How have you felt during the last two weeks?

Please rate all four statements and per statement check the box that reflects your situation best.

1.	I feel tired	Yes, that is true							No, that is not true
2.	I tire easily	Yes, that is true							No, that is not true
3.	I feel fit	Yes, that is true							No, that is not true
4.	Physically I feel exhausted	Yes, that is true							No, that is not true

Scoring:

1, 2 and 4:	Yes, that is true	7	6	5	4	3	2	1	No, that is not true

3: Reversed

Sum scores >18 indicate severe fatigue

FIGURE 464e-1 **Shortened fatigue questionnaire.**

in cytokine production, and shifts in lymphocyte subsets have been described. None of these immune findings appears in most patients, nor does any correlate with the severity of CFS. In theory, symptoms of CFS could result from excessive production of a cytokine, such as interleukin 1, that induces asthenia and other flulike symptoms; however, compelling data in support of this hypothesis are lacking. There is some evidence that CFS patients have mild hypocortisolism, the degree of which is associated with a poorer response to CBT. Discrepancies in perceived and actual cognitive performance are consistent findings in patients with CFS.

DIAGNOSIS

In addition to a thorough history, a systematic physical examination is warranted to exclude disorders causing fatigue (e.g., endocrine disorders, neoplasms, heart failure). The heart rate of CFS patients is often slightly above normal. Laboratory tests serve primarily to exclude other diagnoses; no test can diagnose CFS. The following laboratory screen usually suffices: complete blood count; erythrocyte sedimentation rate; C-reactive protein; serum creatinine, electrolytes, calcium, and iron; blood glucose; creatine kinase; liver function tests; thyroid-stimulating hormone; anti-gliadin antibodies; and urinalysis. Serology for viral or bacterial infections usually is not helpful. No specific abnormalities have been identified on MRI or CT scans. The decrease in gray matter volume observed at a population level by MRI is not useful for diagnosis in the individual patient. Extensive, unfocused, and expensive testing in a search for the "hidden" cause of the fatigue is not productive. CFS is a constellation of symptoms with no pathognomonic features and remains a diagnosis of exclusion.

Bipolar disorders, schizophrenia, and substance abuse exclude a diagnosis of CFS, as do eating disorders, unless these issues have been resolved ≥5 years before symptom onset. In addition, CFS is excluded if the chronic fatigue developed immediately after a depressive episode. Depression developing in the course of the fatigue, however, does not preclude CFS. Concurrent psychiatric disorders, especially anxiety and mood disorders, are present in 30–60% of cases.

INITIAL MANAGEMENT

In cases of suspected CFS, the clinician should acknowledge the impact of the patient's symptoms on daily functioning. Disbelief or denial can provoke an exacerbation of genuine symptoms, which in turn strengthens the clinician's disbelief, leading to an unfortunate cycle of miscommunication. The possibility of CFS should be considered if a patient fulfils all criteria (Table 464e-1) and if other diagnoses have been excluded.

The patient should be asked to describe the symptoms (fatigue and accompanying symptoms) and their duration as well as their consequences (reduction in daily activities). To assess symptom severity and the extent of daily-life impairment, the patient should describe a typical day, from waking to retiring, and, for comparison, an average day prior to symptom onset. Next, potential fatigue-precipitating factors are sought. The severity of fatigue is commonly difficult to assess quantitatively; a brief questionnaire is often helpful (Fig. 464e-1).

The patient should be informed of the current understanding of precipitating and perpetuating factors and effective treatments and should be offered general advice about disease management. If CBT for CFS is not available as an initial option (see below) and depression and anxiety are present, these symptoms should be treated. For patients with headache, diffuse pain, and feverishness, nonsteroidal anti-inflammatory drugs may be helpful. Even modest improvements in symptoms can make an important difference in the patient's degree of self-sufficiency and ability to appreciate life's pleasures.

Controlled therapeutic trials have established that acyclovir, fludrocortisone, galantamine, modafinil, and IV immunoglobulin, among other agents, offer no significant benefit in CFS. Countless anecdotes circulate regarding other traditional and nontraditional therapies. It is important to guide patients away from those therapeutic modalities that are toxic, expensive, or unreasonable.

The patient should be encouraged to maintain regular sleep patterns, to remain as active as possible, and to gradually return to previous levels of exercise and other activity (work).

TREATMENT CHRONIC FATIGUE SYNDROME

CBT and graded exercise therapy (GET) have been found to be the only beneficial interventions in CFS. Some patient groups argue against these approaches because of the implication that CFS is a purely mental disorder. CBT is a psychotherapeutic approach directed at changing unhealthy disease-perpetuating patterns of thoughts and behaviors. It includes educating the patient about the etiologic model, setting goals, restoring fixed bedtimes and wake-up times, challenging and changing fatigue- and activity-related concerns, reducing a focus on symptoms, spreading activities