Symptoms and Signs of Chronic Fatigue Syndrome

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This review summarizes the symptoms and signs seen in patients with chronic fatigue syndrome (CFS). It is based on the authors' experience with two cohorts of ~510 patients with chronic debilitating fatigue and on the reported experience of other investigators with similar patients. The most characteristic symptoms of CFS are the sudden onset of an infectious-type illness, the subsequent chronic and debilitating fatigue, and postexertional malaise; many patients also have recurrent fevers, pharyngitis, adenopathy, myalgias, sleep disorders, and cognitive impairment.

In many respects, the symptoms and signs of chronic fatigue syndrome (CFS) are nonspecific. As outlined in the working case definition of CFS developed under the leadership of the Centers for Disease Control (CDC), many well-recognized organic illnesses can produce chronic fatigue and the associated symptoms and signs of CFS [1] and, obviously, so can primary psychoneuroses.

We believe certain symptoms and signs of CFS may be helpful in distinguishing it from these various organic and psychiatric illnesses. In this review we will synthesize information from the literature [2–7] as well as unpublished data from our own experience.

In our New England practice, we are following ~250 patients with a chronic, debilitating illness of at least 6 months' duration, most of whose illnesses fulfill the CDC working case definition of CFS. Most of these cases appear to be endemic or sporadic: no family members or close contacts appear to have been similarly affected. With the help of colleagues in Nevada, we have also studied a group of ~260 patients who developed a similar illness as part of what may have been an epidemic: the patients all became ill at about the same time. All of these patients have completed detailed initial and follow-up questionnaires regarding their medical histories and current health status. Data on results from physical examinations on initial and subsequent visits have been collected systematically and recorded. All data have been entered into a computerized data base.

Patients for the New England group were chosen on a highly selective basis: before being seen in the practice and studied longitudinally, they completed a questionnaire that indicated they had features suggestive of CFS rather than chronic fatigue alone. Thus, this cohort provides no information as to the prevalence of CFS and may be representative only of more severely affected individuals with CFS. Patients for the Nevada group were chosen on a less-selective basis. All were patients living within a radius of ~100 miles who presented to one general internal medicine practice (that of Daniel Peterson and Paul Cheney) during 1984–1987 with a complaint of debilitating fatigue of at least 3 months' duration along with at least two of the following symptoms: fever, headache, sore throat, earache, rhinorrhea, cough, diarrhea, or myalgias. This cohort provides no information as to the prevalence of CFS in this area of Nevada; also, it cannot be determined whether the cohort is representative of other persons in the community who did not seek care at this particular practice.

In summarizing our own patient cohorts and those reported by other investigators, we may well be describing a heterogeneous group of patients. In this review, we do not exclude from consideration patients who do not fully meet the CDC working case definition of CFS because most of the published literature included in this review preceded the development of the CDC case definition. Also, our cohorts had, for the most part, been assembled before the development of the case definition, and our subsequent experience has indicated that there are virtually no differences between patients who fulfill and those who do not fulfill the case definition with regard to demographic features, symptoms, signs, or laboratory test results [8].

CFS may occur in both an endemic and an epidemic form. Similarities exist between the former and fibrositis; the latter is similar to the illness called myalgic encephalomyelitis. The etiologic agents responsible for these two forms of CFS may be different.

Demographic Data

In our own patient groups, the median age of patients is 37 years and the age at onset has ranged from 11 to 60 years

Supported in part by grants no. RO 1AI26788 and RO 1AI27314 from the National Institute of Allergy and Infectious Diseases, by fellowship support from the Henry J. Kaiser Family Foundation to Dr. Buchwald, by a Young Investigator Award from the National Alliance for Research on Schizophrenia and Depression to Dr. Buchwald, and by funds from the S. Sydney De Young Foundation, M. Palevsky, S. Harris, the Rowland Foundation, and the Minann Foundation.

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Reviews of Infectious Diseases 1991;13(Suppl 1):S8–11

0162-0886/91/1301-0001$02.00

old. This circumstance is similar to that noted by other investigators [2–6]. Jones et al. [4] and Bell (personal communication) have described what seems to be a similar illness in children <11 years old. In our experience and that of others [2–6], ~70% of the patients are women. To place this observation in context, it must be recalled that most (55%–60%) of the patients who have medical conditions and are treated by primary care practitioners are women. Although in our experience all socioeconomic groups are represented, the majority of patients with CFS studied thus far are middle-class. In our experience, no patient has been indigent or unemployed prior to developing CFS and relatively few patients are black. It is quite possible that patients from higher socioeconomic groups are more likely to define themselves as ill when experiencing a chronic, debilitating fatigue and that our experience is not representative of the population at large.

Symptoms

The main symptom of CFS is fatigue. In our studies, the typical patient has been ill for 3.9 years (range, 0.5–14 years). Approximately 25% of our patients describe themselves as regularly bedridden or shut in and unable to work, and one-third can work only on a part-time basis. Before they became ill, the patients generally perceived themselves to be more energetic than most of their friends.

One simple but compelling piece of evidence that these patients are suffering from an organic illness is the sudden onset of the illness in 85% of the patients we have studied. The majority of patients with CFS state that their chronic illness began suddenly on a particular day. Most often the initial illness is flulike, characterized primarily by fever, sore throat, cough, myalgias, and fatigue. Less frequently, the initial illness is gastrointestinal, characterized by fever, diarrhea, nausea, myalgias, and fatigue. In 5%–10% of our New England cohort, the illness started with a case of classic acute infectious mononucleosis. Whatever the nature of the onset, the illness becomes chronic. Typically, the course of the symptoms (individually and collectively) waxes and wanes—patients have good days and bad days. Some patients have periods of weeks or months when they feel essentially healthy again. Most patients never feel that they return to normal health: their good days are only relatively better than their bad days. Some patients, perhaps 10% of the overall group, regain what they perceive to be normal health for periods of at least a year. Some of these patients relapse thereafter; others seem to remain well.

The frequencies of various chronic symptoms that often accompany the fatigue are summarized in table 1. Several points require emphasis. First, these symptoms are experienced not just occasionally but are present to some degree virtually all of the time in most patients. Second, many of these symptoms are severe enough to impair normal functioning. As stated earlier, the severity of any given symptom tends to fluctuate for most patients. Third, in response to explicit questioning, the patients state that these symptoms were typically not a problem before their illness but became common after the illness began. For example, the following are the frequencies of several common chronic symptoms after the illness began vs. before the illness began, as reported by our patients: arthralgias (76% vs. 6%); morning stiffness (62% vs. 3%); distractibility (82% vs. 4%); forgetfulness (71% vs. 2%); dizziness (61% vs. 4%); paresthesias (52% vs. 2%); sleep disorder (90% vs. 7%); irritability (68% vs. 4%); and cough (33% vs. 0%).

Table 1. Frequency of symptoms in patients with CFS.

Symptom	Frequency (%)
Fatigue	100
Low-grade fever	60–95
Myalgias	20–95
Sleep disorder	15–90
Impaired cognition	50–85
Depression	70–85
Headaches	35–85
Pharyngitis	50–75
Anxiety	50–70
Muscle weakness	40–70
Postexertional malaise	50–60
Worsening of premenstrual symptoms	50–60
Stiffness ("gelling")	50–60
Visual blurring	50–60
Nocturia	50–60
Nausea	50–60
Dizziness	30–50
Arthralgias	40–50
Tachycardia	40–50
Paresthesias	30–50
Dry eyes	30–40
Dry mouth	30–40
Diarrhea	30–40
Anorexia	30–40
Cough	30–40
Finger swelling	30–40
Night sweats	30–40
Painful lymph nodes	30–40
Rash	30–40

NOTE. Frequencies are estimated from our own experience and from reports in the literature [2–7].

In our experience, the majority of patients with CFS have an exceptional postexertional malaise. Although patients typically are physically active before the onset of illness (which is usually acute), even modest physical exertion after its onset produces a striking exacerbation of many of their symptoms. Typically, the patient tolerates the physical exertion reasonably well and may even feel energized during and immediately after the exertion. However, 6–24 hours later the patients feel ill: the involved muscle groups feel sore and weak (as can occur with exercise following deconditioning), and 30%–70% of patients experience marked worsening of their

fatigue, cognitive function, adenopathy, pharyngitis, and fevers. In our experience, this postexertional malaise is unusual in healthy individuals or in those with diseases (such as the collagen vascular diseases) that have some clinical similarity to CFS.

As shown in table 1, the majority of patients become depressed and anxious after the illness begins. For most of our patients, the feelings they call depression or anxiety seem to be secondary rather than primary. In the questionnaire that our patients complete, they are asked to describe the presence of all symptoms – including their perception of the presence of anxiety and depression – both before and after the onset of their illness. Whereas depression and anxiety have been experienced chronically by two-thirds of our patients after the onset of CFS, <10% state that they experienced these symptoms chronically before the onset of CFS. We have performed detailed psychiatric evaluations with use of the Diagnostic Interview Survey for ~60 of our patients to date. These data confirm that most patients have no history of psychiatric disease before the onset of their chronic fatigue. The data also suggest, however, that when completing the questionnaire the patients have a tendency to underreport anxiety and depression in the years before the onset of the illness. By self-report ~20% of our patients have first-degree relatives who have been treated for a major affective disorder; other researchers found a higher frequency of major affective disorder among the families of their patients with CFS.

In response to a specific portion of the questionnaire, about one-half of the patients we are following report that they were under unusually severe stress at the time they developed CFS. Is this an unusually high rate of perceived stress, or would age-, sex-, and education-matched individuals who feel healthy report the same level of stress at any given time?

The impaired cognition reported by the great majority of patients (table 1) is a particularly debilitating and disturbing aspect of the illness. Patients describe difficulties such as lack of concentration and attention, impaired verbal expression, and absentmindedness. Like all human beings, they have experienced such mental lapses on occasion, but they state that the frequency and severity of these cognitive lapses have intensified since developing CFS. One-third of our patients responded positively to these two questions: "On occasion, have you not been sure about where you were, or where you were going, for at least five minutes?" "On occasion, have your friends or family said that you were completely confused: not making sense, not recognizing them, not responding normally?"

A few of the individuals in our patient group have had acute neurologic events: primary seizures (7%); acute, profound ataxia (6%); focal weakness (5%); transient blindness (4%); and unilateral paresthesias (not in a dermatomal distribution). For most patients these were single events, whereas for others they recurred on a few occasions. Most often, the events occurred in the first year after the acute onset of illness. In every other respect, the clinical and laboratory findings for these few patients with dramatic neurologic events are similar to those for the larger group of patients with chronic fatigue.

Table 2. Findings from physical examinations of patients with CFS.

Finding	Frequency (%)
Inflamed pharynx	40–60
Posterior cervical adenopathy	20–40
Abnormal Romberg test results	10–20
Impaired tandem gait	15–25
Macular rash	10–20
Fever (>99.6°F at a single office visit)	10–20
Low body temperature (<97.0°F)	20–30
Hepatomegaly (mainly early in disease)	5–20
Splenomegaly (mainly early in disease)	5–20
Axillary adenopathy	5–15

The social consequences of the illness can be severe. The patients feel personally deficient and alienated from their family, friends, and co-workers. Nearly 90% have had to limit their social life. The majority state explicitly that they have been "less able to fulfill my responsibilities to my family." One-third explicitly state that their family, friends, and co-workers "are mad at me for letting them down" and "have thought that I was faking being sick."

The patients' medical histories reveal one clearly striking finding: a high frequency of atopic or allergic illness (for ~40%–70%).

Physical Examination

As shown in table 2, on physical examination unusual and abnormal findings are observed for 10%–50% of patients, i.e., fevers, nonexudative pharyngitis, unusually low basal body temperature (<97°F), posterior cervical and axillary adenopathy, hepatosplenomegaly (which usually disappears after the first 3 months of illness), abnormal Romberg test results, and impaired tandem gait. We have found musculoskeletal tender points characteristic of a similar syndrome called fibrositis or fibromyalgia in most of the patients [9]. For most patients, such findings on physical examination are recurrent or persistent on sequential examinations over time and are noted at more than one examination.

Summary

Fatigue is a common complaint of patients who present at a general medical practice [10, 11]. Most such patients probably are suffering from a primary psychiatric illness [11, 12]. A few may have a well-recognized organic cause of chronic fatigue, such as an occult malignancy, thyroid disease, anemia, or other illness. Probably only a few of the many patients seeking medical care for chronic fatigue have CFS [12].

Moreover, some well-recognized organic illnesses, when

presenting in a mild form, may produce symptoms and signs similar to those seen in patients with CFS, especially systemic lupus erythematosus and multiple sclerosis. CFS also bears a close resemblance to the syndrome called fibrositis or fibromyalgia [13, 14], an illness that is seen frequently by rheumatologists.

CFS is a syndrome with a somewhat heterogeneous presentation. This may well indicate that multiple etiologic agents and pathogenetic derangements also are involved. CFS can present in both an endemic and an epidemic form; the two forms may have different causes. In our experience, however, the clinical and laboratory findings for patients with the endemic and epidemic forms are similar.

We believe the available data on symptoms and signs suggest that CFS is an illness distinct from other known physical and psychological illnesses. In our judgment, the best evidence for this is the sudden onset of the chronic condition after an acute infectious-type illness in the majority of patients; the fevers, pharyngitis, adenopathy, stiffness ("gelling"), arthralgias, cough, night sweats, and neurologic symptoms; physical examination findings such as posterior and axillary adenopathy, abnormal Romberg test results, and impaired tandem gait; and abnormal laboratory results that are described in a separate report [14].

We and other investigators have not yet systematically recorded histories and conducted physical examinations in a blinded manner for matched healthy control subjects. While some of the symptoms and signs described for patients with CFS seem striking and are not likely to be found among healthy individuals, other symptoms and signs are of uncertain significance. The reader is left, as we are, to compare these reported findings with those that would be expected for healthy individuals, from one's own experience.

Although we argue that CFS is likely to be an organic illness, it is nevertheless true that most of the patients suffer from depression and anxiety, which seem in most cases to be secondary to the development of CFS. As in many chronic illnesses, the psychological disorders may become an important part of the illness and require attention and treatment.

The working case definition of CFS [1] is based primarily on the diagnosis of symptoms and signs. However, we believe that the results of laboratory testing also may provide objective evidence that distinguishes patients with CFS from other individuals. We summarize such evidence in another report [9].

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