

FATIGUE

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Overview¹

Fatigue is a common presenting complaint in primary care that can have significant effects on work, family, and social life. Clinical fatigue consists of generalized weakness, poor endurance, and mental exhaustion. It may be categorized as physiologic, secondary, or chronic. In the majority of cases, fatigue is related to underlying medical or psychiatric illness, or its treatment. However, in up to one third of cases, no clear etiology may be found.

Definitions^{1,2}

Physiologic Fatigue: Fatigue due to an unbalanced routine of rest and activity. It may be precipitated by inadequate rest or by excess physical or mental effort, and is relieved by rest.

Secondary Fatigue: Fatigue secondary to an underlying medical condition or its treatment, generally lasting <6 months.

Chronic Fatigue: Fatigue lasting longer than 6 months that is not relieved by rest.

Chronic Fatigue Syndrome: A diagnosis of exclusion characterized by intense fatigue that interferes greatly with daily activities and is not improved by rest. The fatigue is not due to exertion and must have lasted for 6 or more consecutive months. The patient must exhibit 4 or more of the following symptoms during the period of fatigue:

- Post-exertional malaise lasting >24 hr
- Unrefreshing sleep

- Impaired short-term memory or concentration
- Muscle pain
- Multi-joint pain without swelling or erythema
- New onset headaches
- Tender cervical or axillary lymph nodes
- Sore throat

Idiopathic Chronic Fatigue: Fatigue lasting 6 months or more in a patient that does not meet the criteria for chronic fatigue syndrome, and for which no medical or psychiatric explanation can be found.

Diagnostic Considerations^{1,3,4,5,6}

Differential Diagnosis

Infectious	Endocrine	Hematologic	Neurologic
<ul style="list-style-type: none"> • EBV • Influenza • HIV • Hepatitis • TB • Lyme disease • Other infections 	<ul style="list-style-type: none"> • Hypothyroidism • Hyperthyroidism • Cushing's disease • Addison's disease • Diabetes 	<ul style="list-style-type: none"> • Anemia (iron, B12) • Lymphoma • Leukemia 	<ul style="list-style-type: none"> • Sleep disorders (sleep apnea, restless leg syndrome) • Multiple sclerosis • Parkinson's disease • Myasthenia gravis • ALS
Rheumatologic	Psychiatric	Other	
<ul style="list-style-type: none"> • Fibromyalgia • Sjogren's syndrome • Polymyalgia rheumatica • Dermatomyositis • Polymyositis • Giant cell arteritis • Rheumatoid arthritis • SLE 	<ul style="list-style-type: none"> • Depression • Anxiety/stress • Bipolar disorder • Schizophrenia • Delusional disorder • Somatoform disorder • Dementia • Eating disorder • Alcohol/substance abuse • Insomnia 	<ul style="list-style-type: none"> • Pregnancy • Chronic illness (CHF, COPD, coronary artery disease, renal failure, liver disease, autoimmune, Celiac disease) • Medications effects (hypnotics, muscle relaxants, antidepressants, antihistamines, β-blockers, opioids) • Malignancy • Heavy metal toxicity 	

Investigations

History: The history is the main component of investigations into fatigue. Explore the nature of the fatigue (onset, duration, physical vs. mental, recovery period), psychosocial factors, sleep patterns (including quality and quantity of sleep), medication use, and alcohol and drug use.

Physical: The physical exam can help to narrow down the differential diagnosis. Particular attention should be paid to:

General	Head and Neck	Cardiovascular	Respiratory	Neurological
<ul style="list-style-type: none"> Level of alertness Psychomotor agitation/slowing Grooming 	<ul style="list-style-type: none"> Lymphadenopathy Signs of thyroid disease (e.g. goiter, eye findings) 	<ul style="list-style-type: none"> Signs of CHF (e.g. heart rate/rhythm, extra heart sounds, volume overload) 	<ul style="list-style-type: none"> Signs of CHF or lung disease 	<ul style="list-style-type: none"> Muscle bulk, power, tone, and reflexes Sensory exam Cranial nerve exam

Labs and Imaging: Laboratory studies affect management in only about 5 percent of cases. Tests are mainly used to support findings on history or physical exam and are ideally guided by clinical suspicion. Options for initial investigation in a patient with at least a 2 week history of fatigue are given below. Testing for other causes is discouraged unless supported by physical findings or abnormalities in initial testing.

Initial Tests (if >2 week history of fatigue)	Further Tests (if indicated by other findings)
<ul style="list-style-type: none"> CBC Electrolytes Glucose Urea, creatinine Liver enzymes and function tests ESR Ferritin TSH Pregnancy test (if appropriate) 	<ul style="list-style-type: none"> Serum titres (EBV, CMV, HIV, Lyme, hepatitis B/C) Specialized blood testing (iron studies, B12, folate) Toxicology screen Creatine kinase (if muscle pain/weakness) Immunoglobulins ANA, rheumatoid factor Celiac workup PPD skin test ECG Pulmonary functions tests Imaging (chest x-ray, echocardiogram, brain MRI)

Management^{1,3,6}

Physiologic Fatigue: Managed by ensuring an appropriate balance of sleep and activity. The treatment focuses on a combination of proper sleep hygiene and an appropriate level of daily physical activity.

Secondary Fatigue: Should be managed by identifying and treating the root cause. Be alert for signs of underlying medical or psychiatric illness, and be sure to consider the effect of medications the patient may be taking.

Chronic Fatigue: Management can employ several tactics, including cognitive behavioural therapy (CBT) or exercise therapy, and centres around a supportive approach. CBT involves a series of treatment sessions that aim to alter the thinking and behaviour of patients in regards to their illness. Significant improvements in physical functioning have been demonstrated using this therapy. Graded exercise therapy is an option that may or may not have effectiveness equal to CBT. This treatment involves a gentle progression of physical activity over time, with the aim of preventing or reversing deconditioning.

In general, patients should be encouraged to engage in a normal daily routine including attending work and making time for regular physical activity. The short-term prognosis for these individuals is generally poor, but is improved for patients who believe that their fatigue is related to modifiable factors. Progress can be monitored through brief regularly scheduled appointments which can help to foster a supportive doctor-patient relationship. Patient support groups can also be of benefit.

General Approaches: Antidepressants, such as SSRIs, may be used in cases where the patient exhibits features of depression, but should be discontinued if no response is appreciated after 6-8 weeks. Consider vitamin and mineral supplementation where appropriate. Iron therapy may provide some benefit if ferritin is low normal, even in the absence of anemia. Other general treatment options include improved sleep hygiene, diet optimization, and disease education.