Fatigue Clinical Guidelines

Definition

The term “fatigue” can be used to describe difficulty or inability to initiate activity (subjective sense of weakness); reduced capacity to maintain activity (easy fatigability); or difficulty with concentration, memory, and emotional stability (mental fatigue). Twenty-one to 33 percent of patients seeking attention in primary care settings describe fatigue as an important problem (if not always the chief complaint).

Causes

— **Acute fatigue** is most often attributable to an acute medical condition. For example, a patient with influenza will describe fatigue in association with fever and respiratory symptoms. Acute fatigue may also be the result of a recent life stressor. Patients with acute fatigue associated with a recognizable medical or psychosocial condition require little or no evaluation.

— **Subacute and chronic fatigue is likely to be associated with an underlying chronic medical or psychological condition, medication toxicity, or substance use. Etiologies include:**

- **Cardiopulmonary conditions:** Congestive heart failure, chronic obstructive pulmonary disease, sleep apnea
- **Endocrinologic/metabolic conditions:** Hypothyroidism, hyperthyroidism, chronic renal disease, chronic hepatic disease, adrenal insufficiency, electrolyte abnormalities
- **Hematologic/neoplastic conditions:** Anemia, occult malignancy
- **Infectious diseases:** Mononucleosis syndrome, viral hepatitis, human immunodeficiency virus (HIV) infection, subacute bacterial endocarditis, tuberculosis
- **Rheumatologic conditions:** Fibromyalgia, polymyalgia rheumatica, systemic lupus erythematosus, rheumatoid arthritis, Sjogren's syndrome
- **Psychological conditions:** Depression, anxiety disorder, somatization disorder
- **Neurologic conditions:** Multiple sclerosis
- **Medication toxicity:** Benzodiazepines, antidepressants, muscle relaxants, first-generation antihistamines, beta-blockers, opioids
- **Substance use:** Alcohol, marijuana, opioids, cocaine/other stimulants

In a small minority of cases, the presenting complaint of chronic fatigue is explained by **chronic fatigue syndrome (CFS)**, a disorder of unknown cause but with strong evidence of neurologic dysfunction.

Assessment (History and Examination)

History

In taking a history, the clinician should rely upon open-ended questions. Questions such as "What do you mean by fatigue?" or "Please describe what you mean" may elicit responses that help distinguish fatigue from muscle weakness or somnolence.

The history should also determine the characteristics, severity, and temporal pattern of fatigue:

- Onset: Abrupt or gradual, relationship to illness or life event
- Course: Stable, improving, or worsening
- Duration and daily pattern
- Factors that alleviate or exacerbate it
- Impact on daily life: Ability to work, socialize, participate in usual activities

Associated symptoms may suggest specific etiologies. For example, sleep apnea would be suspected in a patient who describe snoring and disrupted sleep, anemia in a patient who reports dizziness and weakness, and fibromyalgia in a patient who describes chronic diffuse muscle pain. The presence of fever may suggest underlying infection, and unintended weight loss may indicate an occult neoplasm or recurrent disease in a patient with a history of malignancy. If history suggests a chronic pattern of unexplained physical symptoms, somatization should also be considered.

The quality and quantity of sleep and substance use (eg, alcohol, marijuana, opioids, cocaine/other stimulants) in patients with fatigue should also be evaluated.

All patients should be asked about symptoms suggestive of depression (eg, sad mood, anhedonia, alteration in sleep and/or eating habits) and anxiety disorder (eg, constant palpitations or sweating, occurrence of panic attacks and/or phobias).

A complete list of medications, including prescription, over-the-counter, and complementary/alternative drugs, should be obtained.

Physical Examination

The physical examination is important to look for evidence of specific causes of fatigue and to establish rapport, assuring the patient that his or her complaint is a concern worth investigating. The physical examination should focus on:

- General appearance: Level of alertness, psychomotor agitation or retardation, grooming
- Evidence of thyroid disease: Bradycardia, tachycardia, goiter, skin changes, ophthalmopathy
- Presence of lymphadenopathy or hepatosplenomegaly
- Cardiopulmonary examination: Signs of congestive heart failure or chronic obstructive pulmonary disease.
- Neuromuscular examination: Muscle bulk, tone, and strength; deep tendon reflexes; sensory and cranial nerve evaluation; cognitive function

Management

Patients with acute fatigue associated with a recognizable medical or psychosocial condition require little or no evaluation. For patients with subacute or chronic fatigue as the primary symptom, we obtain the following initial laboratory studies:

- Complete blood count with differential count
- Chemistries (including glucose, electrolytes, calcium, renal and hepatic function tests)
- Thyroid-stimulating hormone
- Creatine kinase (if muscle pain or weakness present)

Appropriate cancer screening interventions based upon the patient's age and sex should be updated as necessary to exclude common occult malignancies as a potential cause for fatigue.

- **Patients with localized findings:** Additional diagnostic studies should be obtained as warranted in patients with localized findings on history or physical examination or abnormal initial laboratory testing. For example, a patient presenting with fatigue associated with fever/chills, night sweats, and myalgias associated with a new heart murmur should have blood cultures and an echocardiogram performed for evaluation of subacute bacterial endocarditis. A patient presenting with abnormal liver function tests should have viral hepatitis serologies and a hepatic ultrasound performed.
- **Patients without localized findings:** Patients without an identified cause following the initial evaluation should be reassessed in one to three months and have baseline laboratory studies repeated at that time if there continue to be no localizing symptoms or signs.
  Patients who remain undiagnosed with an identifiable condition after six months are designated as having idiopathic chronic fatigue or CFS if they meet diagnostic criteria. Both of these conditions are diagnoses of exclusion.

Treatment

Addressing underlying medical conditions: Patients with an identified cause of chronic fatigue based upon the initial evaluation should be treated specifically for this condition. Their fatigue should be monitored with management of the underlying condition to see if it improves or resolves. If it does not, further evaluation may be warranted to determine if there is an alternative explanation. Repeating the initial evaluation is worthwhile in this setting to make sure that other potential diagnoses were not missed.

Addressing residual or idiopathic fatigue: In patients with residual or idiopathic fatigue, we suggest an empiric trial of antidepressant therapy for patients with depressive symptoms even if they do not meet diagnostic criteria for major depression. We do not suggest the empiric use of stimulants or other drug therapies. If there is no improvement, we suggest a trial of cognitive behavioral therapy (CBT) and/or exercise therapy as tolerated, depending on patient preference.

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