5
Care of the Patient with Fatigue

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Everyone experiences fatigue periodically as a result of hard physical labor or loss of sleep. Fatigue, loss of energy, and lassitude are also common symptoms experienced by patients with any of a large number of diseases. A patient who complains of fatigue presents a difficult problem for the family physician because there are many possible explanations for it. The subjective nature of the complaint and the potential seriousness of some of the diseases in the differential diagnosis compound this difficulty.

Background

Fatigue is common in the general population and is present in at least 20% of the patients who visit a family physician.[1–4] Community-based surveys indicate that as many as 50% of the population report fatigue if asked.[2,3] In the United States, fatigue is responsible for at least 10 million office visits and up to $300 million in health costs each year.[5] Valdini and colleagues[6] determined that 58% of family practice patients with a chief complaint of fatigue were still fatigued 1 year after the initial visit. But, in the absence of identifiable underlying organic diseases, 19 studies examining the prognosis of chronic fatigue found only three deaths among 2075 patients.[7] Chronic fatigue lasting over 6 months has a population prevalence of 1775/100,000 to 6321/100,000.[1] Fatigue consistently ranks among the most common presenting complaints to family physicians re-

gardless of practice setting or culture. A systematic, organized, efficient evaluation of these patients represents an essential skill for all family physicians.

Although fatigue is common and often persistent, many chronically fatigued patients defy diagnostic categorization. For centuries physicians have been perplexed by the diagnostic difficulties inherent in evaluating patients with chronic fatigue. Clinical syndromes have been defined to explain chronic fatigue including terms such as febricula, neurasthenia, nervous exhaustion, Da Costa syndrome, chronic brucellosis, hypoglycemia, total allergy syndrome, chronic candidiasis, and chronic Epstein-Barr virus infection.[8] In 1987 the United States Centers for Disease Control (CDC) established a clinical definition for the chronic fatigue syndrome (CFS).[9] It was hoped that such categorization would facilitate clinical investigation of the causes and most successful treatments for this problem. But the case definition did not clearly identify a clinically useful subset of chronically fatigued patients, and the definition was revised in 1994.[10] This chapter reviews a contextual, biopsychosocial differential diagnosis of fatigue and outlines a practical approach to evaluating and helping patients who complain of fatigue

Clinical Presentation

What are the characteristics of patients who complain of fatigue to the family physician? There is a bimodal distribution of patient age, with a peak between the ages of 15 and 24 and a second peak at 60-plus years. Women complain of fatigue to the physician at least twice as often as men.[3–6,9,11,12] This excess may be explained by a higher incidence of fatigue in women, that women are more likely to tell the physician about fatigue, or that physicians are more sensitive to the ways in which women complain about fatigue. Fatigued patients tend to score lower than nonfatigued patients on tests that measure physical activity. They also score significantly higher than control patients on standardized instruments measuring anxiety and depression, and have a higher lifetime likelihood of being diagnosed with these disorders.[5,13,14]

It is useful to consider the clinical presentation of fatigue in different contexts depending on how the patient describes the problem. Some patients experience fatigue as part of a larger symptom complex in which the fatigue is identified only on detailed history or review of systems by the physician. Other patients present with a chief complaint of fatigue. A third group of patients presents to the physi-

cian specifically with questions about CFS. Patients rarely report acute fatigue to the physician when they have an understanding of why the fatigue is present. For example, a patient who is experiencing a common viral illness usually expects fatigue to be part of the symptom complex and is less likely to be concerned enough to complain about fatigue to the physician. Such patients would not present to the family physician complaining of fatigue but would admit to fatigue on a review of systems. Thus fatigue is a secondary symptom to these patients.

Most studies that have addressed fatigue in family practice have examined only those patients in whom fatigue was the chief or primary complaint. Such a complaint generally causes the physician to consider a long differential diagnosis of diseases that may cause fatigue as a primary symptom. In this clinical situation, the ability to address a broad differential diagnosis in a cost-efficient manner is essential. CFS has received substantial publicity in the lay press. For this reason, a number of patients present to the family physician with questions about this disorder. It is important for the family physician to understand the diagnostic criteria of CFS and to be familiar with the latest research in this area.

Diagnosis

Few patient problems illustrate the inadequacies of the biomedical model of diagnosis more clearly than does fatigue. A diagnostic model that examines the patient's complaint and attempts to determine its cause and then apply a treatment regimen to that cause is called an "epidemiologic model." The traditional biomedical model of diagnosis is largely an epidemiologic model. A contextual model of diagnosis, instead of attempting to identify cause, attempts to identify associated symptoms and factors that make the patient's complaint easier to understand and manage.[15] Contextual diagnosis can include a biomedical approach to the patient but necessarily also includes family, community, and sociocultural considerations. What follows is a contextual approach to diagnosis when a patient complains of fatigue as a secondary concern or chief complaint, or has concerns about CFS.

Fatigue as a Secondary Symptom

Many of the most common problems seen by family physicians are problems associated with fatigue. Chronic medical conditions such

as diabetes, commonly prescribed medications such as antihypertensives, acute illnesses such as viral hepatitis, physiologic changes such as pregnancy, and stressful life situations such as divorce may be associated with fatigue. In these situations, fatigue often is identified as a secondary symptom and, from a diagnostic point of view, may be relatively unimportant. From a contextual point of view, however, the family physician is interested in the degree to which the patient's fatigue is interfering with job performance, family relationships, physical activity, or sexual activity. The contextual approach requires the physician to be as interested in the effects of symptoms as in their cause. Thus when fatigue is a secondary symptom, its importance may rest with its effect on the patient's lifestyle and coping skills for the underlying illness.

Fatigue as a Presenting Complaint

Few clinical situations more fully exercise the skills of a family physician than the patient who presents with a chief complaint of unexplained fatigue. Table 5.1 lists some of the medical and psychosocial problems associated with a chief complaint of fatigue. Evaluation of such a patient begins with a careful, comprehensive medical history, which includes a detailed psychosocial history including symptoms of depression, sleep disorders, anxiety disorders, substance abuse, and the marital and sexual experience.

The most common causes of fatigue as a presenting complaint to a family physician are depression, life stress, chronic medical illnesses, and medication reactions. The history must also include information about the other symptoms of such illnesses as those listed in Table 5.1.

The complete medical history is followed by a careful physical examination. Areas of particular importance on the physical examination are the thyroid gland, cardiovascular system, rectum, pelvis, and mental status (for associated signs of depression or anxiety disorders).

Laboratory evaluation of the patient who presents with chronic fatigue, though important to consider, is unlikely to be helpful in most cases. Sugarman and Berg[16] found that laboratory testing was helpful in securing a diagnosis in only nine of 118 fatigued patients in a university family practice clinic. An appropriate laboratory evaluation is directed by the history and physical examination. For most patients, testing includes a complete blood count, a serum chemistry profile, an erythrocyte sedimentation rate (as a screen for inflammatory disorders), and thyroid-stimulating hormone level (as a screen for hypothyroidism). Other laboratory tests, including a chest radio-

Table 5.1. **Diagnoses Associated with Fatigue**

Infectious diseases
Viral syndromes
Mononucleosis
Hepatitis
Pharyngitis
Endocarditis
Urinary tract infections
HIV infection
Tuberculosis

Toxins and drug effects
Medication side effects
Alcohol and drug abuse
Chronic poisoning

Endocrine and metabolic problems
Electrolyte disturbance
Hypothyroidism
Hypoglycemia
Diabetes
Hyperthyroidism
Starvation or dieting
Obesity
Adrenal insufficiency

Neoplastic conditions
Occult malignancy
Leukemia and lymphoma
Carcinoma of the colon

Vascular disorders
Atherosclerotic heart disease
Valvular heart disease
Congestive heart failure
Cardiomyopathy
Congenital heart disorders

Pulmonary conditions
Asthma/COPD
Allergic disorders
Restrictive lung diseases

Miscellaneous conditions
Anemia
Pregnancy
Systemic lupus erythematosus
Iron deficiency
Renal failure
Chronic liver disease
Multiple sclerosis
Sleep disorders including sleep apnea

Psychosocial problems
Depression
Anxiety disorders
Adjustment reaction
Situational life stress
Alcohol and drug abuse
Sexual dysfunction
Spouse abuse, child abuse, or other family violence
Occupational stress and professional burnout syndrome

HIV = human immunodeficiency virus; COPD = chronic obstructive pulmonary disease.

graph, electrocardiogram, urinalysis, and tuberculin skin testing, may be indicated, depending on the results of the history and physical examination.

Patients without a readily apparent explanation for their fatigue should also be evaluated with a careful family assessment. Such an assessment may include convening a family meeting, preparing a family genogram, or using other family assessment instruments. An assessment of the occupational history, living environment, and social and financial circumstances should also be included in the complete evaluation of patients with fatigue.

Chronic Fatigue Syndrome

The CDC's definition of CFS is outlined in Table 5.2.[10] The purpose of establishing these diagnostic criteria was to identify a subgroup of fatigued patients to direct future research studies. Research projects have since focused on learning more about patients who meet these criteria. Because of obvious similarities to infectious mononucleosis, a number of studies have searched for an association with viral infections. Although these investigations continue, there is no good evidence to link CFS and viral infections.[17–20] Other research has examined the immune function of patients with CFS. Although measurable immune abnormalities have been associated with CFS, no consistent pattern has been delineated from study to study.[17,19,20] Another area of ongoing research has been an attempt to associate connective tissue and autoimmune diseases with CFS. Only a few patients have abnormal autoantibodies, and no association with autoimmune diseases has been clearly established.[21] More recent studies have examined the hypothesis that abnormalities of the central nervous system or changes in the regulation of the hypothalamic-pituitary-adrenal axis might explain chronic fatigue. At this time, evidence of a clinically useful association is inconclusive.[18,19,22,23] Finally, studies have examined the relationship between chronic fatigue and psychiatric disorders. These studies suggest that depression alone is insufficient to explain most cases of chronic or persistent fatigue.[19,22] Several recent studies have raised questions about the degree of diagnostic overlap between chronic fatigue and other conditions such as fibromyalgia and irritable bowel syndrome. Clinically important fatigue is present in over 75% of patients with fibromyalgia and many patients with chronic fatigue have demonstrable trigger points on musculoskeletal exam. Some authors suggest that the family of functional somatic syndromes may in fact be different manifestations of the same process.[24–26] It now seems clear that patients with CFS are not a homogeneous group and are not different from other patients with chronic fatigue in most respects.

It is also clear that chronic fatigue is much more common than CFS. Fewer than 5% of patients who present with chronic fatigue to a family physician ultimately fulfill the diagnostic criteria for CFS.[1,11] Patients who present to the family physician concerned about CFS represent a complex challenge. Some patients are simply looking for information, a need that can be met by discussing questions and providing educational resources. Many patients who are concerned about CFS do not satisfy the criteria listed in Table 5.2 sufficiently to qualify for this diagnosis. These patients require a contextual diagnostic approach from the physician.

Table 5.2. **Case Definition: Chronic Fatigue Syndrome and Idiopathic Chronic Fatigue**

Prolonged fatigue is self-reported, persistent fatigue lasting 1 month or longer. Chronic fatigue is self-reported persistent or relapsing fatigue lasting 6 or more consecutive months.

A case of *chronic fatigue syndrome* is defined as chronic fatigue that is not explained by medical conditions that adequately explain the fatigue (see below) with the presence of the following:

1. clinically evaluated, unexplained, persistent or relapsing chronic fatigue that is of new or definite onset, is not the result of ongoing exertion, is not substantially relieved by rest, and results in substantial reduction in previous levels of occupational, educational, social, or personal activities; and
2. the concurrent occurrence of four or more of the following symptoms, all of which must have persisted or recurred during 6 or more consecutive months and must not have predated the fatigue:
   - self-reported impairment in short-term memory or concentration severe enough to cause substantial reduction in previous levels of occupational, educational, social, or personal activities
   - sore throat
   - tender cervical or axillary lymph nodes
   - muscle pain
   - multijoint pain without joint swelling or redness
   - headaches of a new type, pattern, or severity
   - unrefreshing sleep
   - postexertional malaise lasting more than 24 hours

A case of *idiopathic chronic fatigue* is defined as clinically evaluated, unexplained chronic fatigue that fails to meet the criteria for chronic fatigue syndrome.

The following conditions exclude the patient from being classified as unexplained chronic fatigue:

- Any active medical condition that may explain chronic fatigue including medication side effects
- Any previously diagnosed medical condition whose resolution has not been documented beyond a reasonable doubt and whose continued activity may explain chronic fatigue
- Any past or current diagnosis of a major depressive disorder with psychotic or melancholic features, bipolar affective disorder, schizophrenia of any subtype, delusional disorders of any subtype, dementias of any subtype, or bulimia nervosa
- Alcohol or substance abuse within 2 years before the onset of chronic fatigue or at any time afterward
- Severe obesity defined as a body mass index equal to or greater than 45

(*continued*)

Table 5.2 (Continued).

The following conditions do not exclude the patient from being classified as unexplained chronic fatigue:
Any condition defined primarily by symptoms that cannot be confirmed by diagnostic laboratory tests, including fibromyalgia, anxiety disorders, somatoform disorders, nonpsychotic or nonmelancholic depression, neurasthenia, and multiple chemical sensitivity disorder
Any condition under specific treatment sufficient to alleviate all symptoms related to that condition and for which the adequacy of treatment has been documented
Any condition, such as Lyme disease or syphilis, that was treated with definitive therapy before development of symptomatic sequelae
Any isolated and explained physical examination finding or laboratory or imagining test abnormality that is insufficient to strongly suggest the existence of an exclusionary condition

Evaluation of the chronic fatigue patient should begin with a comprehensive history and physical examination. Most patients have previously seen other physicians for this problem, and copies of previous medical records from these physicians should be obtained. At the initial visit it is imperative that the physician discuss in detail the way in which chronic fatigue has affected and changed the patient's life. A careful family assessment should be completed, including convening the family whenever possible. Although chronic fatigue patients have a high prevalence of depression, anxiety disorders, somatization disorders, and family dysfunction, patients may not be receptive to discussing psychosocial issues early in the process of caring for this problem. Because biomedical evaluation is unlikely to yield a definitive diagnosis, a complete biopsychosocial evaluation beginning at the initial visit is crucial. Patients should be seen frequently, and the laboratory evaluation should include those studies described above for the patient with a chief complaint of chronic fatigue. At the present time there is little justification for extensive immunologic or autoimmune diagnostic testing. Focused laboratory tests should be ordered when indicated from the history and physical examination.

Management

In an epidemiologic model, management of the problem begins after the correct diagnosis has been determined. With a contextual ap-

proach, management begins at the time of initial contact between the patient and physician. Caring for patients with a primary complaint of fatigue requires a contextual approach, which means that the physician's diagnostic inquiry must include the broadest possible scope. The physician begins at the initial visit to assist the patient in delineating ways to cope with the symptoms more effectively. What follows are the basic principles of a systemic management plan for a patient with a primary complaint of chronic fatigue.

1. The physician must be as interested and concerned about the effects of the patient's fatigue as about its cause. Delineating the effects of the symptom on the patient's life is an important step in understanding the symptom and managing the problem.
2. The physician should explain to the patient at the initial visit that the most common causes of fatigue as a presenting complaint are depression and psychosocial problems. The physician should ascertain what this information means to the patient and whether the patient thinks that psychosocial issues may play a role in the fatigue.
3. The physician should discuss the other common causes of fatigue with the patient at the initial visit and ask the patient to think about these possibilities between the initial and first follow-up visit. At the first follow-up visit the physician can then inquire as to whether the patient has had an opportunity to consider possible explanations for the fatigue and if there is new insight into the problem.
4. The physician should continue to return to the discussion of family, occupational, psychosexual, and substance abuse issues at each of the follow-up visits. This can take place while a detailed biomedical evaluation of the patient's symptoms is progressing. Even if fatigue is being caused by a physical disorder, there are important effects on family and job.
5. The physician can consider convening the family to explore the attitudes and ideas of other family members. This point is especially important if the patient has a spouse or significant other.
6. The physician should be able to discuss professional burnout, career dissatisfaction, and other issues that are outside the usual biomedical model of thinking about patient problems. It may be helpful to provide patients with copies of articles about fatigue. Some studies suggest that cognitive-behavioral therapy may be beneficial for patients with chronic fatigue.[27]
7. If the physician believes that a psychosocial problem is of primary importance to the patient's condition but the patient is un-

willing to accept this explanation, the biomedical workup should be paced slowly and scheduled across several follow-up visits. This will allow the doctor–patient rapport to deepen and discussions about psychosocial concerns to continue.

8. The physician should refer the patient to a consultant only for a well-specified purpose. It is essential to communicate with consultants in advance and to avoid using consultants who lack sophistication about psychosocial issues.
9. Prolonged rest is more likely to harm than help patients with chronic fatigue. A gradual program of activity has resulted in improved functional status in some studies.
10. Tricyclic or selective serotonin reuptake inhibitor antidepressants may benefit some patients, particularly those with disturbed sleep patterns. When used, these medications should be started in low doses and their therapeutic effect should be carefully monitored.[28,29]

Summary

Acute fatigue may be a presenting complaint for a large number of important diseases. Fatigue has a large biomedical differential diagnosis and requires a broad contextual approach to optimize diagnosis and management. Although few presenting complaints are more challenging, few patient problems more urgently require the broad contextual diagnostic approach that can best be provided by the family physician.

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http://www.springer.com/978-0-387-22351-3

Taylor's Cardiovascular Diseases
A Handbook
Taylor, R.B.; David, A.K.; Fields, S.A.; Phillips, D.M.;
Scherger, J.E. (Eds.)
2005, XII, 300 p. 10 illus., Softcover
ISBN: 978-0-387-22351-3