT], during and before cardiac surgery, migraine headaches, head trauma, pregnancy, chronic fatigue syndrome [CFS], non-insulin dependent diabetes mellitus [NIDDM], asthma and after excessive dietary intake of Mg). The results indicate that LTRT treated with cyclosporin A, migraine, head trauma, pregnancy, NIDDM, diseased pregnant, and asthmatic patients all on the average, exhibit significant depression in IMg2+ but not total Mg (TMg). Patients with CFS failed to exhibit changes in serum IMg2+ or TMg levels. Increased dietary load of Mg, for only 6 days, resulted in significant elevations of serum IMg2+ but not TMg. Correlations between the clinical course of several of these syndromes and the fall in IMg2+ were found. The Ca2+/Mg2+ ratio appears to be an important guide for signs of peripheral vasoconstriction and or spasm and possibly enhanced atherogenesis. Overall, the data point to important uses for ISE's for IMg2+ in the diagnosis and treatment of disease states. |
| Ambrogetti A, Olson LG. | Sleep Disorders Centre, John Hunter Hospital, New Lambton, NSW. | Consideration of narcolepsy in the differential diagnosis of chronic fatigue syndrome. | Med J Aust 1994 Apr 4;160(7):426-9 | OBJECTIVE: To justify the inclusion of narcolepsy in the differential diagnosis of patients with chronic fatigue. CLINICAL FEATURES: We report three patients aged 17 (two women and one man) and one woman aged 45 who had been diagnosed as having chronic fatigue syndrome (CFS). They had no psychiatric illness. Their main problem was severe daytime sleepiness, presenting as "tiredness and fatigue". The history, sleep study and multiple sleep latency test suggested a diagnosis of narcolepsy. INTERVENTION: Treatment with methylphenidate resulted in complete resolution of symptoms in two patients and significant improvement in the other two. CONCLUSIONS: The differential diagnosis of CFS requires the exclusion of other conditions. If daytime sleepiness is a major complaint, other symptoms of narcolepsy should be sought and the diagnosis confirmed with sleep study and a multiple sleep latency test. |
| Anand AC, Kumar R, Rao MK, Dham SK. | AFMC, Pune. | Low grade pyrexia: is it chronic fatigue syndrome? | J Assoc Physicians India 1994 Aug;42(8):606-8 comment in: J Assoc Physicians India. 1995 Oct;43(10):725-6 | Eighty seven consecutive patients presenting with prolonged low grade pyrexia (99 degrees-101 +/- F) during 1984-93 were followed up for a mean duration of 2.9 years. Mean age was 37.55 years (SD + 10.16) and 66 (75.8%) were females. Onset of pyrexia was acute in 57 patients and was associated with chilly sensation (42), Fatigue (69), Arthralgias (61), myalgias (55) and several other non specific symptoms. Clinical examination showed paucity of physical signs with 7 patients showing tender lymphadenopathy, 7 showing splenomegaly, 5 hepatomegaly, and 1 phlyctenular conjunctivitis. |

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| | | | | Psychiatric examination was within normal limits. Extensive investigations for any viral or other infection, autoimmune disorder or malignancy were unrewarding. Patients were followed up for an average of 2.9 (2 to 5 years). Thirteen patients had become asymptomatic within one year of onset of symptoms, 38 by two years and 45 by the end of three years. This syndrome may be a variant of chronic fatigue syndrome. |
| Anderson N. | | Chronic fatigue syndrome. ...and study them separately. | BMJ 1994 May 14;308(6939):1298 comment on: BMJ. 1994 Mar 19;308(6931):732-3 | |
| Antoni MH, Brickman A, Lutendorf S, Klimas N, Imia-Fins A, Ironson G, Quillian R, Miguez MJ, van Riel F, Morgan R, et al. | Department of Psychology, University of Miami, Coral Gables, Florida 33124. | Psychosocial correlates of illness burden in chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S73-8 | We related reported physical symptoms, cognitive appraisals (e.g., negative style of thinking), and coping strategies (e.g., denial/disengagement strategies) with illness burden across several functional domains separately in subsets of chronic fatigue syndrome (CFS) patients with (n = 26) and without (n = 39) concurrently diagnosed major depressive disorder (MDD). In regard to cognitive appraisal measures, automatic thoughts and dysfunctional attitudes were strongly associated with a higher illness burden, as indicated in sickness impact profile (SIP) scores. Active-involvement coping strategies measured on COPE scales (active coping, planning, and positive reinterpretation and growth) were not associated with SIP scores, while other coping strategies (mental disengagement, behavioral disengagement, and denial) were positively correlated with psychosocial and physical SIP scales, especially those pertaining to interpersonal life-style arenas. After we accounted for the number of different CFS-specific physical complaints reported and DSM-III-R depression diagnosis status, cognitive appraisals and coping strategies predicted a substantial proportion of the variance in the severity of illness burden. For the most part, the magnitude of these relationships between our predictor model variables and illness burden severity was similar in the MDD and non-MDD subgroups. |
| Arber M, Macintyre A. | | Chronic fatigue syndrome or myalgic encephalitis. | Lancet 1994 Jan 22;343(8891):242-3 comment on: Lancet. 1993 Nov 13;342(8881):1247-8 | |
| Artsimovich NG, Chugunov VS, Kornev AV, Ivanova TM, Chugunov AV, Oprishchenko MA. | | [The chronic fatigue syndrome].[article in Russian] | Zh Nevropatol Psikhiatr Im S S Korsakova 1994;94(5):47-50 | CFIDS (chronic fatigue and immune dysfunction syndrome) is also known as CFS (chronic fatigue syndrome), CEBV (chronic Epstein-Barr virus), M.E. (myalgic encephalomyelitis), yuppie flu and by other names. It is a complex illness characterized by incapacitating fatigue (experienced as exhaustion and extremely poor stamina), neurological problems and a constellation of symptoms that can resemble many disorders, including; mononucleosis, multiple sclerosis, fibromyalgia, AIDS-related complex (ARC) and autoimmune diseases such as lupus. These symptoms tend to wax and wane, but any often severely debilitating and may last for many months or years. All sections of the population (including children) are at risk, but women under 45 seem to be most susceptible. The investigators suggest that CFIDS results from dysfunction of the immune system. The exact nature of this dysfunction is not yet well defined, but it can generally be viewed as an unregulated or overactive state which is responsible for most of the symptoms. There is also evidence of some immune suppression in CFIDS. None of the treatments is consistently satisfactory, but some may be helpful: psychotherapy, physiotherapy, exercise programs, acupunctures, small doses of antidepressants, etc. |
| Barker E, Fujimura SF, Fadem MB, Landay AL, Levy JA. | Department of Medicine, University of California, San Francisco 94143-0128. | Immunologic abnormalities associated with chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S136-41 | Several aspects of cellular immunity in patients with clinically defined chronic fatigue syndrome (CFS) were evaluated and compared with those in healthy individuals. Flow cytometric analyses revealed normal expression of total T (CD3+), B (CD19+), and NK (natural killer) (CD16+, CD56+) markers on the surface of peripheral blood mononuclear cells (PMC) from patients with CFS. However, compared with those of healthy individuals, patients' CD8+ T cells expressed reduced levels of CD11b and expressed the activation markers CD38 and HLA-DR at elevated levels. In many of the individuals in whom expression of CD11b was reduced the expression of CD28 was increased. These findings indicate expansion of a population of activated CD8+ cytotoxic T lymphocytes. A marked decrease in NK cell activity was found in almost all patients with CFS, as compared with that in healthy individuals. No substantial abnormalities in monocyte activity or T cell proliferation were observed. The results of this study suggest that immune cell phenotype changes and NK cell dysfunction are common manifestations of CFS. |

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| Bates DW, Buchwald D, Lee J, Kith P, Doolittle TH, Umali P, Komaroff AL. | Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115. | A comparison of case definitions of chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S11-5 | We compared three case definitions of chronic fatigue syndrome (CFS) applied to patients followed in CFS clinics at two institutions. All patients had debilitating fatigue without apparent etiology; patients with medical conditions associated with chronic fatigue and with major psychiatric disorders were stratified and presented separately. Patients were classified according to whether they met case definitions developed by a Centers for Disease Control and Prevention (CDC) Working Group, a British group, or an Australian group. When findings for 805 patients followed at the two clinics were combined, 61% met the CDC criteria, 55% met the British criteria, and 56% met the Australian criteria; these proportions were relatively similar at both sites. In addition, similar laboratory abnormalities were found for all case groups and for fatigued patients who met none of the three case definitions. These data suggest that more inclusive case definitions may be superior. |
| Bearn J, Wessely S. | Bethlem Royal Hospital, London, UK. | Neurobiological aspects of the chronic fatigue syndrome. | Eur J Clin Invest 1994 Feb;24(2):79-90 | |
| Bell DS, Bell KM, Cheney PR. | Department of Pediatrics, Cambridge Hospital, Massachusetts 02139. | Primary juvenile fibromyalgia syndrome and chronic fatigue syndrome in adolescents. | Clin Infect Dis 1994 Jan;18 Suppl 1:S21-3 | Chronic fatigue syndrome (CFS) and primary juvenile fibromyalgia syndrome (PJFS) are illnesses with a similar pattern of symptoms of unknown etiology. Twenty-seven children for whom CFS was diagnosed were evaluated for fibromyalgia by the presence of widespread pain and multiple tender points. Eight children (29.6%) fulfilled criteria for fibromyalgia. Those children who met fibromyalgia criteria had a statistically greater degree of subjective muscle pain, sleep disturbance, and neurological symptoms than did those who did not meet the fibromyalgia criteria. There was no statistical difference between groups in degree of fatigue, headache, sore throat, abdominal pain, depression, lymph node pain, concentration difficulty, eye pain, and joint pain. CFS in children and PJFS appear to be overlapping clinical entities and may be indistinguishable by current diagnostic criteria. |
| Bell DS. | Harvard Medical School, Boston, Massachusetts. | Chronic fatigue syndrome update. Findings now point to CNS involvement. | Postgrad Med 1994 Nov 1;96(6):73-6, 79-81 | Neither Epstein-Barr virus nor human herpesvirus 6 appears to play a causative role in chronic fatigue syndrome. The possibility that a novel human retrovirus may be present in patients with the syndrome needs further study. A number of abnormalities found in patients with chronic fatigue syndrome point to central nervous system (CNS) involvement. These include immunologic abnormalities, indications of pituitary and hypothalamic involvement, abnormal basal plasma levels of certain neurotransmitter metabolites, and cerebral perfusion abnormalities. The symptom pattern of chronic fatigue syndrome may eventually be explainable in terms of CNS dysfunction. |
| Bellanti JA. | | [Chronic fatigue syndrome].[article in Spanish] | 612: Rev Alerg Mex 1994 May-Jun;41(3):65-8 | |
| Bennett AL, Fagioli L, Komaroff AL, Raoult D. | | Persistent infection with Bartonella (Rochalimaea) henselae or Afipia felis is unlikely to be a cause of chronic fatigue syndrome. | Clin Infect Dis 1994 Oct;19(4):804-5 | |
| Bertolin Guillen JM, Bedate Villar J. | Centro de Salud Mental, Diputacion Provincial-Servicio Valenciano de Salud. | [Therapeutic guidelines in chronic fatigue syndrome].[article in Spanish] | Actas Luso Esp Neurol Psiquiatr Cienc Afines 1994 May-Jun;22(3):127-30 | The treatment of CFS is not definitive up till now and it is limited both by ignorance of its causes and by different applicable operative case definitions. It has been etiopathologically related to infectious agents, neuromuscular illnesses, neuro-endocrinous-immunologic alterations and to different psychiatric disorders, particularly depressive disorders. Consequently, a great variety of therapeutic strategies have been tried, most of them with insufficient results. Among the medicamentous ones: immunity activator agents such as recombinant interleukin-2, nonspecific immunitary modulators such as seric gamma globulin, antiviral drugs such as acyclovir, muscular relaxants such as ciclobenzaprime, H2 receptor blockers and steroid and nonsteroid anti-inflammatory drugs such as ibuprofen, naproxen and fulbiprofen. Better results seem to have been obtained with antidepressants, and amfebutamone and serotonin-reuptake selective inhibitors are specially promising. Among the nonmedicamentous strategies, cognitive behavioural treatment can be effective and the so called "psychiatric management of the patient with CFS" has been proposed as a global, pragmatic, individualized, comprehensive approach which must be completed with other interdisciplinary interventions on the patient and his environment. |
| Blatch C, Blatt T. | | Chronic fatigue syndrome. Role of psychological factors | BMJ 1994 May 14;308(6939):1297 comment | |

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| | | overemphasised. | in: BMJ. 1994 Jul 23;309(6949):275 comment on: BMJ. 1994 Mar 19;308(6931):756-9 | |
| Bonner D, Ron M, Chalder T, Butler S, Wessely S. | Maudsley Hospital, London, UK. | Chronic fatigue syndrome: a follow up study. | J Neurol Neurosurg Psychiatry 1994 May;57(5):617-21 comment in: J Neurol Neurosurg Psychiatry. 1995 Jun;58(6):764-5 | Forty-six of 47 patients diagnosed as having chronic fatigue and offered treatment four years previously were followed up. Twenty-nine patients were interviewed, three patients refused an interview, and information on the remaining 14 was obtained from their general practitioners. All the instruments used at interview had been used in the initial study. The long-term prognosis for patients with chronic fatigue syndrome who have initially responded to treatment is good. Spontaneous recovery in those who declined or who did not benefit from treatment is unlikely. Patients who continue to fulfil the criteria for chronic fatigue syndrome four years after they were initially diagnosed are likely to have had more somatic disorders, to have been more fatigued, and to have had a previous psychiatric history when they were initially assessed. |
| Branco JC, Tavares V, Abreu I, Humbel RL. | Unidade de Reumatologia, Hospital de Egas Moniz, Lisboa. | [Viral infection and fibromyalgia].[article in Portuguese] | Acta Med Port 1994 Jun;7(6):337-41 | Fibromyalgia (FM) is a very frequent syndrome of unknown cause, characterized by generalized pain, fatigue and a number of tender points to palpation. Among the several etiopathogenic hypotheses discussed, the association of FM with some viral infections has been the object of multiple studies due to its relation and similarity with the chronic fatigue syndrome, acknowledges as being related, although not exclusively, with the chronic infection by the Epstein-Barr virus. Many individual descriptions of association between infection with the human parvovirus B19 and FM led us to carry out this study, comparing the serology for that virus in 52 patients with FM and 39 healthy controls. The titers of specific IgG anti-parvovirus B19 antibodies, indicating previous infection with that virus, were determined in all 91 individuals through ELISA method and at the same laboratory. Results revealed, though not significantly, a greater prevalence of positive titers, of which the mean was also higher, in patients than in controls. When comparing the women from both groups, this tendency was even less perceptible. These data imply that there is no etiologic association between infection with the human parvovirus B19 and FM. |
| Briggs NC, Levine PH. | Viral Epidemiology Branch, NCI/NIH, Bethesda, Maryland 20892. | A comparative review of systemic and neurological symptomatology in 12 outbreaks collectively described as chronic fatigue syndrome, epidemic neuromyasthenia, and myalgic encephalomyelitis. | Clin Infect Dis 1994 Jan;18 Suppl 1:S32-42 | Outbreaks of illnesses of unknown etiology typified by a chronic relapsing course of constitutional symptoms and nervous system involvement have collectively been referred to as chronic fatigue syndrome, epidemic neuromyasthenia, and myalgic encephalomyelitis. To examine heterogeneity of clinical presentation, a comparative review was undertaken for 12 well-documented outbreaks reported since 1934. A systemic syndrome characterized by excessive fatigue, myalgias, headache, low-grade fever, and other constitutional symptoms was common to cases in all outbreaks. However, marked heterogeneity in the range of neurological features was apparent. On the basis of predominant neurological manifestations, outbreaks could be grouped into four levels of increasing neurological involvement: affective neuropsychological changes (level I); prominent cutaneous sensory symptoms with both affective and cognitive neuropsychological changes (level II); marked objective paresis with cutaneous sensory as well as affective and cognitive neuropsychological changes (level III); and cutaneous sensory, affective and cognitive neuropsychological, posterior column, cranial nerve, and mixed upper and lower motor neuron changes (level IV). Groups with the most prominent objective neurological findings (levels III and IV) comprised exclusively outbreaks reported between the 1930s and 1950s. All but one outbreak in groups with less prominent neurological findings (levels I and II) were reported between the 1960s and 1980s; a range of neurological features was observed for these groups. Because a complete neurological examination is not emphasized as part of the diagnostic workup in current outbreaks, it is possible that less obvious neurological findings may be overlooked. Careful evaluation of neurological features in epidemic and endemic cases of what is now called chronic fatigue syndrome may be one approach to distinguishing subtypes of what has been described in the past as a nosological entity. Review Review, Tutorial |
| Brouwer B, Packer T. | School of Rehabilitation Therapy, Division of Occupational Therapy, Queen's University, Kingston, Ontario, Canada. | Corticospinal excitability in patients diagnosed with chronic fatigue syndrome. | Muscle Nerve 1994 Oct;17(10):1210-2 | |

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| Buchwald D, Garrity D. | Department of Medicine, Harborview Medical Center, Seattle. | Comparison of patients with chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities. | Arch Intern Med 1994 Sep 26;154(18):2049-53 comment in: Arch Intern Med. 1995 Sep 25;155(17):1913 | BACKGROUND: Chronic fatigue syndrome (CFS), fibromyalgia (FM), and multiple chemical sensitivities (MCS) are conditions associated with fatigue and a variety of other symptoms that appear to share many clinical and demographic features. Our objectives were to describe the similarities and differences among patients with CFS, FM, and MCS. Additional objectives were to determine how frequently patients with MCS and FM met the criteria for CFS and if they differed in their health locus of control. METHODS: Demographic, clinical, and psychosocial measures were prospectively collected in 90 patients, 30 each with CFS, FM, and MCS. Patients were recruited from a university-based referral clinic devoted to the evaluation and treatment of chronic fatigue and three private practices. Variables included demographic features, symptoms characteristic of each condition, psychological complaints, a measure of health locus of control, and information on health care use. RESULTS: Overall, the three patient groups were remarkably similar in demographic characteristics and the presence of specific symptoms. Patients with CFS and FM frequently reported symptoms compatible with MCS. Likewise, 70% of patients with FM and 30% of those with MCS met the criteria for CFS. Health care use was substantial among patients with CFS, FM, and MCS, with an average of 22.1, 39.7, and 23.3 visits, respectively, to a medical provider during the prior year. Health locus of control did not differ among the three populations. CONCLUSIONS: In general, demographic and clinical factors and health locus of control do not clearly distinguish patients with CFS, FM, and MCS. Symptoms typical of each disorder are prevalent in the other two conditions. |
| Buchwald D, Pascualy R, Bombardier C, Kith P. | Department of Medicine, University of Washington, Seattle. | Sleep disorders in patients with chronic fatigue. | Clin Infect Dis 1994 Jan;18 Suppl 1:S68-72 | This prospective, cohort study examined the prevalence of sleep disorders among highly selected patients with chronic fatigue. On the basis of responses suggestive of sleep pathology on a screening questionnaire, 59 patients from a university-based clinic for chronic fatigue who had undergone a medical and psychiatric evaluation underwent polysomnography. Criteria for chronic fatigue syndrome (CFS) were met by 64% of patients and those for a current psychiatric disorder were met by 41%. Overall, 41% of patients had abnormal results for a multiple sleep latency test and 81% had at least one sleep disorder, most frequently sleep apnea (44%) and idiopathic hypersomnia (12%). In comparing patients who did and did not meet CFS criteria, no significant differences were found in individual sleep symptoms or sleep disorders. Likewise, symptoms and sleep disorders were unrelated to psychiatric diagnoses. In conclusion, chronically fatigued patients with suggestive symptoms may have potentially treatable coexisting sleep disorders that are not associated with meeting criteria for CFS or a current psychiatric disorder. |
| Buchwald D, Pearlman T, Kith P, Schmaling K. | Department of Medicine, University of Washington, Seattle. | Gender differences in patients with chronic fatigue syndrome. | J Gen Intern Med 1994 Jul;9(7):397-401 | OBJECTIVE: To determine whether there are differences between men and women patients who have chronic fatigue syndrome (CFS) and, if so, to ascertain whether a gender-related pattern exists. DESIGN: A descriptive study of demographic, clinical, and psychosocial measures, the results of which were prospectively collected for patients who had CFS. SETTING: A university-based referral clinic devoted to the evaluation and management of chronic fatigue. PATIENTS: 348 CFS patients who had undergone complete medical evaluations. MEASURES: Clinical variables included symptoms, physical examination findings, and laboratory results. Psychosocial assessment consisted of a structured psychiatric interview, the Medical Outcomes Study Short-form General Health Survey to assess functional status, the General Health Questionnaire to ascertain psychological distress, the Multidimensional Health Locus of Control, and measures of attribution, social support, and coping. MAIN RESULTS: Overall, few gender-related differences were identified. Women had a higher frequency of tender or enlarged lymph nodes (60% versus 33%, $p < 0.01$) and fibromyalgia (36% versus 12%, $p < 0.001$) and lower scores on the physical functioning subscale of the Medical Outcomes Study Short-form General Health Survey (37.6 versus 52.2, $p < 0.01$); men more often had pharyngeal inflammation (42% versus 22%, $p < 0.001$) and reported a higher lifetime prevalence of alcoholism (20% versus 9%, $p < 0.01$). CONCLUSIONS: In general, demographic, clinical, and psychosocial factors do not distinguish men from women CFS patients. |
| Caffery BE, Josephson JE, Samek MJ. | | The ocular signs and symptoms of chronic fatigue syndrome. | J Am Optom Assoc 1994 Mar;65(3):187-91 | BACKGROUND: Chronic Fatigue syndrome (CFS) is a relatively newly defined clinical entity that affects multiple systems including the ocular system. These effects have not been well documented. METHODS: 25 consecutive CFS patients were evaluated and the ocular signs and symptoms were described. RESULTS: Significant ocular symptoms were present in all 25 patients. The most common clinical findings were abnormalities of the preocular tear film and ocular surface (19 patients) and |

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| | | | | reduced accommodation for age (18 patients). CONCLUSIONS: CFS affects the ocular system in many ways. Eye care practitioners should pay particular attention to accommodative needs, ocular surface disease and tear film dysfunction when examining these patients. Further research into the pathophysiology of these ocular findings may lead to a better understanding of the pathophysiology of CFS. |
| Calabrese LH, Davis ME, Wilke WS. | Department of Rheumatic and Immunologic Disease, Cleveland Clinic Foundation, Ohio 44195-5028. | Chronic fatigue syndrome and a disorder resembling Sjogren's syndrome: preliminary report. | Clin Infect Dis 1994 Jan;18 Suppl 1:S28-31 | Chronic fatigue syndrome (CFS), as currently described in the working criteria proposed by the Centers for Disease Control and Prevention (Atlanta), may be associated with multiple, distinct, and possibly unique clinical and/or etiopathogenic subsets. Sjogren's syndrome (SS) is a disease of unknown etiology that is characterized by dryness of the mucous membranes and a variety of autoimmune phenomena and conditions. Subjective manifestations of SS such as neurocognitive dysfunction and fatigue have been stressed by some observers. We have detected a large number of patients with unrecognized SS-like illness in a clinical specializing in CFS and believe the relationship to be more than casual. From January 1991 through April 1992, 172 patients were evaluated for CFS; the SS cohort consisted of 27 females (mean age, 41.9 years). Sixteen of these patients had previously been found to have CFS by a physician, and 11 were self-referred. All patients complained of severe, dominating, chronic fatigue. Complaints of myalgia were prominent; 20 of 27 patients met the criteria for fibromyalgia. Neurocognitive complaints and/or a history of neuropsychiatric disease was frequent. Results of Schirmer's test were abnormal for 16 of 27, and results of minor salivary-gland biopsy were abnormal for 20 of 25. Antibodies to nuclear antigen were present in 16 of 27, but anti-Ro was present in only 1 of 21. In the SS group, 13 of 27 patients met eight or more CDC minor criteria for CFS, and 18 of 27 met six or more of the criteria.(ABSTRACT TRUNCATED AT 250 WORDS) |
| Carver LA, Connallon PF, Flanigan SJ, Crossley-Miller MK. | 159th MASH, Louisiana Army National Guard, Jackson Barracks, New Orleans 70146. | Epstein-Barr virus infection in Desert Storm reservists. | Mil Med 1994 Aug;159(8):580-2 | Approximately 150 U.S. Army reservists from Indiana reported symptoms consistent with chronic fatigue syndrome after returning stateside from the tour of duty in Saudi Arabia. A psychiatric team confirmed the diagnosis, evaluated possible etiology, and treated the service members when appropriate. Those available service members who met the study's diagnostic criteria for chronic fatigue syndrome (n = 37) received an Epstein-Barr virus panel. Seventy-three percent of these selected service members were positive either for an acute or reactivated Epstein-Barr viral infection. These data suggest that service members who suffer from chronic fatigue syndrome may have their symptoms increased and prolonged by secondary viral infections. |
| Chester AC, Levine PH. | Georgetown University Medical Center, Washington, D.C. | Concurrent sick building syndrome and chronic fatigue syndrome: epidemic neuromyasthenia revisited. | Clin Infect Dis 1994 Jan;18 Suppl 1:S43-8 | Sick building syndrome (SBS) is usually characterized by upper respiratory complaints, headache, and mild fatigue. Chronic fatigue syndrome (CFS) is an illness with defined criteria including extreme fatigue, sore throat, headache, and neurological symptoms. We investigated three apparent outbreaks of SBS and observed another more serious illness (or illnesses), characterized predominantly by severe fatigue, that was noted by 9 (90%) of the 10 teachers who frequently used a single conference room at a high school in Truckee, California; 5 (23%) of the 22 responding teachers in the J wing of a high school in Elk Grove, California; and 9 (10%) of the 93 responding workers from an office building in Washington, D.C. In those individuals with severe fatigue, symptoms of mucous membrane irritation that are characteristic of SBS were noted but also noted were neurological complaints not typical of SBS but quite characteristic of CFS. We conclude that CFS is often associated with SBS. |
| Conference proceedings. Albany New York, | | Chronic Fatigue Syndrome: Current Concepts. Conference proceedings. Albany New York, 3-4 October 1992. Overall | Clin Infect Dis 1994 Jan;18 Suppl 1:S1-167 | |
| Connolly S, Fowler CJ. | | Single fibre EMG studies in chronic fatigue syndrome: a reappraisal. | J Neurol Neurosurg Psychiatry 1994 Sep;57(9):1157 comment on: J Neurol Neurosurg Psychiatry. 1994 Mar;57(3):375-6 | |
| Conti F, Priori R, De Petrillo G, Rusconi AC, Arpino C, | Istituto di Clinica Medica I, Universita degli Studi La | Prevalence of chronic fatigue syndrome in Italian patients | Ann Ital Med Int 1994 Oct-Dec;9(4):219-22 | Our study was carried out to determine the prevalence of chronic fatigue syndrome (CFS) within a selected population of patients suffering from persistent fatigue. We studied subjects with recurrent or |

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| Valesini G. | Sapienza di Roma. | with persistent fatigue. | | persistent fatigue lasting 6 months and fulfilling at least four minor Center for Disease Control (CDC) criteria for the diagnosis of CFS. Evaluation included both clinical examination and laboratory testing. All subjects filled out a questionnaire specifically designed to gain information about the length and severity of symptoms, and patients with a previously diagnosed illness associated with fatigue were excluded. The study was carried out at the Fatigue Clinic of an internal medicine unit (Clinica Medica I) of the University of Rome "La Sapienza". Sixty-three subjects, residents of the Lazio region (central Italy), completed the diagnostic assessment. Alternative diagnoses were established in 37 (59%) of the 63 patients. A diagnosis of CFS based on the CDC criteria was established in only 6 cases. In 2 subjects, CFS had appeared following infectious mononucleosis, and no definitive diagnosis could be formulated for 18 patients. In Italy, CFS seems to be an infrequent cause of severe and persistent fatigue in a selected population. Numerous morbid conditions may be responsible for a clinical picture closely resembling CFS. We recommend that patients suffering from fatigue be thoroughly evaluated. |
| Cox D, Findley L. | | Chronic fatigue syndrome in adolescence. | Br J Hosp Med 1994 Jun 1-14;51(11):614 comment on: Br J Hosp Med. 1994 Feb 2-15;51(3)::110-2 | |
| Dantzer R. | INRA-INSERM U 176, Bordeaux. | [Current studies on the neurobiology of chronic fatigue syndrome]. [article in French] | Encephale 1994 Nov;20 Spec No 3:597-602 | Cytokines are soluble mediators which are released by activated immune cells during infection and inflammation. The possibility that fatigue is mediated by the effects of cytokines on the central nervous system is supported by several converging lines of evidence: 1) infusions of cytokines to immunocompromised patients induce flu-like symptoms including fatigue and malaise; 2) peripheral and central injection of cytokines to laboratory rodents induce sickness behaviour; 3) symptoms of sickness behaviour occurring during experimental infections can be abrogated by administration of anti-cytokine treatments; 4) although many pitfalls in the detection of cytokines still exist, patients afflicted with the chronic fatigue syndrome have been found in some studies to display instances of excessive production of cytokines. Experimental studies have confirmed that cytokines are interpreted by the brain as internal signals for sickness. Furthermore, there is evidence that sickness is a motivation which reorganizes the organism's priorities in face of this particular threat which is represented by infectious pathogens. The elucidation of the mechanisms that are involved in these effects and in particular, the role of the cytokines which are produced in the brain in response to peripheral immune stimuli and to stressors, should give new insight on the way sickness and recovery processes are organized in the brain. |
| Deale A, David AS. | Department of Psychological Medicine, King's College Hospital, London, United Kingdom. | Chronic fatigue syndrome: evaluation and management. | J Neuropsychiatry Clin Neurosci 1994 Spring;6(2):189-94 | |
| Deluca J, Johnson SK, Natelson BH. | Kessler Institute for Rehabilitation, Department of Research, West Orange, New Jersey 07052, USA. | Neuropsychiatric status of patients with chronic fatigue syndrome: an overview. | Toxicol Ind Health 1994 Jul-Oct;10(4-5):513-22 | Chronic fatigue syndrome (CFS) is an illness that results in debilitating fatigue as well as rheumatological, infectious, and neuropsychiatric symptoms. The present paper is a brief overview of the neuropsychological and psychiatric research on CFS. Studies from our laboratory contrasting CFS with patients with multiple sclerosis, depression, and healthy controls are detailed. Our hypothesis of neuropsychological impairments in CFS is discussed. |
| Demitrack MA, Engleberg NC. | University of Michigan Medical School, Ann Arbor. | Chronic fatigue syndrome. | Curr Ther Endocrinol Metab 1994;5:135-42 | |
| Demitrack MA. Review Review, Tutorial | | Chronic fatigue syndrome: a disease of the hypothalamic-pituitary-adrenal axis? | Ann Med 1994 Feb;26(1):1-5 | |
| Dworkin HJ, Lawrie C, Bohdiewicz P, Lerner AM. | William Beaumont Hospital, Nuclear Medicine Department, Royal Oak, MI 48073. | Abnormal left ventricular myocardial dynamics in eleven patients with chronic fatigue syndrome. | Clin Nucl Med 1994 Aug;19(8):675-7 | Eleven patients diagnosed with chronic fatigue syndrome were found to have abnormal left ventricular myocardial dynamics as indicated on MUGA studies. Among the abnormalities noted were abnormal wall motion at rest and stress, dilatation of the left ventricle, and segmental wall motion abnormalities. |
| Eicosanoids and essential fatty acid modulation in | Gray JB, Martinovic AM. | Erratum in: Med Hypotheses 1995 Aug;45(2):219 | Med Hypotheses 1994 Jul;43(1):31-42 | Abnormalities of Essential Fatty Acid (EFA) incorporation into phospholipid are found in chronic diseases. More recently changes in circulating EFA metabolites (EFAM) together with EFAM hypo- |

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| chronic disease and the chronic fatigue syndrome. | | | | responsiveness of immune cells and EFAM production from cells have been found associated with disease. We hypothesize that changes in ratio of EFAMs are the normal physiological responses to stressors, but when stressors are excessive or prolonged, EFAM systems may become unpredictably hypo-responsive owing to factors such as receptor down regulation and substrate depletion. In time, many homeostatic system become deranged and held in that state by minor stressors. Literature review of chronic fatigue syndrome (CFS) shows hyper and hypo-responsiveness in immune function, several Hypothalamo-Pituitary (HP) axes and sympathetic nervous system, all relatable to dysfunctional changes in EFA metabolism. For the first time, we explain chronic immune system activation and hypo-responsive immune function in CFS; through EFAMs. Dietary EFA modulation (DEFA) can alter ratios of both membrane EFAs and produced EFAMs, and if maintained can restore hypo-responsive function. We discuss dietary strategies and relevance in CFS, and a case series of CFS patients applying DEFA with other titrated published managements which saw 90% gaining improvement within 3 months and more than 2/3 fit for full time duties. This hypothesis and DEFA may have relevance in other chronic conditions. Review, Academic |
| Fenske TK, Davis P, Aaron SL. | Department of Medicine, University of Alberta, Edmonton, Canada. | Human adjuvant disease revisited: a review of eleven post-augmentation mammoplasty patients. | Clin Exp Rheumatol 1994 Sep-Oct;12(5):477-81 | OBJECTIVES: We have reviewed 11 women post-augmentation mammoplasty who were referred to our clinic with diffuse rheumatic complaints. All patients had undergone mammoplasty with silicone gel-filled implants prior to the onset of their locomotor symptoms (mean latency time 7.8 years). One physician interviewed and examined each of these patients following a standardized format for clinical retrieval. RESULTS: Of the patients reviewed, 6 patients had clinical fibromyalgia based on the ACR criteria, and the remaining 5 patients had symptoms consistent with the "chronic fatigue syndrome." None of our patients were found to have evidence of a defined connective tissue disease. Antinuclear antibodies were detected in 4 (36%) patients and low level titres of extractable nuclear antigens in only 2 (18%). CONCLUSIONS: Previously a causal relationship between the use of silicone gel-filled breast implants and the subsequent development of symptoms referred to as human adjuvant disease (HAD) has been proposed. On the basis of currently accepted criteria we have preferred to diagnose our post-mammoplasty patients without specific connective tissue disease, as having chronic fatigue syndrome (CFS), or when tender points are present, as having fibromyalgia (FMS), rather than implying that such cases represent a separate and unique rheumatological disease entity. In the light of our current understanding of CFS and FMS, a relationship between them and the previous silicone mammoplasty seems possible. |
| Fiedler N, Kipen H, Deluca J, Kelly-McNeil K, Natelson B. | UMDNJ-Robert Wood Johnson Medical School, Environmental and Occupational Health Sciences Institute, Piscataway 08855, USA. | Neuropsychology and psychology of MCS. | Toxicol Ind Health 1994 Jul-Oct;10(4-5):545-54 | Neurological symptoms are frequently reported by patients with multiple chemical sensitivities (MCS). Methods to compare the psychiatric, personality, and neuropsychological function of patients with MCS, chronic fatigue syndrome (CFS), and normal controls are described. Increased rates of Axis I psychiatric diagnoses are observed in the literature for MCS and CFS subjects relative to controls. Findings on the MMPI-2 and the Toronto Alexithymia Scale reveal profiles consistent with the tendency to report somatic rather than emotional symptoms in response to stress. However, many of the reported somatic symptoms also coincide with those found in neurologic disorders. The overall neuropsychological profile for MCS subjects does not reflect cognitive impairment. Relative to normal controls, the only difference in neuropsychological performance observed is reduced recognition of nontarget designs on a visual memory task. More fruitful areas for future psychological research will include measurement of the interaction between behavioral response styles and attentional processes in cognition, as well as observations under controlled challenge conditions. |
| Fox DS. | | Chronic fatigue syndrome: a review and practical guide. | J Am Acad Nurse Pract 1994 Dec;6(12):565-70 | Diagnosis and management of chronic fatigue syndrome (CFS) is a difficult challenge for nurse practitioners. The syndrome is widespread, poorly-defined, and problematic. Despite extensive etiologic research, no cause has been identified. Each case should be carefully evaluated for possible organic, psychiatric, and other factors reported as potential causes. Clinical manifestations, possible causes, and options for management are reviewed. |
| Friedberg F, Krupp LB. | Department of Psychiatry, State University of New York at Stony Brook. | A comparison of cognitive behavioral treatment for chronic fatigue syndrome and primary depression. | Clin Infect Dis 1994 Jan;18 Suppl 1:S105-10 comment in: Clin Infect Dis. 1995 Mar;20(3):717-8 | To evaluate the effect of cognitive behavioral intervention on chronic fatigue syndrome (CFS), we studied three patient groups: a CFS-treatment group (n = 22), a primary depression-treatment group (n = 20), and a no-treatment control group of subjects with CFS (n = 22). For the CFS-treatment group, a trend toward reduced depression-symptom scores was noted, but there were no significant changes in stress-related symptoms or fatigue severity. For the most depressed treated subjects with CFS, |

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| | | | | significant score reductions were observed in measures of depression, stress, fatigue severity, and fatigue-related thinking. In the depression group, significant reductions in depression, stress, and fatigue severity scores were found. No significant changes in any measure were observed in the CFS control group. A new fatigue-related cognitions scale, developed to assess cognitive and emotional reactions to fatigue, showed a significant reduction in such reactions in the CFS-treatment group, a finding suggesting that depression in this group was mediated by maladaptive thinking. The results suggest that a subset of CFS patients with cognition-related depressive symptomatology may respond to short-term behavioral intervention. |
| Fudenberg NH. | | Treatment for chronic fatigue syndrome. | Am J Med 1994 Nov;97(5):493-4 comment on: Am J Med. 1993 Feb;94(2):197-203 | |
| Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. | Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333. | The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. | Ann Intern Med 1994 Dec 15;121(12):953-9 comment in: Ann Intern Med. 1995 Jul 1;123(1):74-5 Ann Intern Med. 1995 Jul 1;123(1):75; discussion 76 | The complexities of the chronic fatigue syndrome and the methodologic problems associated with its study indicate the need for a comprehensive, systematic, and integrated approach to the evaluation, classification, and study of persons with this condition and other fatiguing illnesses. We propose a conceptual framework and a set of guidelines that provide such an approach. Our guidelines include recommendations for the clinical evaluation of fatigued persons, a revised case definition of the chronic fatigue syndrome, and a strategy for subgrouping fatigued persons in formal investigations. |
| Gardner W. | | Hyperventilation and chronic fatigue syndrome. | QJM 1994 Jul;87(7):443 | |
| Goldenberg DL. | Newton-Wellesley Hospital, Massachusetts. | Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome. | Curr Opin Rheumatol 1994 Mar;6(2):223-33 | No major pathophysiologic or therapeutic findings have appeared over the past year regarding fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome, three poorly understood, controversial, and overlapping syndromes. The frequent prevalence of these disorders in association with Lyme disease and other medical and psychiatric illness was emphasized. New studies demonstrated the potential role for central nervous system activation in fibromyalgia and chronic fatigue syndrome. |
| Goudsmit EM. | | Chronic fatigue syndrome. Distinguish between syndromes... | BMJ 1994 May 14;308(6939):1297-8 comment in: BMJ. 1994 Jul 23;309(6949):275 comment on: BMJ. 1994 Mar 19;308(6931):756-9 | |
| Gow JW, Behan WM, Simpson K, McGarry F, Keir S, Behan PO. | Department of Neurology, University of Glasgow, Scotland, United Kingdom. | Studies on enterovirus in patients with chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S126-9 | A large study on 121 patients with the chronic fatigue syndrome (CFS) that examined muscle biopsy samples for enterovirus by means of polymerase chain reaction analysis was carried out. The results were compared with those obtained from 101 muscle biopsy specimens from patients with a variety of other neuromuscular disorders (OND), including neurogenic atrophies, dystrophies, and mitochondrial, metabolic, and endocrine myopathies. Thirty-two (26.4%) of the biopsy specimens from the group of patients with CFS were positive, compared with 20 (19.8%) from the group of patients with OND, a difference that was not significant. This finding is in contrast to those of our previous smaller study in which significantly more patients with CFS than control subjects (53% [32 of 60] vs. 15% [6 of 41]) had enterovirus RNA sequences in their muscle. It was concluded that it is unlikely that persistent enterovirus infection plays a pathogenetic role in CFS, although an effect in initiating the disease process cannot be excluded. |
| Hauben M. | | Quinacrine and chronic fatigue syndrome. | Am Fam Physician 1994 May 1;49(6):1354 | |
| Henderson DA. | Executive Office of the President, Office of Science and Technology Policy, Washington, D.C. | Reflections on epidemic neuromyasthenia (chronic fatigue syndrome). | Clin Infect Dis 1994 Jan;18 Suppl 1:S3-6; discussion S7-9 | Personal Name as Subject: Henderson DA |
| Heneine W, Woods TC, Sinha SD, Khan AS, | Retrovirus Diseases Branch, Centers for Disease Control | Lack of evidence for infection with known human and animal | Clin Infect Dis 1994 Jan;18 Suppl 1:S121-5 | We investigated 21 patients with chronic fatigue syndrome who were identified through the surveillance system of the Centers for Disease Control and Prevention (CDC) in Atlanta for the |

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| Chapman LE, Schonberger LB, Folks TM. | and Prevention, Atlanta, Georgia 30333. | retroviruses in patients with chronic fatigue syndrome. | | presence of several human and animal retroviruses. In addition, we evaluated 21 CDC employee controls matched with the patients for age (+/- 5 years), gender, and race. The viruses tested included human T-lymphotropic viruses types I and II; human spuma retrovirus; simian T-lymphotropic virus type I; simian retroviruses types 1, 2, and 3; bovine leukemia virus; feline leukemia virus; and gibbon ape leukemia virus. Samples of peripheral blood lymphocytes and leukocytes from patients and controls were analyzed in a blinded fashion for retroviral sequences; polymerase chain reaction (PCR) amplification assays and Southern blot hybridization to 32P-labeled internal oligoprobes were used. All PCR assays were optimized for maximal sensitivity on respective infected cell lines or plasmids, and sensitivity controls were included in each experiment. All samples from patients and controls were negative for the tested retroviral sequences. Our data indicate that none of these retroviruses plays an etiologic role or is a cofactor in the chronic fatigue syndrome illnesses of our study population. |
| Hilgers A, Frank J. | Institut fur angewandte Immunologie und Umweltmedizin, Dusseldorf. | [Chronic fatigue syndrome: immune dysfunction, role of pathogens and toxic agents and neurological and cardiac changes].[article in German] | Wien Med Wochenschr 1994;144(16):399-406 | 375 patients with chronic fatigue syndrome (CFS) were examined using a standardized questionnaire and subsequent interview on 11 risk factors and 45 symptoms. Additionally immunologic, serologic, toxicologic, neuroradiologic, neurophysiologic and cardiologic investigations were performed. Immunologic tests showed cellular immunodeficiencies particularly in functional regard (pathological lymphocyte stimulation in 50% of the patients, disorders of granulocyte function in 44%). Furthermore variable deviations were found in the lymphocyte subpopulations (CD3, CD4, CD8, CD19, DR, Leu 11 + 19). In the humoral part tendencies to low IgG-3- and IgG-1-subclass-levels occurred (59% respectively 11% of the patients) also as decreases in complement system (CH50, C3, C4, C1-esterase-inhibitor). In the group of activation markers and cytokines 42% of the investigated patients had circulating immune complexes (CIC), 47% increases of tumor-necrosis-factor (TNF-a) and 21% increases of soluble interleukin-2-receptor (IL-2-R). The increased occurrence of autoantibodies in the CFS-patients (specially antinuclear anti-bodies [ANA], microsomal thyroid antibodies) suggest, that CFS is associated with or the beginning of manifest autoimmune disease. Under the pathogens 78% of the patients had a striking serological constellation of Epstein-Barr-Virus (EBV-EA positive, low EBNA-titers), in the HHV-6-Virus 47% showed increased antibody-titers. Tests on further herpes viruses and on Borreliae, Chlamydiae, Candida and Amoebae were positive in 8 to 36% of the examined patients. Furthermore there were found variable deficits of vitamins and trace elements also as hormonal disturbances.(ABSTRACT TRUNCATED AT 250 WORDS) |
| Hinds G, Bell NP, McMaster D, McCluskey DR. | Department of Medicine, Queen's University of Belfast, Northern Ireland, UK. | Normal red cell magnesium concentrations and magnesium loading tests in patients with chronic fatigue syndrome. | Ann Clin Biochem 1994 Sep;31 (Pt 5):459-61 | Red blood cell magnesium concentrations were measured in samples from 89 patients who fulfilled the diagnostic criteria for chronic fatigue syndrome and the results compared to those found in an age and sex matched group selected from the normal population. No significant difference was found. Six patients were further investigated using a magnesium loading test to determine if there was any evidence of magnesium deficiency associated with this disorder. None was found. There is therefore no indication for the use of magnesium therapy in the management of this condition. |
| Hoey M. | | Chronic fatigue syndrome. What is happening to M.E.? | Aust Nurs J 1994 Oct;2(4):18-20 | |
| Howes S. | | Chronic fatigue syndrome. ME Association is honest about prognosis. | BMJ 1994 May 14;308(6939):1299-300 comment on: BMJ. 1994 Mar 19;308(6931):732-3 | |
| Howes S. | | Chronic fatigue syndrome or myalgic encephalitis. | Lancet 1994 Jan 22;343(8891):243 comment on: Lancet. 1993 Nov 13;342(8881):1247-8 | |
| Ho-Yen DO, Grant A. | | Chronic fatigue syndrome. Self help groups give valuable support. | BMJ 1994 May 14;308(6939):1298-9 | |
| Ho-Yen DO, Shanks M. | | Chronic fatigue syndrome. Prevalence study overlooked. | BMJ 1994 May 14;308(6939):1299 comment on: BMJ. 1994 Mar | |

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| Ho-Yen DO. | | Chronic fatigue syndrome and fibromyalgia. | BMJ 1994 Dec 3;309(6967):1515 comment on: BMJ. 1994 Sep 17;309(6956):696-9 | |
| Jason LA, Taylor SL. | Department of Psychology, DePaul University, Chicago, Illinois 60614, USA. | Monitoring chronic fatigue syndrome. | J Nerv Ment Dis 1994 Apr;182(4):243-4 | |
| Jefferies WM. | Case-Western Reserve University School of Medicine, Cleveland, Ohio. | Mild adrenocortical deficiency, chronic allergies, autoimmune disorders and the chronic fatigue syndrome: a continuation of the cortisone story. | Med Hypotheses 1994 Mar;42(3):183-9 | The possibility that patients with disorders that improve with administration of large, pharmacologic dosages of glucocorticoids, such as chronic allergies and autoimmune disorders, might have mild deficiency of cortisol production or utilization has received little attention. Yet evidence that patients with rheumatoid arthritis improved with small, physiologic dosages of cortisol or cortisone acetate was reported over 25 years ago, and that patients with chronic allergic disorders or unexplained chronic fatigue also improved with administration of such small dosages was reported over 15 years ago, suggesting that these disorders might be associated with mild adrenocortical deficiency. The apparent reasons for the failure of these reports to be confirmed or mentioned in medical textbooks and the facts needed to restore perspective are reviewed, and the need for further studies of the possible relationship of a mild deficiency of the production or utilization of cortisol and possibly other normal adrenocortical hormones to the development of these disorders is discussed. |
| Johnson SK, DeLuca J, Fiedler N, Natelson BH. | Department of Physical Medicine, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark. | Cognitive functioning of patients with chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S84-5 | Neuropsychological problems are a distressing and frequent component of the symptom complex associated with chronic fatigue syndrome. Objective assessment of these difficulties is essential to understanding the nature of this illness. Results of the studies discussed in this paper suggest that impaired information processing, rather than primary memory dysfunction, may be at the root of the cognitive problems that afflict so many patients with CFS. |
| Johnston JH. | | Chronic fatigue syndrome in Army general practice. | J R Army Med Corps 1994 Jun;140(2):59-60 comment in: J R Army Med Corps. 1996 Jun;142(2):85 | |
| Khoury PB. | | Chronic fatigue syndrome (CFS) and psychiatric disorders. | Am J Med 1994 May;96(5):485-6 comment on: Am J Med. 1991 Oct;91(4):335-44 Am J Med. 1992 Jun;92(6):710 | |
| Kim E. | University of South Florida College of Medicine. | A brief history of chronic fatigue syndrome. | JAMA 1994 Oct 5;272(13):1070-1 | |
| King JC, Goddard MJ. | University of Texas Health Science Center, San Antonio 78284. | Pain rehabilitation. 2. Chronic pain syndrome and myofascial pain | Arch Phys Med Rehabil 1994 May;75(5 Spec No):S9-14. | This article highlights chronic pain syndrome and myofascial pain. It is part of the chapter on pain rehabilitation in the Self-Directed Medical Knowledge Program for practitioners and trainees in physical medicine and rehabilitation. This article discusses behavioral maladaptations to chronic pain which lead to global physical, psychologic, social, and vocational impairments--the chronic pain syndrome. The spectrum of myofascial pain syndromes, contributing factors, and interventions are detailed. New advances that are covered in this section include controversies in long-term use of opioids and muscle relaxants; differentiating fibromyalgia, myofascial pain syndromes, and chronic fatigue syndrome; pathophysiology of myofascial pain; and beneficial treatments. |
| Kohler D. | | [Sleep apnea as the cause of chronic fatigue syndrome]. [article in German] | Med Klin 1994 Aug 15;89(8):457 | |
| Krueger GR, Klueppelberg U, Hoffmann A, Ablashi DV. | Immunopathology Section, University of Cologne, Germany. | Clinical correlates of infection with human herpesvirus-6. | In Vivo 1994 Jul-Aug;8(4):457-85 | Human herpesvirus-6 is a lymphotropic virus which infects susceptible individuals during the first year of life and usually causes life-long latency. In a variable percentage primary infections are followed by a short acute disease, exanthema subitum. Older individuals may suffer from infectious mononucleosis-like illnesses or from Kikuchi-Fujimoto's disease. In addition, there is a fairly wide spectrum of lymphoid and hematopoietic diseases or autoimmune disorders, which are associated with |

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| | | | | elevated titers of HHV-6 antibody, and from which replicating virus may be isolated. Such diseases include atypical polyclonal lymphoproliferation, Hodgkin's disease, chronic fatigue syndrome and systemic lupus erythematosus. The present article reviews the current knowledge of such associations. Review, Academic |
| Krupp LB, Sliwinski M, Masur DM, Friedberg F, Coyle PK. | Department of Neurology, State University of New York-Stony Brook. | Cognitive functioning and depression in patients with chronic fatigue syndrome and multiple sclerosis. | Arch Neurol 1994 Jul;51(7):705-10 | OBJECTIVE: To assess cognitive function in patients with chronic fatigue syndrome (CFS) and multiple sclerosis (MS) and to evaluate the role of depressive symptoms in cognitive performance. DESIGN: Case-control. All subjects were given a neuropsychological battery, self-report measures of depression and fatigue, and a global cognitive impairment rating by a neuropsychologist "blinded" to clinical diagnosis. Patients with MS and CFS were additionally evaluated with a Structured Clinical Interview for DSM-III-R (Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition) disorders. SETTING: Institutional and private neurological practices and the community at large. PATIENTS: Twenty patients with CFS diagnosed in accord with the Centers for Disease Control and Prevention-revised criteria who had cognitive complaints; 20 patients with clinically definite MS who were ambulatory and were matched for fatigue severity, age, and education to CFS subjects; and 20 age- and education-matched healthy controls. RESULTS: Patients with CFS had significantly elevated depression symptoms compared with patients with MS and healthy controls ($P < .001$) and had a greater lifetime prevalence of depression and dysthymia compared with MS subjects. Patients with CFS, relative to controls, performed more poorly on the Digit Symbol subtest ($P = .023$) and showed a trend for poorer performance on logical memory ($P = .087$). Patients with MS compared with controls had more widespread differences of greater magnitude on the Digit Span ($P < .004$) and Digit Symbol ($P < .001$), Trail Making parts A ($P = .022$) and B ($P = .037$), and Controlled Oral Word Association ($P = .043$) tests. Patients with MS also showed a trend of poorer performance on the Booklet Category Test ($P = .089$). When patients with CFS and MS were directly compared, MS subjects had lower scores on all measures, but the differences reached significance only for the Digit Span measure of attention ($P = .035$). CONCLUSIONS: Patients with CFS compared with MS have more depressive symptoms but less cognitive impairment. Relative to controls, a subset of CFS subjects did poorly on tests of visuomotor search and on the logical memory measure of the Wechsler Memory Scale-revised. Poor performance of logical memory in CFS appears to be related to depression, while visuomotor deficits in CFS are unrelated. Cognitive deficits in patients with MS are more widespread compared with those in patients with CFS and are independent of depressive symptoms. |
| Kuratsune H, Yamaguti K, Takahashi M, Misaki H, Tagawa S, Kitani T. | Osaka University Medical School, Japan. | Acylcarnitine deficiency in chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S62-7 | One of the characteristic complaints of patients with chronic fatigue syndrome (CFS) is the skeletal muscle-related symptom. However, the abnormalities in the skeletal muscle that explain the symptom are not clear. Herein, we show that our patients with CFS had a deficiency of serum acylcarnitine. As carnitine has an important role in energy production and modulation of the intramitochondrial coenzyme A (CoA)/acyl-CoA ratio in the skeletal muscle, this deficiency might induce an energy deficit and/or abnormality of the intramitochondrial condition in the skeletal muscle, thus resulting in general fatigue, myalgia, muscle weakness, and postexertional malaise in patients with CFS. Furthermore, the concentration of serum acylcarnitine in patients with CFS tended to increase to the normal level with the recovery of general fatigue. Therefore, the measurement of acylcarnitine would be a useful tool for the diagnosis and assessment of the degree of clinical manifestation in patients with CFS. |
| Lane RJ, Woodrow D, Archard LC. | | Lactate responses to exercise in chronic fatigue syndrome. | J Neurol Neurosurg Psychiatry 1994 May;57(5):662-3 comment on: J Neurol Neurosurg Psychiatry. 1993 Sep;56(9):993-8 | |
| Lanham RJ. | Division of General Medicine, University at Buffalo, Erie County Medical Center, New York 14215, USA. | Chronic fatigue syndrome: a diagnostic challenge for the laboratory. | Clin Lab Sci 1994 Sep-Oct;7(5):279-82 | OBJECTIVE: To review the literature and current research about the causes of chronic fatigue syndrome (CFS). DATA SOURCES: Recent research articles about CFS and data gathered by the author. STUDY SELECTION: Performed by the author. DATA EXTRACTION: Performed by the author. DATA SYNTHESIS: Chronic fatigue syndrome (CFS) is a disease of pain, excessive fatigue after minor exertion, cognitive difficulties, and other symptoms-all occurring in cycles. While its |

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| | | | | etiology is unclear, CFS is associated with abnormal results of immune system tests. There is no specific marker for the illness. Treatment is symptomatic, and the long-term outlook for recovery is good. CONCLUSION: A rational, symptomatic approach to treating CFS patients can be made using the model developed at the author's institution. Research into the causes of CFS must continue. |
| Lawrie SM, MacHale SM. | | Chronic fatigue syndrome. | Lancet 1994 Nov 26;344(8935):1514 comment in: Lancet. 1995 Jan 14;345(8942):131 comment on: Lancet. 1994 Sep 24;344(8926):864-8 | |
| Lawrie SM, Pelosi AJ. | | Chronic fatigue syndrome and myalgic encephalomyelitis. | BMJ 1994 Jul 23;309(6949):275 comment on: BMJ. 1994 May 14;308(6939):1297 BMJ. 1994 May 14;308(6939):1297-8 | |
| Lawrie SM, Pelosi AJ. Editorial | | Chronic fatigue syndrome: prevalence and outcome. | BMJ 1994 Mar 19;308(6931):732-3 comment in: BMJ. 1994 May 14;308(6939):1298 BMJ. 1994 May 14;308(6939):1299 BMJ. 1994 May 14;308(6939):1299-300 comment on: BMJ. 1994 Mar 19;308(6931):776-7 | |
| Levine PH, Atherton M, Fears T, Hoover R. | Viral Epidemiology Branch, National Cancer Institute, Bethesda, Maryland 20892. | An approach to studies of cancer subsequent to clusters of chronic fatigue syndrome: use of data from the Nevada State Cancer Registry. | Clin Infect Dis 1994 Jan;18 Suppl 1:S49-53 | Chronic fatigue syndrome (CFS) has been increasingly associated with immune dysregulation, including depressed natural killer cell activity; this phenomenon is associated with increased susceptibility to cancer. Although anecdotal reports have suggested an association between CFS and cancer, particularly non-Hodgkin's lymphoma and brain cancer, there has been no a priori justification for evaluating such an association and no consideration of relevant parameters, such as length of latent period vs. tumor type. We reviewed data from the Nevada State Cancer Registry subsequent to a reported outbreak of a CFS-like illness in Nevada that occurred during 1984-1986. We concentrated on non-Hodgkin's lymphoma and brain/CNS tumors, with particular emphasis on persons 15-34 and 35-54 years of age. An upward trend in the incidence of brain/CNS tumors, which could be related to a national upward trend for this disease, was noted. No consistent trends were noted for non-Hodgkin's lymphoma. Because of the difficulties inherent in studies of cancer subsequent to various exposures, we evaluated the methodology for determining an association between outbreaks of CFS-like disease and cancer. We propose several approaches that should be considered in future studies for investigation of possible associations between CFS and cancer, including expected latent periods for specific tumors. |
| Levine PH. | Viral Epidemiology Branch, National Cancer Institute, Bethesda, Maryland 20892. | Epidemiology of chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S57-60 | |
| Levine PH. | Viral Epidemiology Branch, National Cancer Institute, Bethesda, Maryland 20892. | Epidemic neuromyasthenia and chronic fatigue syndrome: epidemiological importance of a cluster definition. | Clin Infect Dis 1994 Jan;18 Suppl 1:S16-20 | Outbreaks of illness variously identified by a number of terms, including epidemic neuromyasthenia, myalgic encephalomyelitis, Iceland disease, and atypical poliomyelitis, have been reported from many countries during the past 45 years. Since the first well-described outbreak occurring in 1934, > 60 outbreaks have been reported, but few of these have been described in considerable detail. These outbreaks are usually cited in historical reports of chronic fatigue syndrome (CFS) since each of these outbreaks appears to contain a number of cases meeting the current case definition of CFS. There has been inadequate attention given to the fact that epidemic neuromyasthenia and related clusters characterized by various complaints, including fatigue, do not have an accepted epidemiological or clinical definition, and only rarely have descriptions of these clusters included a specific case definition. When such case definitions have been applied, the occurrence of cases meeting the current |

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| | | | | case definition for CFS appears to be both variable and infrequent. This report utilizes examples of several well-documented outbreaks to emphasize specific aspects that should be considered in the investigation of future clusters. |
| Levy JA. | Department of Medicine, University of California School of Medicine, San Francisco. | Viral studies of chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S117-20 | Chronic fatigue syndrome (CFS) has many characteristics suggesting persistent fatigue following a viral illness. At least nine different RNA and DNA viruses have been considered to be associated with this disease, but none of these viruses has been found to be the etiologic agent. Immunologic studies have demonstrated activated CD8+ cells and reduced function of natural killer cells suggesting a host response to an infection that has led to persistent immune disorders. Some of the symptoms of CFS may be due to cytokines produced by this hyperactive immune response to a virus that is still present in the host or that has been eliminated but leaves abnormal immunologic sequelae. These possibilities offer directions for future studies of CFS and therapeutic approaches to this condition. |
| Lewis S, Cooper CL, Bennett D. | Department of Psychology and Speech Pathology, Manchester Metropolitan University. | Psychosocial factors and chronic fatigue syndrome. | Psychol Med 1994 Aug;24(3):661-71 | This study investigated the number and severity of life events, Type A behaviour, coping strategies and social support differences between chronic fatigue and irritable bowel syndrome patients prior to illness and between these groups and healthy controls. Although few differences were found between the groups for life events, a number of interesting results emerged with regard to different aspects of Type A behaviour, various coping strategies and social support. These findings are discussed with respect to existing research in the field. |
| Lloyd A, Gandevia S, Brockman A, Hales J, Wakefield D. | Department of Infectious Diseases, Prince Henry Hospital, Little Bay, New South Wales, Australia. | Cytokine production and fatigue in patients with chronic fatigue syndrome and healthy control subjects in response to exercise. | Clin Infect Dis 1994 Jan;18 Suppl 1:S142-6 | We have studied the relationship between the cytokine production induced in vivo by prolonged isometric exercise and the symptom complex marked by fatigue in patients with chronic fatigue syndrome (CFS). Twelve male patients and 13 matched male control subjects undertook an isometric hand-grip exercise protocol utilizing dynamometers. Subjects undertook 30 minutes of exercise, for which the target force was set at 40% of the maximal voluntary contraction and the duty cycle was 50%. Prior to, during, and for 24 hours following the exercise, blood samples were collected and assayed for the presence of cytokines, including interferon-gamma and interferon-alpha, interleukin-1 beta, and tumor necrosis factor-alpha. At those times subjects also completed the Profile of Mood States (POMS) questionnaire, which served as a measure of changes in subjective fatigue. No significant alteration in the level of any of the cytokines in the plasma of patients or control subjects was detected before, during, or after exercise. Surprisingly, the patients' levels of fatigue, depression, and confusion, as measured by the POMS, decreased in response to the exercise. These data do not confirm the presence of an immunologic process correlating with the exacerbation of fatigue after exercise experienced by patients with CFS. Limitations in the study design and in the sensitivity of the cytokine assays may have affected our results. |
| Lloyd A, Pender H. | | Chronic fatigue syndrome: does it need more healthcare resources? | Pharmacoeconomics 1994 Jun;5(6):460-4 | |
| Lund-Olesen LH, Lund-Olesen K. | Department of Radiology, Svendborg Hospital, Denmark. | The etiology and possible treatment of chronic fatigue syndrome/fibromyalgia. | Med Hypotheses 1994 Jul;43(1):55-8 | It is suggested that chronic fatigue syndrome/fibromyalgia is caused by virus injury to the calcium channels leading to larger quantities than usual of calcium ions entering the striated muscle cells. Should this be true, then treatment with a calcium antagonist (CA) may possibly be of value. |
| MacLean G, Wessely S. | Academic Department of Psychological Medicine, King's College School of Medicine and Dentistry, London. | Professional and popular views of chronic fatigue syndrome. | BMJ 1994 Mar 19;308(6931):776-7 comment in: BMJ. 1994 Mar 19;308(6931):732-3 BMJ. 1995 Jul 29;311(7000):329 | OBJECTIVE--To study the coverage of the chronic fatigue syndrome in the popular and professional press. DESIGN--Search of all original research papers on the chronic fatigue syndrome published in British journals from 1980 onwards and of professional trade papers, national newspapers, and women's magazines. Interviews with six medical journalists. SETTING--British scientific, medical, and popular press. RESULTS--37 (49%) articles in research journals did not favour organic causes and 23 (31%) favoured organic causes. By contrast 31 (55%) articles in the medical trade press and 118 (69%) in national newspapers and women's magazines favoured organic causes. CONCLUSIONS--Press coverage of chronic fatigue syndrome has amplified and distorted divisions in the research community concerning the chronic fatigue syndrome. Articles in the press concentrate on a simple medical model of illness reinforcing the stigma of psychological illness and dissatisfaction with traditional medical authority. Review Literature |
| Makela EH. | | Understanding chronic fatigue syndrome. | Am Pharm 1994 Apr;NS34(4):45-54; quiz 55-6 | |

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| Manian FA. | Division of Infectious Diseases, St. John's Mercy Medical Center, St. Louis, Missouri. | Simultaneous measurement of antibodies to Epstein-Barr virus, human herpesvirus 6, herpes simplex virus types 1 and 2, and 14 enteroviruses in chronic fatigue syndrome: is there evidence of activation of a nonspecific polyclonal immune response? | Clin Infect Dis 1994 Sep;19(3):448-53 comment in: Clin Infect Dis. 1995 Sep;21(3):708-9 | As a test of the hypothesis that elevated titers of viral antibodies in patients with chronic fatigue syndrome (CFS) are due to a nonspecific polyclonal immune response, antibodies to Epstein-Barr virus (EBV), human herpesvirus 6 (HHV-6), and 14 enteroviruses in 20 patients with CFS and 20 age- and gender-matched controls were simultaneously measured. Similarly, titers of IgG to herpes simplex virus (HSV) types 1 and 2 were measured in 18 of these cases and in the respective controls. IgG to EBV viral capsid antigen (VCA) was present at titers > or = 1:320 in 55% of cases vs. 15% of controls (P = .02). The geometric mean titers of early antigen antibody to EBV, HHV-6 IgG, and HSV-1 and HSV-2 IgG were not significantly different among cases and controls. Of the 14 enteroviral antibodies tested for, only those to coxsackieviruses B1 and B4 were present at significant titers (> or = 1:8) in cases vs. controls (P = .02 and P = .001, respectively). Of the cases, 19 (95%) had either an EBV VCA IgG titer > or = 1:320 or a coxsackievirus B1 or B4 antibody titer > or = 1:8, a percentage significantly higher than that of controls (40%; P = .0004). Titers of EBV VCA IgG and coxsackievirus B1 and B4 antibodies were simultaneously elevated in only 20% of cases. There was no correlation between elevated titers of EBV VCA IgG and IgG to HHV-6, HSV-1, and HSV-2 or antibody to coxsackieviruses B1 and B4 in the cases. The prevalence of reported allergies to medications or other substances was identical in both groups (60%). These findings suggest that in the majority of cases of CFS, elevation of viral antibody titers is not due to a nonspecific polyclonal immune response. |
| Mann AH, Mc Donald E, Cope H, Pelosi A, David A. | Section of Epidemiology & General Practice, Institute of Psychiatry, London, United Kingdom. | [Epidemiologic study of chronic fatigue in primary care (general practice)].[article in French] | Encephale 1994 Nov;20 Spec No 3:575-9 | The results of a cross sectional study of fatigue in two large samples of patients attending primary care physicians are reported. The level of complaint of fatigue was higher in the prospective sample, which consisted of patients who had been diagnosed as suffering from a viral infection six months earlier. Duration and frequency of experience of fatigue correlated with severity in both samples. Severity, duration and frequency were continuously distributed in these populations. Attribution of fatigue in these two samples was mixed: social stresses, current physical illness and psychological problems all being offered as explanations. 11% of the cross sectional sample and 17% of the prospective sample met study operational criteria for a possible chronic fatigue state. These patients were assessed in greater detail. The majority had a diagnosable psychiatric disorder, predominantly depression. Physical illnesses were not adequate to explain these fatigue states. These studies in primary care do not support a clinical entity of a "chronic fatigue syndrome". Some patients in primary care settings have complaints of fatigue that are both disabling and long lasting, but they do not form a distinct group although the majority are likely however to be suffering from a concurrent psychiatric disorder. In contrast to similar patients with chronic fatigue syndromes attending hospital clinics, primary care patients with complaints of fatigue are much more varied in their ideas of causation with considerable less evidence of disease conviction. |
| Mant D. | University of Southampton, UK. | Chronic fatigue syndrome. | Lancet 1994 Sep 24;344(8926):834-5 comment on: Lancet. 1994 Sep 24;344(8926):864-8 | |
| Manu P, Lane TJ, Matthews DA, Castriotta RJ, Watson RK, Abeles M. | Department of Medicine, University of Connecticut School of Medicine, Farmington. | Alpha-delta sleep in patients with a chief complaint of chronic fatigue. | South Med J 1994 Apr;87(4):465-70 comment in: South Med J. 1994 Dec;87(12):1289-90 | Our prospective, standardized cohort study was designed to assess the presence of alpha wave intrusions during non-rapid eye movement sleep (alpha-delta sleep) and its relationship to fibromyalgia, major depression, and chronic fatigue syndrome (CFS) in patients with a chief complaint of chronic fatigue. The study group comprised 30 consecutive patients seen at a university hospital referral clinic for evaluation of chronic fatigue. All patients had nocturnal polysomnography, dolorimetric tender point assessment for fibromyalgia, a comprehensive history, physical, and laboratory evaluation, and a structured psychiatric interview. Alpha-delta sleep was identified in 8 of the 30 patients (26%), major depression in 20 (67%), CFS in 15 (50%), and fibromyalgia in 4 (13%). Ten of the 30 patients (33%) had a primary sleep disorder (sleep apnea, periodic limb movements, or narcolepsy). Alpha-delta sleep was not significantly correlated with fibromyalgia, CFS, major depression, or primary sleep disorders, but was significantly more common among patients who had chronic fatigue without major depression. We conclude that primary sleep disorders are relatively common among patients with chronic fatigue and must be diligently sought and treated. Alpha-delta sleep is not a marker of fibromyalgia or CFS, but may contribute to the illness of nondepressed patients with these conditions. |

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| Martin WJ, Zeng LC, Ahmed K, Roy M. | Department of Pathology, USC School of Medicine, Los Angeles 90033. | Cytomegalovirus-related sequence in an atypical cytopathic virus repeatedly isolated from a patient with chronic fatigue syndrome. | Am J Pathol 1994 Aug;145(2):440-51 | An atypical virus, cytopathic for human and animal fibroblasts, was repeatedly cultured from a patient with chronic fatigue syndrome. Viral particles, suggestive of cytomegalovirus (CMV) were seen by electron microscopy. Infected cells did not, however, stain with antisera specific for CMV, herpes, simplex virus, or human herpes-virus-6. Polymerase chain reaction (PCR) assays for these viruses were also negative. Two distinct products of approximately 1.5 kilobase pairs were amplified from virally infected cells using the human T lymphotropic virus-II tax gene reactive primer, SK44, in low stringency PCR. Sequencing of one of the amplified products showed a region of highly significant partial homology with the UL34 gene of CMV. The sequence of the other PCR product did not correspond with CMV or any other virus. DNA was extracted from the material pelleted by ultracentrifugation of filtered culture supernatants. It migrated in agarose gels as a single band of approximately 20 kpb. The banded DNA was digested with EcoRI and cloned. A 2.2 kbp plasmid containing the CMV-related sequence identified within the PCR product was recovered. Sequencing of this plasmid extended the region of partial sequence homology with CMV to include a portion of the UL35 gene of CMV. Initial sequencing of additional plasmids has confirmed the partial relatedness to CMV. The data indicate a novel type of CMV-related "stealth" virus that is able to establish a clinically persistent human infection. |
| Martin WJ. | University of Southern California School of Medicine, Los Angeles 90033, USA. | Stealth viruses as neuropathogens. | CAP Today 1994 Oct;8(10):67-70 | Neuropsychiatric diseases viewed as multifaceted expression of a dysfunctional brain in which atypical responses are evoked by various sensory inputs. Disease entities have traditionally been classified according to the predominant manifestation () without regard to the overlapping features of many of the diseases (+/-). Thus, mild to moderate pain, mood, cognitive, and neurosomatic symptoms are frequently present in chronic fatigue syndrome (CFS) patients. Fibromyalgia syndrome (FMS) is listed as an example of a predominantly chronic pain syndrome. Affect (mood) disorders include depression (Depress.), anxiety, panic reactions, blunted affect, mania, etc. Schizophrenia (Schizo.) is listed as an example of a major cognitive psychosis. Autism as well as various forms of dementia would be included in this category. Irritable bowel syndrome (IBS) is an example of a neurosomatic disease. |
| Masuda A, Nozoe SI, Matsuyama T, Tanaka H. | First Department of Internal Medicine, Faculty of Medicine, Kagoshima University, Japan. | Psychobehavioral and immunological characteristics of adult people with chronic fatigue and patients with chronic fatigue syndrome. | Psychosom Med 1994 Nov-Dec;56(6):512-8 | The psychobehavioral responses and cellular immune function were investigated in healthy people (control, N = 21), adult people with chronic fatigue (fatigue-non-CFS group, N = 24), and patients with chronic fatigue syndrome (CFS, N = 10). Based on psychobehavioral responses, the fatigue-non-CFS group had low general activity levels ($p < .05$) and slightly depressive tendencies ($p < .01$) compared with the control. They had many life event stresses ($p < .05$) and sleep disturbances ($p < .01$), and they could not cope appropriately with stresses. The fatigue-non-CFS group also showed significantly lower natural killer (NK) cell activity ($p < .01$) and decreased numbers of CD16+ and CD56+ cells ($p < .05$). Compared with the fatigue-non-CFS group, patients with CFS had higher degrees of physical fatigue ($p < .01$) and more life event stresses ($p < .05$). They had lower general activity levels and social introversion. They were also in a depressive state. NK cell activity and the numbers of CD16+ and CD56+ cells were significantly reduced in patients with CFS ($p < .01$). These findings suggest that adult people with chronic fatigue may be in an intermediate state between the healthy control and patients with CFS in terms of psychobehavioral responses and low NK cell activity. We observed three cases in such an intermediate state in whom CFS subsequently developed. Randomized Controlled Trial |
| Matsuda J, Gohchi K, Gotoh N. | | Serum concentrations of 2',5'-oligoadenylate synthetase, neopterin, and beta-glucan in patients with chronic fatigue syndrome and in patients with major depression. | J Neurol Neurosurg Psychiatry 1994 Aug;57(8):1015-6 | |
| Matsuda J. | | [Chronic fatigue syndrome: fictitious or true disease?][article in Japanese] | Ryumachi 1994 Oct;34(5):921-8 | |
| Matsuno T, Hikita K, Matsuo T. | Department of Neuropsychiatry, Faculty of Medicine, Kyushu University. | [Chronic fatigue syndrome and psychiatric diseases].[article in Japanese] | Nippon Rinsho 1994 May;52(5):1339-44 | The chronic fatigue syndrome consists of a combination of non-specific symptoms. Some believe that the CFS is subcategory of major depression, because the symptoms are similar to those of major depression. We believe that the CFS is quite different from major depression or neurotic depression, |

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| | | | | since the CFS has no lack of initiative and effort, no inhibition which is seen in endogenous depression, and sharp fluctuations in general fatigue, anxiety, and various persisting somatic symptoms, such as, malaise and mild fever. CFS seems to be similar to the neurasthenia. It is harmful, at least, in aetiology and treatment, to neglect the diagnosis of the CFS. |
| McGarry F, Gow J, Behan PO. | | Enterovirus in the chronic fatigue syndrome. | Ann Intern Med 1994 Jun 1;120(11):972-3 | |
| Millner L, Widerman E. | Temple University, School of Social Administration, Philadelphia, PA 19122. | Women's health issues: a review of the current literature in the social work journals, 1985-1992. | Soc Work Health Care 1994;19(3-4):145-72 | To assess the ways in which social work is addressing issues in women's health care, the profession's journals from 1985-1992 were searched, yielding 36 articles. Over half addressed issues of reproduction and sexuality including pregnancy, family planning, abortion, substance abuse in pregnancy, and fetal protection policies. Remaining articles addressed medical diagnoses; including AIDS/HIV/STDs, cancer, illnesses associated with aging, PMS, Turner's Syndrome, and chronic fatigue syndrome. Foci, methodologies, and recommendations are discussed and the authors critically analyze the articles' reflections of the status of women's health as a social work concern. |
| Moutschen M, Triffaux JM, Demonty J, Legros JJ, Lefebvre PJ. | Department of Internal Medicine, CHU Sart-Tilman, Liege, Belgium. | Pathogenic tracks in fatigue syndromes. | Acta Clin Belg 1994;49(6):274-89 | This review analyses the recent literature devoted to two related fatigue syndromes: chronic fatigue syndrome (CFS) and acute onset postviral fatigue syndrome (PVFS). The articles are grouped into five pathogenic tracks: infectious agents, immune system, skeletal muscle, hypothalamo-pituitary-adrenal (HPA) axis and psychiatric factors. Although a particular infectious agent is unlikely to be responsible for all CFS cases, evidence is shown that host-parasite relationships are modified in a large proportion of patients with chronic fatigue. Antibody titres against infectious agents are often elevated and replication of several viruses could be increased. Chronic activation of the immune system is also observed and could be due to the reactivation of persistent or latent infectious agents such as herpes viruses (i.e. HHV-6) or enteroviruses. It could also be favoured by an impaired negative feedback of the HPA axis on the immune system. A model is proposed where the abnormalities of the HPA axis are primary events and are mainly responsible for a chronic activation of the immune system which in turn induces an increased replication of several viruses under the control of cellular transcription factors. These replicating viruses together with cytokines such as TNF-alpha would secondarily induce functional disorders of muscle and several aspects of asthenia itself. |
| Natelson BH, Ye N, Moul DE, Jenkins FJ, Oren DA, Tapp WN, Cheng YC. | Chronic Fatigue Syndrome Center, UMDNJ-New Jersey Medical School, Newark. | High titers of anti-Epstein-Barr virus DNA polymerase are found in patients with severe fatiguing illness. | J Med Virol 1994 Jan;42(1):42-6 | Forty-one patients with chronic fatigue syndrome (CFS), 76 healthy controls matched with the patient group for age range, sex, race, and socioeconomic class, and 22 symptomatic patients with seasonal affective disorder (SAD) had serum sampled for antibodies against 2 Epstein-Barr virus (EBV) replicating enzymes. Abnormal titers of antibodies were found twice as often in CFS patients as controls (34.1% vs. 17.1%), with SAD patients having an intermediate frequency (27.3%). Stratifying for disease severity sharpened the differences considerably, with the sicker CFS and SAD patients having 52% and 50% abnormal tests, respectively; more mildly afflicted CFS and SAD patients had a frequency of abnormal tests in the normal range. Antibodies to EBV DNA polymerase (DNAP) were the more sensitive of the two tests in that they were positive in all cases but one. These findings suggest that antibodies against EBV DNAP may be a useful marker in delineating a subset of patients with severe fatiguing illness for appropriate treatment trials and for monitoring their outcomes. |
| Neutra RR. | Special Epidemiological Studies Program, California Department of Health Services, Albany 94706. | Some preliminary thoughts on the potential contribution of epidemiology to the question of multiple chemical sensitivity. | Public Health Rev 1994;22(3-4):271-8 | Epidemiology has played a role in clarifying mysterious symptom complexes such as AIDS, Chronic Fatigue Syndrome, and Psychiatric Disease. Is Multiple Chemical Sensitivity a new environmental disease or another in the parade of psychosomatic syndromes which have come and gone in history. It is proposed that epidemiology can: (1) Describe quantitatively the relative frequency of presenting symptoms and natural history. (2) Work with experimental psychologists to develop double-blind protocols for the "environmental unit" where chemical challenges are said to reveal chemical etiology. (3) Develop an epidemiological definition in a clinical series. (4) Develop an epidemiological definition in cohorts recently exposed to chemicals. (5) Apply the epidemiological definitions in descriptive studies and around hazardous waste sites. |
| Nixon PG. | Charing Cross Hospital, London, England. | Effort syndrome: hyperventilation and reduction of anaerobic threshold. | Biofeedback Self Regul 1994 Jun;19(2):155-69 | Effort syndrome is an entity in danger of being subsumed into "chronic fatigue syndrome" and lost to sight. Its distinctive feature is the reduction of the anaerobic threshold for work by depletion of the body's alkaline buffering systems through hyperventilation. This article describes the history and clinical features of effort syndrome and reports a study in which capnography is used to identify the |

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| | | | | anaerobic threshold by registering the respiratory response to the onset of metabolic acidosis. The patients' thresholds are low, and provide a goal for rehabilitation. In other forms of chronic fatigue syndrome, the pathogenesis and logic of therapy are unclear. |
| Packer TL, Sauriol A, Brouwer B. | Division of Occupational Therapy, School of Rehabilitation Therapy, Queen's University, Kingston, Ontario, Canada. | Fatigue secondary to chronic illness: postpolio syndrome, chronic fatigue syndrome, and multiple sclerosis. | Arch Phys Med Rehabil 1994 Oct;75(10):1122-6 | Estimates of the percentage of patients with postpolio syndrome, chronic fatigue syndrome, and multiple sclerosis who experience fatigue range from approximately 75% to 100%. In this study we describe the severity of fatigue and its impact on subjects with these three diagnoses. The Fatigue Severity Scale, the Human Activity Profile, and the Nottingham Health Profile were used to measure fatigue, activity, and health status respectively of each diagnostic group as well as a control group. Using a Kruskal-Wallis one-way analysis of variance followed by a Bonferroni-adjusted Mann Whitney U test all diagnostic groups reported significantly higher levels ($p = .0000$ to $p = .002$) of fatigue and lower perceived health status than the control group. Subjects with chronic fatigue and multiple sclerosis also had significantly reduced activity levels ($p = .002$ to $p = .01$) compared with the control group. Further attention should be directed toward understanding the relationship between fatigue and ability to engage in activities as well as strategies for remediation and/or compensation of the fatigue. |
| Pagani M, Lucini D, Mela GS, Langewitz W, Malliani A. | Centro Ricerche Cardiovascolari, CNR, Ospedale L Sacco, University of Milano, Italy. | Sympathetic overactivity in subjects complaining of unexplained fatigue. | Clin Sci (Colch) 1994 Dec;87(6):655-61 | 1. Theoretical and practical considerations suggest that in subjects complaining of fatigue, in the absence of evident organ dysfunction, an alteration in the autonomic nervous system might be present as a functional correlate. 2. Autoregressive spectral analysis of R-R interval variability from a surface ECG, was used in healthy control subjects ($n = 24$, age 45 ± 4 years) and in subjects complaining of unexplained fatigue ($n = 53$, age 46 ± 9 years) to obtain quantitative indices of the state of the sympathovagal balance, both at rest and during a mental stimulus (mental arithmetic), capable of enhancing sympathetic drive. Sympathetic and vagal modulations were inferred from the normalized powers of the low frequency and high frequency spectral components respectively. 3. We observed in patients, at rest, a prevailing low frequency component of R-R variability (patients low frequency = 73 ± 11 , control subjects 51 ± 10 normalized units, $P < 0.05$). The responsiveness to mental arithmetic was reduced in patients as compared with controls. Systolic blood pressure variability did not differ. This suggested a selective imbalance in autonomic control of the sinoatrial node, characterized by sympathetic predominance as well as by vagal withdrawal, at rest. 4. The possibility of discriminating patients from control subjects on the basis of simple non-invasive functional markers might provide a better understanding of the mechanisms, clinical evolution and outcome of conditions such as the chronic fatigue syndrome, which lack ordinary evidence of disease, but comprise, as physiopathological correlate, a quantitative alteration of autonomic control. |
| Patarca R, Klimas NG, Lugtendorf S, Antoni M, Fletcher MA. | E. M. Papper Laboratory of Clinical Immunology, University of Miami School of Medicine, Florida. | Dysregulated expression of tumor necrosis factor in chronic fatigue syndrome: interrelations with cellular sources and patterns of soluble immune mediator expression. | Clin Infect Dis 1994 Jan;18 Suppl 1:S147-53 | Among a group of 70 individuals who met the criteria established by the Centers for Disease Control and Prevention (Atlanta) for chronic fatigue syndrome (CFS), 12%-28% had serum levels exceeding 95% of control values for tumor necrosis factor (TNF) alpha, TNF-beta, interleukin (IL) 1 alpha, IL-2, soluble IL-2 receptor (sIL-2R), or neopterin; overall, 60% of patients had elevated levels of one or more of the nine soluble immune mediators tested. Nevertheless, only the distributions for circulating levels of TNF-alpha and TNF-beta differed significantly in the two populations. In patients with CFS--but not in controls--serum levels of TNF-alpha, IL-1 alpha, IL-4, and sIL-2R correlated significantly with one another and (in the 10 cases analyzed) with relative amounts (as compared to beta-globin or beta-actin) of the only mRNAs detectable by reverse transcriptase-coupled polymerase chain reaction in peripheral-blood mononuclear cells: TNF-beta, unspliced and spliced; IL-1 beta, lymphocyte fraction; and IL-6 (in order of appearance). These findings point to polycellular activation and may be relevant to the etiology and nosology of CFS. |
| Pawlikowska T, Chalder T, Hirsch SR, Wallace P, Wright DJ, Wessely SC. | Department of General Practice, St Mary's Hospital Medical School, London. | Population based study of fatigue and psychological distress. | BMJ 1994 Mar 19;308(6931):763-6 comment in: BMJ. 1995 Jul 29;311(7000):329 BMJ. 2000 Feb 19;320(7233):515-6 BMJ. 2000 May 13;320(7245):1343 | OBJECTIVES--To determine the prevalence of fatigue in the general population and the factors associated with fatigue. DESIGN--Postal survey. SETTING--Six general practices in southern England. SUBJECTS--31,651 men and women aged 18-45 years registered with the practices. MAIN OUTCOME MEASURES--Responses to the 12 item general health questionnaire and a fatigue questionnaire which included self reported measures of duration, severity, and causes of fatigue. RESULTS--15,283 valid questionnaires were returned, giving a response rate of 48.3%, (64% after adjustment for inaccuracies in the practice registers). 2798 (18.3%) of respondents reported substantial fatigue lasting six months or longer. Fatigue and psychological morbidity were moderately correlated |

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| | | | | ($r = 0.62$). Women were more likely to complain of fatigue than men, even after adjustment for psychological distress. The commonest cited reasons for fatigue were psychosocial (40% of patients). Of 2798 patients with excessive tiredness, only 38 (1.4%) attributed this to the chronic fatigue syndrome. CONCLUSION--Fatigue is distributed as a continuous variable in the community and is closely associated with psychological morbidity. |
| Peterson PK, Sirr SA, Grammith FC, Schenck CH, Pheley AM, Hu S, Chao CC. | Department of Medicine, Hennepin County Medical Center, Minneapolis, MN 54415, USA. | Effects of mild exercise on cytokines and cerebral blood flow in chronic fatigue syndrome patients. | Clin Diagn Lab Immunol 1994 Mar;1(2):222-6 | Chronic fatigue syndrome (CFS) is an idiopathic disorder characterized by fatigue that is markedly exacerbated by physical exertion. In the present study, we tested the hypothesis that mild exercise (walking 1 mph [1 mile = 1.609 km] for 30 min) would provoke serum cytokine and cerebral blood flow abnormalities of potential pathogenic importance in CFS. Interleukin-1 beta, interleukin-6, and tumor necrosis factor alpha were nondetectable in sera of CFS patients (n = 10) and healthy control subjects (n = 10) pre- and postexercise. At rest, serum transforming growth factor beta (TGF-beta) levels were elevated in the CFS group compared with the control group (287 +/- 18 versus 115 +/- 5 pg/ml, respectively; $P < 0.01$). Serum TGF-beta and cerebral blood flow abnormalities, detected by single-photon emission-computed tomographic scanning, were accentuated postexercise in the CFS group. Although these findings were not significantly different from those in the control group, the effect of exercise on serum TGF-beta and cerebral blood flow appeared magnified in the CFS patients. Results of this study encourage future research on the interaction of physical exertion, serum cytokines, and cerebral blood flow in CFS that will adopt a more rigorous exercise program than the one used in this study. |
| Pichot P. | | [Neurasthenia, yesterday and today]. [article in French] | Encephale 1994 Nov;20 Spec No 3:545-9 | Neurasthenia was described and explained in very mechanistic terms, at the end of the 19th century, by G.M. Beard to account for physical and mental exhaustion and for varied somatic troubles imputed to failure of too much solicited nervous resources. This concept was then universally adopted and gave rise to diverse interpretations, among which was the Freud's one. Later, in Occident, came a deterioration, the diagnostic of neurasthenia giving way to those of anxious or affective disorders. In the same time, at least for ideological and cultural reasons, the concept remained lively in Russia and in Asia. During the last decade the western psychiatry has been led to accept that there are clinical situations focussed on fatigue and fatigability, even if it coined for them new terminologies (post-infectious fatigue, chronic fatigue syndrome, etc.) and while DSMs keep on ignoring neurasthenia, the ICD 10 gives it an important place. |
| Priori R, Conti F, Luan FL, Arpino C, Valesini G. | Istituto di Clinica Medica I, Universita La Sapienza, Roma, Italy. | Chronic fatigue: a peculiar evolution of eosinophilia myalgia syndrome following treatment with L-tryptophan in four Italian adolescents. | Eur J Pediatr 1994 May;153(5):344-6 | We describe four Italian adolescents in whom a persistent, debilitating fatigue appeared after therapeutic ingestion of products containing L-tryptophan and subsequent to the development of a transient rise in eosinophil count and severe myalgia (Eosinophilia Myalgia Syndrome-EMS). Their clinical picture was indistinguishable from that of the so-called Chronic Fatigue Syndrome. A chronic fatigue may occur after diverse triggering agents and its represents the peculiar clinical evolution of these four paediatric cases of EMS. |
| Przewlocka M. | Katedry i Kliniki Kardiologii AM we Wroclawiu. | [Chronic fatigue syndrome]. [article in Polish] | Pol Tyg Lek 1994 Jun 20-27;49(25-26):593-5 | |
| Raanani P, Martinowitz U. | | [Chronic fatigue syndrome]. [article in Hebrew] | Harefuah 1994 Dec 1;127(11):467-71 | |
| Raik E. | | Chronic fatigue syndrome and the medical referee. | Med J Aust 1994 Jan 3;160(1):47-8 comment on: Med J Aust. 1993 Sep 20;159(6):432 | |
| Rasmussen AK, Andersen V, Nielsen H, Wiik A. | Medicinsk afdeling TTA, Rigshospitalet, Kobenhavn. | [Chronic fatigue syndrome--a defined entity]? [article in Danish] | Ugeskr Laeger 1994 Nov 14;156(46):6832-6 comment in: Ugeskr Laeger. 1995 Feb 6;157(6):756-7 Ugeskr Laeger. 1995 Feb 6;157(6):757 | Chronic fatigue syndrome (CFS) is characterized by a sudden onset of an influenza-like illness followed by marked chronic fatigue and abnormal exercise-induced exhaustion. The precise pathogenesis of this disorder is unknown, but viral infection triggering immune imbalance has been suggested. The literature on CFS is reviewed. We find no consistent support for chronic viral infection or immunological dysfunction. The data in the published studies are rather conflicting, and further research in order to identify parameters that differentiate CFS from other disorders is necessary. |
| Rasmussen AK, Nielsen H, Andersen V, Barington T. | Medicinsk afdeling TTA og infektionsmedicinsk afdeling | [Chronic fatigue syndrome--a controlled cross-sectional | Ugeskr Laeger 1994 Nov 14;156(46):6836-40 comment | Twenty-one patients fulfilling the Center for Disease Control criteria for chronic fatigue syndrome (CFS) were examined in a controlled study. Viral antibodies and tests evaluating the immune system |

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| Bendtzen K, Hansen MB, Nielsen L, Pedersen BK, Wiik A. | M, Rigshospitalet, Kobenhavn. | study].[article in Danish] | in: Ugeskr Laeger. 1995 Feb 6;157(6):756-7 | were investigated in the patients and in a control group of 21 sex- and age-matched individuals. Production in vitro of the predominantly T-cell-derived cytokines interleukin-2 and interferon-gamma was significantly higher in patients with CFS compared the control group. Furthermore, the serum concentrations of IgA and IgE were significantly lower in patients with CFS; however, the values were within the normal reference range. All other variables were similar in the two groups. This study does not suggest a clearly disordered immune system or a chronic viral infection as a major pathogenetic factor in CFS. Longitudinal studies of immunological and virological parameters in CFS are warranted as are studies on patients that are severely handicapped. |
| Rasmussen AK, Nielsen H, Andersen V, Barington T, Bendtzen K, Hansen MB, Nielsen L, Pedersen BK, Wiik A. | Medical Department TTA M. Rigshospitalet, Copenhagen, Denmark. | Chronic fatigue syndrome--a controlled cross sectional study. | J Rheumatol 1994 Aug;21(8):1527-31 | OBJECTIVE. To look for signs of immunodeficiencies and/or longstanding infections underlying chronic fatigue syndrome (CFS). METHODS. Twenty-one patients fulfilling the Centers for Disease Control criteria for CFS were compared to 21 age and sex matched controls. A number of viral antibodies as well as the following tests evaluating the immune system were studied: autoantibody profile, cell surface markers on isolated blood mononuclear cells, cytokine production, lymphocyte proliferative responses, natural killer cell activity and quantitation of immunoglobulin secreting cells. RESULTS. Production in vitro of the predominantly T cell derived cytokines interleukin 2 and interferon gamma was significantly higher in patients with CFS compared to the control group. Furthermore, the serum concentrations of IgA and IgE were lower in patients with CFS; however, this difference was caused by a larger number with values of IgA and IgE above the upper limit of the normal range among the controls than among the patients with CFS. All other variables were similar in the 2 groups. CONCLUSION. A pathogenically significant imbalance of the immune system in patients with CFS cannot be excluded. However, evidence of a causal link between abnormal immunity and CFS was not obtained. |
| Rebora A, Drago F. | Department of Dermatology, University of Genoa, Italy. | Chronic fatigue syndrome: a novel disorder with cutaneous manifestations. | Dermatology 1994;188(1):3-5 | Persistent and disabling fatigue associated with low-grade fever and other constitutional symptoms, without any known disorder that accounts for it, is recognized as chronic fatigue syndrome (CFS). Skin lesions occur in 10-35% of patients, but their description is inaccurate. Recurrent aphthous stomatitis or persistent Epstein-Barr virus (EBV)-related erythema multiforme have also been reported. Patients may be diagnosed as having CFS only when they fulfill at least 2 major and 8 minor criteria. Major criteria are the presence of debilitating fatigue persisting or recurring for at least 6 months and the absence of any other medical disorder that may explain it. Although different viral or nonviral etiologies have been documented, evidence implicating EBV is gaining support. |
| Rest J. | | The chronic fatigue syndrome. | 955: Ann Intern Med 1995 Jul 1;123(1):75; discussion 76 comment on: Ann Intern Med. 1994 Dec 15;121(12):953-9 | |
| Richman JA, Flaherty JA, Rospenda KM. | Department of Psychiatry, University of Illinois at Chicago 60612. | Chronic fatigue syndrome: have flawed assumptions been derived from treatment-based studies? | Am J Public Health 1994 Feb;84(2):282-4 | Chronic fatigue syndrome is a disabling disorder that has been studied primarily in clinical settings. In the absence of an adequate epidemiological database, cultural stereotypes have influenced the characterization of chronic fatigue syndrome as "the yuppie flu," similar to the 19th century characterization of neurasthenia as a disease of the affluent. The limited epidemiological data available and the overall medical-sociological literature call this assumption into question. Only a community "true" prevalence study that is unbiased by help seeking and access to health care can provide an accurate assessment of the risk factors for and the public health ramifications of this disease. |
| Roberts L, Byrne E. | Department of Neurology, St Vincent's Hospital, Fitzroy, Melbourne, Australia. | Single fibre EMG studies in chronic fatigue syndrome: a reappraisal. | J Neurol Neurosurg Psychiatry 1994 Mar;57(3):375-6 comment in: J Neurol Neurosurg Psychiatry. 1994 Sep;57(9):1157 | Single fibre EMG studies were carried out on the right extensor digitorum communis muscle in 30 subjects with chronic fatigue syndrome and in 30 age and sex matched controls. Abnormal jitter was seen in five patients with chronic fatigue syndrome. Slight but significant differences between the mean consecutive differences in the remainder of the chronic fatigue subjects and the control subjects were recorded. Overall the differences were so minor that it seems unlikely that a disturbance of neuromuscular function as reflected by jitter measurement has a pathogenetic role. It is suggested that the increased jitter seen may be explained by the effects of the variability of motor unit firing rates on the myogenic component of the jitter. |
| Rosen SD. | | Hyperventilation and the chronic fatigue syndrome. | Q J Med 1994 Jun;87(6):373-4 comment on: Q J Med. 1994 | |

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| Saisch SG, Deale A, Gardner WN, Wessely S. | Department of Thoracic Medicine, Kings College School of Medicine and Dentistry, London, UK. | Hyperventilation and chronic fatigue syndrome. | Jan;87(1):63-7 Q J Med 1994 Jan;87(1):63-7 comment in: Q J Med. 1994 Jun;87(6):373-4 | We studied the link between chronic fatigue syndrome (CFS) and hyperventilation in 31 consecutive attenders at a chronic fatigue clinic (19 females, 12 males) who fulfilled criteria for CFS based on both Oxford and Joint CDC/NIH criteria. All experienced profound fatigue and fatigability associated with minimal exertion, in 66% developing after an infective episode. Alternative causes of fatigue were excluded. Hyperventilation was studied during a 43-min protocol in which end-tidal PCO ₂ (PETCO ₂) was measured non-invasively by capnograph or mass spectrometer via a fine catheter taped in a nostril at rest, during and after exercise (10-50 W) and for 10 min during recovery from voluntary overbreathing to approximately 2.7 kPa (20 mmHg). PETCO ₂ < 4 kPa (30 mmHg) at rest, during or after exercise, or at 5 min after the end of voluntary overbreathing, suggested either hyperventilation or a tendency to hyperventilate. Most patients were able voluntarily to overbreathe, but not all were able to exercise. Twenty-two patients (71%) had no evidence of hyperventilation during any aspect of the test. Only four patients had unequivocal hyperventilation, in one associated with asthma and in three with panic. Only one patient with severe functional disability and agoraphobia had hyperventilation with no other obvious cause. A further five patients had borderline hyperventilation, in which PETCO ₂ was < 4 kPa (30 mmHg) for no more than 2 min, when we would have expected it to be normal. There was no association between level of functional impairment and degree of hyperventilation. There is only a weak association between hyperventilation and chronic fatigue syndrome.(ABSTRACT TRUNCATED AT 250 WORDS) |
| Schmalig KB, DiClementi JD, Cullum CM, Jones JF. | Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle 98105. | Cognitive functioning in chronic fatigue syndrome and depression: a preliminary comparison. | Psychosom Med 1994 Sep-Oct;56(5):383-8 | This study used a brief battery of neuropsychological measures to examine the performance of patients with chronic fatigue syndrome (CFS) (N = 16) and patients in a major depressive episode (N = 23). The overall neuropsychological performance of the CFS group was not significantly different from depressed patients, and both groups scored within normal limits on most measures. Variability of neuropsychologic performance was in general unrelated to level of depressive symptoms. The results are discussed in terms of the validity of the cognitive criterion for the CFS diagnosis. Subjective complaints of cognitive dysfunction by CFS patients in light of the lack of objective evidence for the same are considered in terms of a somatic vigilance hypothesis. |
| Schmidley JW, Hines J. | | Folate and chronic fatigue syndrome. | Neurology 1994 Nov;44(11):2214-5 comment on: Neurology. 1993 Dec;43(12):2645-7 | |
| Schmitz S, Tesch H, Bohlen H, Engert A, Diehl V. | Klinik I für Innere Medizin, Universität zu Köln. | [Chronic fatigue syndrome]. [article in German] | Med Klin 1994 Mar 15;89(3):154-9 | |
| Schwartz RB, Garada BM, Komaroff AL, Tice HM, Gleit M, Jolesz FA, Holman BL. | Department of Radiology, Brigham and Women's Hospital, Boston, MA 02115. | Detection of intracranial abnormalities in patients with chronic fatigue syndrome: comparison of MR imaging and SPECT. | AJR Am J Roentgenol 1994 Apr;162(4):935-41 | OBJECTIVE. Chronic fatigue syndrome is a recently characterized condition of unknown origin that is manifested by fatigue, flu-like complaints, and neurologic signs and symptoms, including persistent headache, impaired cognitive abilities, mood disorders, and sensorimotor disturbances. This syndrome can be difficult to diagnose clinically or by standard neuroradiologic tests. We performed MR imaging and single-photon emission computed tomography (SPECT) in patients with chronic fatigue syndrome to compare the usefulness of functional and anatomic imaging in the detection of intracranial abnormalities. SUBJECTS AND METHODS. Sixteen patients who fulfilled the Centers for Disease Control, British, and/or Australian criteria for chronic fatigue syndrome had MR and SPECT examinations within a 10-week period. Axial MR and SPECT scans were analyzed as to the number and location of focal abnormalities by using analysis of variance with the Student-Newman-Keuls option. MR imaging findings in patients with chronic fatigue syndrome were compared with those in 15 age-matched control subjects, and SPECT findings in the patients with chronic fatigue syndrome were compared with those in 14 age-matched control subjects by using Fisher's exact test. The findings on MR and SPECT scans in the same patients were compared by using the Wilcoxon matched-pairs signed-ranks test. RESULTS. MR abnormalities consisted of foci of T2-bright signal in the periventricular and subcortical white matter and in the centrum semiovale; there were 2.06 foci per patient, vs 0.80 foci per control subject. MR abnormalities were present in eight (50%) of 16 patients, compared with three (20%) of 15 age-matched control subjects. Neither of these differences reached significance, although the power of the study to detect differences between groups was small. Patients |

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| | | | | with chronic fatigue syndrome had significantly more defects throughout the cerebral cortex on SPECT scans than did normal subjects (7.31 vs 0.43 defects per subject, $p < .001$). SPECT abnormalities were present in 13 (81%) of 16 patients, vs three (21%) of 14 control subjects ($p < .01$). SPECT scans showed significantly more abnormalities than did MR scans in patients with chronic fatigue syndrome ($p < .025$). In the few patients who had repeat SPECT and MR studies, the number of SPECT abnormalities appeared to correlate with clinical status, whereas MR changes were irreversible. CONCLUSION. SPECT abnormalities occur more frequently and in greater numbers than MR abnormalities do in patients with chronic fatigue syndrome. SPECT may prove to be useful in following the clinical progress of patients with this syndrome. |
| Schwartz RB, Komaroff AL, Garada BM, Gleit M, Doolittle TH, Bates DW, Vasile RG, Holman BL. | Department of Radiology, Brigham and Women's Hospital, Boston, MA 02215. | SPECT imaging of the brain: comparison of findings in patients with chronic fatigue syndrome, AIDS dementia complex, and major unipolar depression. | AJR Am J Roentgenol 1994 Apr;162(4):943-51 | OBJECTIVE. Chronic fatigue syndrome is an illness of unknown origin that begins abruptly with a flulike state and has symptoms suggesting both a chronic viral encephalitis and an affective disorder. We compared single-photon emission computed tomography (SPECT) scans of patients with chronic fatigue syndrome with those of patients with AIDS dementia complex and unipolar depression. SUBJECTS AND METHODS. We used 99mTc-hexamethylpropyleneamine oxime to examine 45 patients with chronic fatigue syndrome, 27 patients with AIDS dementia complex, and 14 patients with major unipolar depression. Scans of 38 healthy persons were used as controls. Comparison of regional defects between groups, as well as midcerebral uptake indexes (an objective measure of global radionuclide uptake), was performed by using analysis of variance with the Student-Newman-Keuls option. Correlation between the number of regional defects and the midcerebral uptake index was determined by using the Spearman rank-correlation test. RESULTS. Patients with AIDS dementia complex had the largest number of defects (9.15 per patient) and healthy patients had the fewest defects (1.66 per patient). Patients with chronic fatigue syndrome and depression had similar numbers of defects per patient (6.53 and 6.43, respectively). In all groups, defects were located predominantly in the frontal and temporal lobes. The midcerebral uptake index was found to be significantly lower ($p < .002$) in the patients with chronic fatigue syndrome (.667) and patients with AIDS dementia complex (.650) than in patients with major depression (.731) or healthy control subjects (.716). Also, a significant negative correlation was found between the number of defects and midcerebral uptake index in patients with chronic fatigue syndrome and AIDS dementia complex, but not in depressed patients or control subjects. CONCLUSION. These findings are consistent with the hypothesis that chronic fatigue syndrome may be due to a chronic viral encephalitis; clinical similarities between chronic fatigue syndrome and depression may be due to a similar distribution and number of defects in the two disorders. |
| Schweitzer R, Robertson DL, Kelly B, Whiting J. | Department of Psychology, University of Queensland, Australia. | Illness behaviour of patients with chronic fatigue syndrome. | J Psychosom Res 1994 Jan;38(1):41-9 | The study examines the illness behaviour of patients with Chronic Fatigue Syndrome (CFS). The Illness Behaviour Questionnaire (IBQ), the twenty-eight version of the General Health Questionnaire (GHQ-28), and the Beck Depression Inventory (BDI) were administered to forty patients with a diagnosis of CFS. The results revealed that CFS patients in comparison with general practice patients, scored significantly higher on the IBQ sub-scales of General Hypochondriasis, $t(188) = 5.2$, $p < 0.001$ and Disease Conviction, $t(188) = 13.28$, $p < 0.001$ but lower on the Psychological/Somatic sub-scale, $t(188) = -5.88$, $p < 0.001$. The CFS and psychiatric patients did not differ significantly on the general hypochondriasis sub-scale. Results of the GHQ-28 revealed 66.7% of the CFS patients scored above the cut-off for psychiatric morbidity. In comparison to a previous study of CFS patients [1], the current findings indicate a significantly higher score on general hypochondriasis. The implications of these findings are discussed. |
| Secchiero P, Berneman ZN, Gallo RC, Lusso P. | Laboratory of Tumor Cell Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892. | Biological and molecular characteristics of human herpesvirus 7: in vitro growth optimization and development of a syncytia inhibition test. | Virology 1994 Jul;202(1):506-12 | Two isolates of human herpesvirus 7 (HHV-7) were recovered from phytohemagglutinin-activated peripheral blood mononuclear cells of a patient with chronic fatigue syndrome and of a healthy blood donor. A genetic polymorphism between the two isolates was detected by Southern blot analysis using a novel HHV-7 genomic clone (pVL8) as a probe. We developed optimized conditions for the in vitro propagation of HHV-7 by using enriched populations of activated CD4+ T lymphocytes derived from normal peripheral blood, resulting in the production of high-titered extracellular virus ($> 10^6$ cell culture infectious doses/ml). Bona fide syncytia formation was documented both in normal CD4+ T lymphocytes and in the Sup-T1 CD4+ T-cell line following infection with high-titered HHV-7. To identify neutralizing antibodies to HHV-7, a syncytia-inhibition test was developed. Variable titers of |

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| | | | | syncytia-neutralizing antibodies were detected in all the human sera tested, thus confirming the high prevalence of HHV-7 in the human population. |
| Shepherd C. | | Chronic fatigue syndrome or myalgic encephalitis. | Lancet 1994 Jan 22;343(8891):243 comment on: Lancet. 1993 Nov 13;342(8881):1247-8 | |
| Sidebotham PD, Skeldon I, Chambers TL, Clements S, Culling J. | | Refractory chronic fatigue syndrome in adolescence. | Br J Hosp Med 1994 Feb 2-15;51(3):110-2 comment in: Br J Hosp Med. 1994 Jun 1-14;51(11):614 | |
| Steere AC. | Division of Rheumatology/Immunology, Tufts University School of Medicine, New England Medical Center, Boston, MA 02111. | Lyme disease: a growing threat to urban populations. | Proc Natl Acad Sci U S A 1994 Mar 29;91(7):2378-83 | Lyme disease or Lyme borreliosis, which is caused by three groups of the spirochete <i>Borrelia burgdorferi</i> , is transmitted in North America, Europe, and Asia by ticks of the <i>Ixodes ricinus</i> complex. The primary areas around the world that are now affected by Lyme disease are near the terminal moraine of the glaciers 15,000 years ago. The emergence of Lyme disease in the United States in this century is thought to have occurred because of ecological conditions favorable for deer. From 1982 through 1991, 40,195 cases occurring in 47 states were reported to the Centers for Disease Control, but enzootic cycles of <i>B. burgdorferi</i> have been identified in only 19 states. During the last several decades, the disease has spread to new areas and has caused focal outbreaks, including locations near Boston, New York, and Philadelphia. Lyme disease is like syphilis in its multisystem involvement, occurrence in stages, and mimicry of other diseases. Diagnosis of late neurologic abnormalities of the disorder has created the most difficulty. A recent phenomenon is that a number of poorly understood conditions, such as chronic fatigue syndrome or fibromyalgia, are misdiagnosed as "chronic Lyme disease." Part of the reason for misdiagnosis is due to problems associated with diagnostic tests. The various manifestations of Lyme disease can usually be treated successfully with oral doxycycline or amoxicillin, except for objective neurologic manifestations, which seem to require intravenous therapy. Vector control of tick-borne diseases has been difficult and, therefore, reduction of the risk of infection has been limited primarily to personal protection measures. |
| Sternon J, Decaux G, Hoffmann G. | Service de Medecine Interne, Hopital Erasme. | [Chronic fatigue syndrome].[article in French] | Rev Med Brux 1994 Sep-Oct;15(5):311-5 | The major and minor diagnostic criteria of the chronic fatigue syndrome are described. The stages of the differential diagnosis, the diagnostic strategies and the controversies, while insisting on certain sleeping disorders are discussed. The cause of the syndrome may be a viral infection, and an anxious-depressive state may increase somatic complaints. Patients with chronic fatigue syndrome did not demonstrate a specific response to therapy. Spontaneous remission after a few years is a typical feature of this syndrome. |
| Straus SE, Komaroff AL, Wedner HJ. | Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892. | Chronic fatigue syndrome: point and counterpoint. | J Infect Dis 1994 Jul;170(1):1-6 | Two clinical investigators with divergent views on chronic fatigue syndrome (CFS) were invited to debate their positions at the 1993 annual meeting of The Infectious Disease Society of America. Major points of the discourse focused on the value of the US Centers for Disease Control and Prevention case definition of CFS, the potential roles of infectious and allergic problems in the syndrome, the confounding problem of concurrent psychiatric problems, and the utility of diagnostic tests. |
| Strayer DR, Carter WA, Brodsky I, Cheney P, Peterson D, Salvato P, Thompson C, Loveless M, Shapiro DE, Elsasser W, et al. | School of Medicine, Hahnemann University, Philadelphia, Pennsylvania 19102. | A controlled clinical trial with a specifically configured RNA drug, poly(I).poly(C12U), in chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S88-95 | Chronic fatigue syndrome (CFS) is a physically debilitating illness associated with immunologic abnormalities, viral reactivation, and impairment of cognition. In a randomized, multicenter, placebo-controlled, double-blind study of 92 patients meeting the CFS case definition of the Centers for Disease Control and Prevention, the response of several laboratory and clinical variables to an antiviral and immunomodulatory drug, poly(I).poly(C12U), was determined. Measures of clinical response included Karnofsky performance score, a cognition scale derived from a self-administered instrument assessing symptomatology (SCL-90-R), an activities of daily living scale, and exercise treadmill performance. After 24 weeks, patients receiving poly(I).poly(C12U) had higher scores for both global performance and perceived cognition than did patients receiving placebo. In particular, patients given poly(I).poly(C12U) had increased Karnofsky performance scores ($P < .03$), exhibited a greater ability to do work during exercise treadmill testing ($P = .01$), displayed an enhanced capacity to perform the activities of daily living ($P < .04$), had a reduced cognitive deficit ($P = .05$), and required less use of |

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| | | | | other medications ($P < .05$). Multicenter Study Randomized Controlled Trial |
| Suhadolnik RJ, Reichenbach NL, Hitzges P, Adelson ME, Peterson DL, Cheney P, Salvato P, Thompson C, Loveless M, Muller WE, et al. | Department of Biochemistry, Temple University School of Medicine, Philadelphia, Pennsylvania 19140. | Changes in the 2-5A synthetase/RNase L antiviral pathway in a controlled clinical trial with poly(I)-poly(C12U) in chronic fatigue syndrome. | In Vivo 1994 Jul-Aug;8(4):599-604 | Latent 2', 5'-oligoadenylate (2-5A) synthetase activity, bioactive 2-5A and RNase L activity were measured in extracts of peripheral blood mononuclear cells (PMBC) before and during a randomized, multicenter, placebo-controlled, double-blind study of poly(I)-poly(C12U) in individuals with chronic fatigue syndrome (CFS) as defined by the Centers for Disease Control and Prevention. The mean values for bioactive 2-5A and RNase L activity were significantly elevated at baseline compared to controls ($p < .0001$ and $p = .001$, respectively). In individuals that presented with elevated RNase L activity at baseline, therapy with poly(I)-poly(C12U) resulted in a significant decrease in both bioactive 2-5A and RNase L activity ($p = .09$ and $p = .005$, respectively). Decrease in RNase L activity in individuals treated with poly(I)-poly(C12U) correlated with cognitive improvement ($p = .007$). Poly(I)-poly(C12U) therapy resulted in a significant decrease in bioactive 2-5A and RNase L activity in agreement with clinical and neuropsychological improvements (Strayer DR, et al., Clin. Infectious Dis. 18:588-595, 1994). The results described show that poly(I)-poly(C12U) is a biologically active drug in CFS. Multicenter Study Randomized Controlled Trial |
| Suhadolnik RJ, Reichenbach NL, Hitzges P, Sobol RW, Peterson DL, Henry B, Ablashi DV, Muller WE, Schroder HC, Carter WA, et al. | Department of Biochemistry, Temple University School of Medicine, Philadelphia, Pennsylvania 19140. | Upregulation of the 2-5A synthetase/RNase L antiviral pathway associated with chronic fatigue syndrome. | Clin Infect Dis 1994 Jan;18 Suppl 1:S96-104 | Levels of 2',5'-oligoadenylate (2-5A) synthetase, bioactive 2-5A, and RNase L were measured in extracts of peripheral blood mononuclear cells (PBMCs) from 15 individuals with chronic fatigue syndrome (CFS) before and during therapy with the biological response modifier poly(I).poly(C12U) and were compared with levels in healthy controls. Patients differed significantly from controls in having a lower mean basal level of latent 2-5A synthetase ($P < .0001$), a higher pretreatment level of bioactive 2-5A ($P = .002$), and a higher level of pretherapy RNase L activity ($P < .0001$). PBMC extracts from 10 persons with CFS had a mean basal level of activated 2-5A synthetase higher than the corresponding control value ($P = .009$). All seven pretherapy PBMC extracts tested were positive for the replication of human herpesvirus 6 (HHV-6). Therapy with poly(I).poly(C12U) resulted in a significant decrease in HHV-6 activity ($P < .01$) and in downregulation of the 2-5A synthetase/RNase L pathway in temporal association with clinical and neuropsychological improvement. The upregulated 2-5A pathway in CFS before therapy is consistent with an activated immune state and a role for persistent viral infection in the pathogenesis of CFS. The response to therapy suggests direct or indirect antiviral activity of poly(I).poly(C12U) in this situation. |
| Swanink CM, Melchers WJ, van der Meer JW, Vercoulen JH, Bleijenberg G, Fennis JF, Galama JM. | Department of Medical Microbiology, University Hospital Nijmegen, The Netherlands. | Enteroviruses and the chronic fatigue syndrome. | Clin Infect Dis 1994 Nov;19(5):860-4 | The possible role of enteroviral persistence in the etiology of the chronic fatigue syndrome (CFS) was investigated by serological testing, VP-1 antigen testing, and polymerase chain reaction (PCR) analysis of stool specimens as well as by viral cultures of stool--both direct and after acid treatment. No differences between 76 patients with disabling unexplained fatigue and 76 matched controls were found by serological or antigen testing. Furthermore, no enteroviruses were isolated from any stool culture. Enterovirus was detected by PCR in one stool specimen from a patient with CFS but was not detectable in a second sample obtained from the same patient 3 months later. All stool specimens from controls were PCR-negative. These results argue against the hypothesis that enteroviruses persist in patients with CFS and that their persistence plays a role in the pathogenesis of this syndrome. |
| Swanink CM, Vercoulen JH, Bazelmans E, Fennis JF, Bleijenberg G, van der Meer JW, Galama JM. | | Viral antibodies in chronic fatigue syndrome. | 938: Clin Infect Dis 1995 Sep;21(3):708-9 comment on: Clin Infect Dis. 1994 Sep;19(3):448-53 | |
| Taerk G, Gnam W. | Department of Psychiatry, Toronto Hospital, Ontario, Canada. | A psychodynamic view of the chronic fatigue syndrome. The role of object relations in etiology and treatment. | Gen Hosp Psychiatry 1994 Sep;16(5):319-25 comment in: Gen Hosp Psychiatry. 1998 Nov;20(6):382-4 | The chronic fatigue syndrome (CFS) is a constellation of physical and psychological symptoms including incapacitating fatigue associated with a marked reduction in activity. Although the etiology of CFS is unclear, reports in the literature suggest the presence of both physical and psychological dysfunction in this patient population. These findings have led to a debate between those who consider CFS to be primarily organic in origin and those who view CFS as a primary psychiatric disorder characterized by somatic preoccupations. This debate led the authors to develop a working model for CFS designed to integrate the psychological and physiological findings, based on the hypothesis that early object relations have an etiologic relationship to CFS. This hypothesis then formed the rationale for a psychoanalytic treatment approach which will be described. There are no published case reports describing psychoanalytic psychotherapy as a primary treatment modality for this patient population. The current paper attempts to fill a void. Two case reports of long-term (> 18 months), intensive (2-3 |

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| | | | | times per week) psychoanalytic psychotherapy with CFS patients referred by infectious disease specialists at a university teaching hospital will be presented. The following aspects of the treatment will be highlighted: 1) the unique opportunity afforded by this treatment to view the nature of CFS, namely, the intimate relationship over time of fatigue symptoms to disturbances in object relationships, particularly within the transference; (2) the improvement in symptoms when this relationship is seen and understood by the patient; (3) the importance of the patient-therapist bond as a facilitating medium for clinical improvement; (4) the challenges involved in treating CFS patients with psychotherapy. |
| Tannock C, Costa DC, Brostoff J. | | Chronic fatigue syndrome. Preliminary report misrepresented. | BMJ 1994 May 14;308(6939):1298 comment in: BMJ. 1994 Jun 25;308(6945):1716-7 | |
| Tirdei G, Ruta SM, Popescu AE. | Institut de Virologie, Stefan S. Nicolau, Bucarest, Roumanie. | [Human herpesvirus 6. General overview].[article in French] | Rev Roum Virol 1994 Jan-Jun;45(1-2):83-95 | Human herpesvirus 6 (HHV6) was first isolated in 1985 and included in the Herpesviridae family and the beta-herpes virinae subfamily, mainly due to its genomic similarities to the human cytomegalic virus (HCMV). HHV6 is largely disseminated in the population. The contamination takes place very early, most frequently before the age of three. In some very rare cases, a benign illness is produced, known since 1911 as Roseolum infantum or Exanthemum subitum. Seroepidemiological surveys showed that anti-HHV6 IgG antibodies were present in more than 60% of the adult population. By now, there are good information about in vitro cultivability of the virus, viral genome and proteins, epidemiology of the infection and etiopathogenic relation between virus and Exanthemum subitum. Relations between virus and lymphoproliferative diseases, some auto-immune diseases, chronic fatigue syndrome and some other diseases are less clear. Relation between this virus and HIV-infection is another problem requiring more research. |
| Tirelli U, Marotta G, Improta S, Pinto A. | CFS Unit, Division of Medical Oncology and AIDS, Centro di Riferimento Oncologico (CRO), Aviano, Italy. | Immunological abnormalities in patients with chronic fatigue syndrome. | Scand J Immunol 1994 Dec;40(6):601-8 | Between January 1991 and January 1993, 265 patients who fulfilled the CDC criteria of the working case definition of Chronic Fatigue Syndrome (CFS) have been observed at our Institution and submitted for clinical and laboratory evaluation. One hundred and sixty-three patients were females and 102 males, the median age was 35 years (range 4-55 years); all patients reported profound and prolonged fatigue, lasting for a median of 3 years (range 6 months-10 years), preceded or accompanied at appearance by fever in 185 cases, and neuropsychologic problems including inability to concentrate, difficulty in thinking, confusion, irritability, forgetfulness, and depression. The fatigue was so severe that it required 102 patients to stop their working activities for a period of time ranging from 3 months to 2 years (range 7 months). In 40 consecutive patients a comprehensive immunologic testing by single and two-colour flow cytometry was performed and results compared with a group of 35 healthy, age- and sex-matched controls. Whilst no significant differences were found in the absolute numbers of circulating total T cells (CD3+) and of total helper/inducer (CD4+) or suppressor/cytotoxic (CD8+) T cells, an evident reduction in CD3-/CD16+ and CD57+/CD56+ NK lymphocytes along with an expansion of the CD8+/CD56+ and CD16-/CD56+ NK subsets, were found in the CFS group. In addition, CD56+ NK cells from CFS subjects were found to express an increased amount of cell adhesion molecules (CD11b, CD11c, CD54) and activation antigens (CD38). Both the percentage and absolute numbers of CD4+ T cells bearing the CD45RA antigen appeared significantly reduced in CFS patients, and CD4+ T lymphocytes from CFS subjects displayed an increased expression of the intercellular adhesion molecule-1 (ICAM-1/CD54). Finally, the total numbers of circulating (CD19+) B lymphocytes, were significantly higher in CFS cases than in controls, and in 11 out of 30 CFS patients the increase in circulating B cells was sustained by the expansion of the CD5+/CD19+ subset of B lymphocytes. We conclude that CFS is a syndrome not previously described in Italy, with already known clinical characteristics and appears to be associated with several immunologic abnormalities, including those reported previously in cohort of patients from different countries. We also show for the first time that CD56- NK cell subsets from CFS patients display an abnormally increased expression of cell adhesion molecules and activation markers. |
| Trevor A. | | Chronic fatigue syndrome: what's in a name? | Can Fam Physician 1994 Jun;40:1088-9 comment on: Can Fam Physician. 1993 Dec;39:2586-92, 2595-7 | |

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| Trinidad EE, Ramirez-Ronda C. | Programa de Enfermedades Infecciosas Universidad de Puerto Rico, San Juan. | [Chronic fatigue syndrome].[article in Spanish] | Bol Asoc Med P R 1994 Jul-Sep;86(7-9):56-61 | The Chronic Fatigue Syndrome is a disease that originates in the 18th Century of unknown etiology. The chronic fatigue is a common complain with an estimate prevalence of 24%. In 1988 the Chronic Fatigue Syndrome was define by the experts due to an increase in the recognition of the disease. Is a disease that possess similar characteristics to other conditions for which the diagnosis is one of exclusion. Cases has been reported around the world been most common in women between 20-50 years of age. The treatment is mostly supportive. |
| Trojani FT. | | [The chronic fatigue syndrome].[article in Italian] | Clin Ter 1994 Apr;144(4):373-6 | |
| Trojani FT. | | [Chronic fatigue syndrome].[article in Italian] | Clin Ter 1994 Mar;144(3):269-72 | |
| Trojani FT. | | [Chronic fatigue syndrome].[article in Italian] | Clin Ter 1994 Feb;144(2):163-6 | |
| Valesini G, Conti F, Priori R. Review Review, Tutorial | | Chronic fatigue syndrome: what factors trigger it off? | Clin Exp Rheumatol 1994 Sep-Oct;12(5):473-6 | |
| Vercoulen JH, Swanink CM, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G. | Department of Medical Psychology, University Hospital, Nijmegen, The Netherlands. | Dimensional assessment of chronic fatigue syndrome. | J Psychosom Res 1994 Jul;38(5):383-92 | The absence of laboratory tests and clear criteria to identify homogeneous (sub)groups in patients presenting with unexplained fatigue, and to assess clinical status and disability in these patients, calls for further assessment methods. In the present study, a multi-dimensional approach to the assessment of chronic fatigue syndrome (CFS) is evaluated. Two-hundred and ninety-eight patients with CFS completed a set of postal questionnaires that assessed the behavioural, emotional, social, and cognitive aspects of CFS. By means of statistical analyses nine relatively independent dimensions of CFS were identified along which CFS-assessment and CFS-research can be directed. These dimensions were named: psychological well-being, functional impairment in daily life, sleep disturbances, avoidance of physical activity, neuropsychological impairment, causal attributions related to the complaints, social functioning, self-efficacy expectations, and subjective experience of the personal situation. A description of the study sample on these dimensions is presented. |
| Wassif WS, Sherman D, Salisbury JR, Peters TJ. | Department of Clinical Biochemistry, Kings College School of Medicine and Dentistry, London, UK. | Use of dynamic tests of muscle function and histomorphometry of quadriceps muscle biopsies in the investigation of patients with chronic alcohol misuse and chronic fatigue syndrome. | Ann Clin Biochem 1994 Sep;31 (Pt 5):462-8 | Ischaemic lactate/ammonia tests, serum carnosinase and creatine kinase assays and percutaneous needle muscle biopsies were performed on 10 patients with chronic fatigue syndrome (CFS), and 10 with chronic alcohol misuse complaining of muscular symptoms. Basal serum lactate levels were significantly elevated in the alcohol misusers compared to the CFS patients, but all were within the reference range. Lactate profiles after ischaemic forearm exercise did not differ significantly for the two patient groups. In one patient previously diagnosed as having CFS, myoadenylate deaminase deficiency was identified on the basis of a flat ammonia response to ischaemia and absent muscle adenosine monophosphate deaminase activity. In addition, two further patients in the CFS group were subsequently shown to have other disorders: one had polymyositis and one had myopathy with mild type II fibre atrophy of unknown cause. Histomorphometric examination of muscle needle biopsy in the alcohol misusers showed features of chronic alcohol-induced skeletal myopathy in six patients and polymyositis in one patient. Type II fibre atrophy factors were significantly elevated in the alcohol group but were within the reference range in CFS patients. Dynamic tests of muscle function and muscle histology are valuable tools in excluding alternative pathology in CFS, whereas muscle histomorphometry is of the greatest value in the diagnosis of chronic alcoholic myopathy. |
| Wessely S. | Academic Dpt of Psychologic, King's College Hospital, London, United Kingdom. | [Chronic fatigue syndrome. Clinical, social psychological problems and management].[article in French] | Encephale 1994 Nov;20 Spec No 3:581-95 | Fatigue chronic syndrome (SFC) is the heir-at-law of neurasthenia. Both are seen like physical diseases and share certain therapeutic measures, such as sleep; they have the same symbolic function and enable patients as well as doctors reluctant to psychological dimensions of pathology, to get and express sympathy and attention. A strong controversy developed these last years concerning the SFC physiopathology particularly concerning the responsibility of viral infectious agents or psychiatric troubles. The SFC fatigue is unlikely hysterical or neuromuscular but it probably depends on several associated factors; cerebral neurobiochemistry anomalies (possibly induced by an infection or immune reactions), effort perception trouble, affective trouble, lack of physical activity. The handicap seems to be worse on account of unsuitable care and inefficacious treatment. Especially sleep, which is often beneficial in a short term, is source of ulterior chronicisation. Antidepressants are the only justified pharmacological treatment for SFC at the moment. Referring to the existence and the nature of |

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| | | | | cognitive distortions, the author suggests a cognitive-behavioural therapy, whose aim is a progressive activity resumption. |
| Wilborn F, Schmidt CA, Brinkmann V, Jendroska K, Oettle H, Siegert W. | Universitätsklinikum Rudolf Virchow, Innere Medizin und Poliklinik mit Schwerpunkt Hamatologie und Onkologie, Berlin, Germany. | A potential role for human herpesvirus type 6 in nervous system disease. | J Neuroimmunol 1994 Jan;49(1-2):213-4 | Human herpesvirus type 6 (HHV-6) is a new representative of the herpesvirus family which was associated with a spectrum of diseases, including myalgic encephalitis, meningitis and the chronic fatigue syndrome. We set out to study the potential role of HHV-6 in multiple sclerosis (MS) (n = 21), facial palsy (FP) (n = 19) and Guillain-Barre-syndrome (GBS) (n = 7). Results were compared with a control group (CG) (n = 16). We analyzed paired samples of serum and cerebrospinal fluid (CSF) with the polymerase chain reaction (PCR) for the presence of HHV-6 DNA. The studies were complemented by ELISA determination of serum antibodies against HHV-6. In the MS group we detected HHV-6 DNA in the CSF from three of 21 (14.3%) patients but not in the corresponding serum samples. In FP, GBS and controls CSF and serum PCRs were negative in all cases. HHV-6 serum antibody titers were significantly higher in MS compared with FP, GBS and controls. These findings suggest that HHV-6 may play a role in MS. |
| Wilson A, Hickie I, Lloyd A, Hadzi-Pavlovic D, Boughton C, Dwyer J, Wakefield D. | Department of Psychiatry, Prince Henry Hospital, Little Bay, NSW, Australia. | Longitudinal study of outcome of chronic fatigue syndrome. | BMJ 1994 Mar 19;308(6931):756-9 comment in: BMJ. 1994 May 14;308(6939):1297 BMJ. 1994 May 14;308(6939):1297-8 BMJ. 1994 May 14;308(6939):1299 | OBJECTIVE--To examine the predictors of long term outcome for patients with the chronic fatigue syndrome. DESIGN--Cohort study. SUBJECTS--139 subjects previously enrolled in two treatment trials; 103 (74%) were reassessed a mean of 3.2 years after start of the trials. SETTING--University hospital referral centre. MAIN OUTCOME MEASURES--Age at onset, duration of illness, psychological and immunological status at initial assessment. Ongoing symptom severity, levels of disability, and immunological function at follow up. RESULTS--65 subjects had improved but only six reported no current symptoms. An alternative medical diagnosis had been made in two and psychiatric illness diagnosed in 20. The assignment of a primary psychiatric diagnosis at follow up and the strength of the belief that a physical disease process explained all symptoms at entry to the trials both predicted poor outcome. Age at onset of illness, duration of illness, neuroticism, premorbid psychiatric diagnoses, and cell mediated immune function did not predict outcome. CONCLUSION--Though most patients with the chronic fatigue syndrome improve, a substantial proportion remain functionally impaired. Psychological factors such as illness attitudes and coping style seem more important predictors of long term outcome than immunological or demographic variables. |
| Wilson A, Hickie I, Lloyd A, Wakefield D. | Department of Psychiatry, Prince Henry Hospital, Little Bay NSW, Australia. | The treatment of chronic fatigue syndrome: science and speculation. | Am J Med 1994 Jun;96(6):544-50 | The chronic fatigue syndrome (CFS) is a heterogeneous disorder characterized by fatigue, neuropsychiatric symptoms, and various other somatic complaints. Treatment studies to date reflect both the diversity of medical disciplines involved in the management of patients with CFS and the multiple pathophysiologic mechanisms proposed. There have been few attempts to study integrated treatment programs, and although several controlled studies have been reported, no treatment has been shown clearly to result in long-term benefit in the majority of patients. Good clinical care integrating medical and psychologic concepts, together with symptomatic management, may prevent significant secondary impairment in the majority of patients. Future treatment studies should examine differential response rates for possible subtypes of the disorder (eg, documented viral onset, concurrent clinical depression), evaluate the extent of any synergistic effects between therapies (ie, medical and psychologic), and employ a wide range of biologic and psychologic parameters as markers of treatment response. |
| Yalcin S, Kuratsune H, Yamaguchi K, Kitani T, Yamanishi K. | Department of Virology, Osaka University Medical School, Japan. | Prevalence of human herpesvirus 6 variants A and B in patients with chronic fatigue syndrome. | Microbiol Immunol 1994;38(7):587-90 | Peripheral blood mononuclear cells collected from 13 patients with chronic fatigue syndrome and 13 healthy controls were analyzed for the presence of human herpesvirus 6 (HHV-6) DNA by variant-specific polymerase chain reaction and dot blot hybridization. HHV-6 DNA was detected in 7 of 13 (53%) patients, and of those 7 patients, 4 were positive for HHV-6 variant A DNA and 3 were for variant B. No HHV-6 DNA was detected in the controls. Serum antibody titers to the late antigen and antibody prevalence to the early antigen of HHV-6 were significantly higher in the patient group. These results suggest active replication of HHV-6 in patients with chronic fatigue syndrome. |
| Zavalishin IA, Zakharova MN. | | [The chronic fatigue syndrome]. [article in Russian] | Zh Nevropatol Psikhiatr Im S S Korsakova 1994;94(5):44-6 | |
| Zubieta JK, Engleberg NC, Yargic LI, Pande AC, Demitrack MA. | Department of Psychiatry, University of Michigan Medical Center, Ann Arbor | Seasonal symptom variation in patients with chronic fatigue: comparison with major mood | J Psychiatr Res 1994 Jan-Feb;28(1):13-22 | The psychobiology of idiopathic fatigue has received renewed interest in the medical literature in recent years. In order to examine the relation between chronic, idiopathic fatigue and specific subtypes of depressive illness, we characterized the pattern and severity of seasonal symptom variation in 73 |

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| | 48109-0116. | disorders. | <p>patients with chronic, idiopathic fatigue, compared to patients with major depression (n = 55), atypical depression (n = 35), and seasonal affective disorder (n = 16) Fifty of the fatigued subjects also met the specific Centers for Disease Control and Prevention case criteria for chronic fatigue syndrome, though this definition was unable to discriminate a distinct subgroup of patients, based on their seasonality scores alone. As a group, the fatigued subjects reported the lowest levels of symptom seasonality of any of the study groups. Further, even in those fatigued subjects with scores in the range of those seen in patients with seasonal affective disorder, seasonality was not reported to be a subjectively distressing problem. These findings lend support to the idea that although chronic fatigue shares some clinical features with certain mood disorders, they are not the same illnesses. These data are also consistent with the emerging view that chronic fatigue represents a heterogeneously determined clinical condition.</p> |
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