

A Historical Review of Chronic Fatigue Syndrome

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I. Introduction

Chronic fatigue syndrome is an illness characterized by profound disabling fatigue lasting at least 6 months and accompanied by numerous rheumatological, infectious, and neuropsychiatric symptoms (Fukuda K. et al.1994). As the name implies, chronic fatigue syndrome is a symptom-based or clinical diagnosis without distinguishing physical examination or routine laboratory findings. Infectious, immunological, neuroendocrine, sleep, and psychiatric mechanisms have been investigated; however, a unifying etiology for chronic fatigue syndrome has yet to emerge. It seems likely that chronic fatigue syndrome is a heterogeneous disease with different pathophysiological disturbances that manifest with similar symptoms. Regardless of the pathogenesis, persons with chronic fatigue syndrome, like those with other chronic diseases, have a substantially impaired functional status that results in significant personal and economic morbidity (Bombardier C.H.& Buchwald D. 1996; & Buchwald D. et al.1996). Bell D.S. in 1995 has defined chronic fatigue syndrome (CFS) as, "A complex symptom pattern, characterized by functional limitations and dominated by debilitating fatigue". As a result of a lack of explicit laboratory markers to diagnose CFS, the diagnosis is strictly clinical (Bell D.S., 1995; & Smith M.S. et al.1991). For research purposes, descriptive criteria have been defined by the Centers for Disease Control and Prevention (CDC) (Holmes G.P., Kaplan J.E., Nelson M., et al.1988; Fukuda K., Straus S.E., Hickie I., et al.1994).The major criteria consist of fatigue persisting for at least 6 months, seriously interfering with the patient's daily activities, and without evidence of organic or psychiatric illnesses that can produce chronic fatigue. Minor symptom criteria include impaired memory or concentration, sore throat, tender cervical or axillary lymph nodes, muscle pain, multijoint pain, new headaches, unrefreshing sleep, and post exertion malaise (Fukuda K. et al.1994).Chronic fatigue syndrome (CFS), otherwise known as myalgic encephalomyelitis or post-viral fatigue syndrome, is an illness characterized by persistent debilitating fatigue of uncertain origin. A multiplicity of other symptoms are associated with CFS such as muscle and joint pain, fever, sleep disruption, and impaired memory and concentration. Prevalence rates for this disorder have been quoted between 7.4 and 37 per 100,000, depending on the sampling procedures and diagnostic criteria used (Gunn, Connel & Randall, 1993; Lloyd, Hickie, Boughton, Spencer & Wakefield, 1990; Price, North, Wessely & Fraser, 1992). The average age of onset is approximately 30 years, with well-educated white women being over represented in patient samples (Gunn et al., 1993). CFS in adolescence mostly has an acute onset, presenting as a flu- or mononucleosis-like image, e.g., Epstein-Barr virus infection (Bell D.S.1995; Smith M.S. et al.1991; Jordan K.M. et al. 1998; & Carter B.D. et al. 1995). In ~25% of cases, the onset is insidious. Depending on the diagnostic criteria and age ranges used, prevalence estimates for adolescents vary from 23/100 000 to 116.4/100 000 in children from 6 to 19 years old. In the literature a predominance is reported of CFS in adult women (ratio 4:1 for women vs. men) and this also seems to be the case in pediatric CFS (Bell D.S.1995; Jordan K.M. et al. 1998; & Kennedy J.L, Pearce J.B.1995). Although in young children the distribution seems to be more equal, after puberty adolescent girls seem to outnumber adolescent boys. The middle and upper socioeconomic classes are slightly overrepresented in research on chronically fatigued patients (Jordan K.M. et al. 1998; Carter B.D. et al. 1995; & Kennedy J.L. & Pearce J.B.1995).

Fatigue is the hallmark of chronic fatigue syndrome. Patients often report excellent pre-illness physical fitness and energy (MacDonalld et al.1996) and an abrupt onset of fatigue, typically with a flu-like illness (Salit I.E. 1997& Schluederberg A. 1992). After illness onset, however, patients indicate that physical exertion tends to exacerbate the fatigue. Many patients with chronic fatigue syndrome also often experience anorexia, nausea, drenching night sweats, dizziness, and intolerance to alcohol and other pharmaceuticals that affect the central nervous system (Komaroff A.L. et al.1996). Finally, those with chronic fatigue syndrome have significant functional impairment. Nearly all patients with chronic fatigue syndrome note a decrease in social relationships in addition to other unwanted consequences of illness (Sharpe M.C. et al.1991); about one-third are unable to work, and another one-third can only work part-time (Bombardier C.H. & Buchwald D.1996).

There is some support for this model of CFS. Investigations into CFS patients' symptom experience have frequently demonstrated that subjective reports of cognitive difficulties and neuromuscular symptoms are incongruent with objective test results (e.g. Altay, Toner, Brooker, Abbey, Salit & Garfinkel, 1990; Grafman, Schartz, Dale, Scheffers, Houser & Straus, 1993; Lloyd, Hales & Gandevia, 1988). These studies suggest that CFS patients have distorted perceptions of effort and sensation which may contribute to their functional disability. Other investigators have focused on coping styles and beliefs about CFS. Two longitudinal studies of patients with chronic fatigue found that patients who strongly believed their condition was caused by a physical agent were more functionally impaired (Sharpe, Hawton, Seagroatt & Pasvol, 1992; Wilson et al., 1994). Sharpe et al. (1992) also established that coping with chronic fatigue by avoiding exercise was predictive of disability. A cross-sectional study of coping in CFS reported that patients who coped with the illness by maintaining high activity had higher levels of functioning, while focusing on symptoms and accommodating to the illness were associated with greater functional impairment (Ray, Weir, Stewart, Miller & Hyde, 1993).

History of Chronic Fatigue Syndrome

The history of chronic fatigue syndrome (CFS, also known by many other names) is thought to date back to the 19th century and before. Several descriptions of illness resembling those of chronic fatigue syndrome have been reported for at least two hundred years (Lorusso L. et al. 2009). In the 19th century neurologist George Miller Beard popularised the concept of neurasthenia with symptoms including fatigue, anxiety, headache, impotence, neuralgia and depression (Beard G. 1869). This concept remained popular well into the 20th century, eventually coming to be seen as a behavioural rather than physical condition, with a diagnosis that excluded post viral syndromes. Neurasthenia has largely been abandoned as a medical diagnosis (Evangard B. et al. 1999). The ICD-10 system of the World Health Organization now categorizes neurasthenia under (F48 other neurotic disorders) which specifically excludes chronic fatigue syndrome (WHO 2007).

In 1938, Alexander Gilliam described an illness that resembled poliomyelitis, interviewing patients and reviewing records of one of several clusters which had occurred in Los Angeles, United States in 1934 (Gilliam A.G. 1938). The Los Angeles County Hospital outbreak included all or most of its nurses and doctors (Roberto Patarca-Montero 2004). Gilliam called the outbreak "atypical poliomyelitis" and described the symptoms as: rapid muscle weakness, vasomotor instability, clonic twitches and cramps, ataxia, severe pain (usually aggravated by exercise), neck and back stiffness, menstrual disturbance and dominant sensory involvement. In the 1960s and 1970s, chronic fatigue symptoms were often attributed to chronic brucellosis, but typically people were seen as having psychiatric disorders, in particular depression (Roberto Patarca-Montero 2004). Epidemic cases of benign myalgic encephalomyelitis were called mass hysteria by psychiatrists McEvedy and Beard in 1970, provoking criticism in letters to the editor of the British Medical Journal by outbreak researchers, attending physicians, and physicians who fell ill. (Scott B.D. 1970; Compston N. D., 1970; Acheson E. D. 1970; Gosling P. H. 1970; Purke G. J. 1970; Hopkins E. J. 1970; Galpine J. F. 1970; Poskanzer D. C. 1970 & Parish J. G. 1970). The psychiatrists were faulted for not adequately investigating the patients they described (Hooper M. 2006) and their conclusions have been refuted (Evangard B. et al. 1999; David A. S. et al. 1988; Stricklin A. et al. 1990). The illness gained national attention in the United States when the popular magazine *Hippocrates* ran a cover story of an epidemic at Lake Tahoe Nevada in the mid-1980s (Johnson Hilary 1996). The designation Chronic Epstein-Barr Virus was in use in the U. S. (Jones J. et al. 1985; Straus S. et al. 1985) but the magazine used the term "Raggedy Ann Syndrome" to note the fatigue and loss of muscle power patients felt (Day W (1987). Researchers investigating the Lake Tahoe cluster did not find evidence that EBV was involved, and they proposed the name chronic fatigue syndrome, describing the main symptom of the illness (Sharpe Michael & Frankie Campling 2000; Packard R. M. et al. 2004). They published the first working case definition for CFS in 1988 (Holmes G. et al. 1988). Research increased considerably, and more so after the criteria were relaxed in 1994 (Fukuda K. et al. 1994). In 1990, researchers presented evidence they found DNA sequences very similar to the human HTLV-II retrovirus in some CFS patients, at a conference in Kyoto, Japan (Palca J. 1990 & Altman Lawrence K. 1990). Their study was later published in the Proceedings of the National Academy of Sciences (DeFreitas E., Hilliard B., Cheney P. R. et al. 1991). A reporter on Prime Time Live stated the announcement made headlines all over the world. The CDC first ignored their findings (Sam Donaldson et al. 1996) then later conducted a study and published a paper that refuted the hypothesis (CDC 1993). In the United Kingdom, Royal Colleges (1996) published a joint report in which the term "chronic fatigue syndrome" was found to be most representative (Royal Colleges of Physicians, Psychiatrists and General Practitioners (1996). This was followed in 2002 by a further report by the new CMO, Liam Donaldson (CFS/ME Working Group 2002). The U.S. Centers for Disease Control & Prevention (CDC) recognize CFS as a serious illness and launched a campaign in June 2006 to raise public and medical awareness about it (CDC 2006 & Gerberding 2008). Lombardi V.C. et al. (2009) has identified the XMRV retrovirus in a population of people with CFS (Morgan David 2009). Other studies failed to reproduce those findings, sparking a controversy about XMRV's purported association with CFS. The 2009 paper was retracted by *Science* in December 2011. At the same time -

in December 2011 - the Proceedings of the National Academy of Sciences published a similar retraction for an August 2010 paper. The DSM-IV-TR (American Psychiatric Association, 2000) classifies chronic Fatigue Syndrome as 'undifferentiated Somatoform disorder', with the following diagnostic criteria.

A. One or more physical complaints (e.g., fatigue, loss of appetite, gastrointestinal or urinary complaints).

B. Either:

(1) After appropriate investigation, the symptoms cannot be fully explained by a known general medical condition or the direct effects of a substance (e.g., a drug of abuse, a medication).

(2) When there is a related general medical condition, the physical complaints or resulting social or occupational impairment is in excess of what would be expected from the history, physical examination, or laboratory findings.

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The duration of the disturbance is at least 6 months.

E. The disturbance is not better accounted for by another mental disorder (e.g., another Somatoform Disorder, Sexual Dysfunction, Mood Disorder, Anxiety Disorder, Sleep Disorder, or Psychotic Disorder).

F. The symptom is not intentionally produced or feigned (as in Factitious Disorder or Malingering).

Although the intent is that each disorder can be classified in only one place in the ICD-10 classification system (WHO, 2007), in practicality 96% of the symptoms of Chronic Fatigue Syndrome overlap between two codes in the diagnostic classification. The recommendation currently is that Chronic Fatigue Syndrome is classified as G93.3 (Benign myalgic encephalomyelitis), however the description of the other relevant code (F48) has been included below for reference. G93.3 Benign myalgic encephalomyelitis - to be used where specific trigger such as a viral disease and/or where the symptoms do not fulfill the criteria for F48.0 (World Health Organization - UK Collaborating Centre, 2004).

F48.0 Neurasthenia – which has the following diagnostic features:

A. Either persistent and distressing complaints of increased fatigue after mental effort, or persistent and distressing complaints of bodily weakness and exhaustion after minimal effort;

B. At least two of the following: feelings of muscular aches and pains; dizziness; tension headaches; sleep disturbance; inability to relax; irritability & dyspepsia;

C. Any autonomic or depressive symptoms present are not sufficiently persistent and severe to fulfill the criteria for any of the more specific disorders in this classification.

It should be noted that the code F48.0 is little used in practice now (WHO, 2007).

In DSM-5 (APA 2013) chronic fatigue syndrome has been categorized under 'Somatic Symptom Disorder' 300.82 (F45.1), with the following diagnostic criteria: A) One or more symptoms that are distressing or resulting in significant disruption of daily life. B) Excessive thoughts, feelings, or behaviors related to the somatic symptom or associated health concerns as manifested by at least one of the following; 1) Disproportionate and persistent thoughts about the seriousness of one's symptoms, 2) Persistently high level of anxiety about health or symptoms. C) Although any one somatic symptom may not be continuously present, the state of being symptomatic is persistent (typically more than 6 months). *Specific if:* With predominant pain (previously pain disorder): This specifier is for individuals whose somatic symptom predominantly involves pain. *Specific if:* Persistent: A persistent course is characterized by severe symptoms, marked impairment, and long duration (more than 6 months). *Specific current severity:* Mild: Only one of the following symptoms specified in criteria B are fulfilled. Moderate: Two or more of the symptoms specified in criterion B are fulfilled. Severe: Two or more of the symptoms specified in criterion B are fulfilled, plus there are multiple somatic complaints (or one very severe somatic symptom). The idiopathic nature of CFS has resulted in a decade-long debate about whether the aetiology of this disorder is organic or psychological. Those favouring an organic cause have linked CFS to viral pathogens, muscle abnormalities and immunological disorders (for a review, see Buchwald & Kornaroff, 1991). Advocates of the psychological position have suggested that CFS is a psychiatric syndrome, such as depression, which presents with prominent somatic features (Kruesi, Dale & Straus, 1989; Manu, Lane & Mathews, 1988, 1993). Inconclusive results in both these fields have led others to propose that CFS may be caused by an interaction of both physical and psychosocial factors (Ray, 1991; Ware, 1993). In accordance with this thinking, Wessely and his colleagues have developed a model of CFS which suggests that a cycle of cognitive and behavioural responses mediates between the acute organic illness and the chronic syndrome (Butler, Chalder, Ron & Wessely, 1991; Wessely, Butler, Chalder & David, 1991).

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