Fatigue

Notes by Shaila Gunn

Definitions

Fatigue: feeling exhausted during or after activity, or as a feeling of not having enough energy to even start activities It is a significant chief complaint in family practice and comprises 10-30% of visits.

* distinguish this from related complaints like daytime sleepiness or objective weakness, which might steer you down a different path.*

Acute fatigue: Fatigue lasting less than a month. This will often be secondary to an acute medical condition or a change in life circumstances.

Sub-acute or chronic fatigue: Usually defined as lasting one to six months or longer. Often requires more work-up.

Approach

1. Starts with the history
    a. Usual OPQRSTAAA
    b. Differentiate fatigue from sleepiness and weakness
    c. Note that fatigue that does not improve with rest is often associated with psychological conditions, medication side effects or substance use
    d. Ask about sleep, especially sleep apnea
        i. Snoring
        ii. Waking up from sleep
        iii. Daytime sleepiness
    e. Constitutional symptoms
        i. Weightless
        ii. Fever
        iii. Night sweats
    f. Dyspnea
    g. Chest pain
    h. Rheumatologic ROS i.e. muscle pain, rashes etc.
    i. Heart/cold intolerance

Red Flags

Table 1: RED FLAGS THAT RAISE SUSPICION OF SERIOUS UNDERLYING DISEASE†

Red flags	Examples of potential serious underlying disease
Unintentional weight loss	• Malignancy • HIV infection • Diabetes mellitus • Hyperthyroidism
Abnormal bleeding	• Anaemia • Gastrointestinal malignancy
Shortness of breath	• Anaemia • Heart failure • Chronic obstructive pulmonary disease
Lymphadenopathy	• Malignancy
Fever	• Hidden infection or abscess
Concurrent cardiovascular, gastroenterological, neurological or rheumatological symptoms	• Autoimmune disease e.g. rheumatoid arthritis • Malignancy • Coeliac disease • Multiple sclerosis
Recent onset of fatigue in a previously well older patient	• Malignancy • Anaemia • Renal failure • Diabetes mellitus

† Adapted from the Australian Family Physician 2014.[9]

Differential Diagnosis

Note that this chart is not exhaustive. The differential is massive. But this is a good starting point.

Condition	Symptoms	Physical findings	Supportive diagnostic studies
Cardiopulmonary			
Congestive heart failure	Dyspnea on exertion, orthopnea, leg swelling	S3 gallop, inspiratory rales, elevated jugular venous distension, peripheral edema	Chest radiograph, echocardiogram
Chronic obstructive pulmonary disease	Dyspnea, chronic cough, sputum production	Evidence of hyperinflation, wheezing, rales	Chest radiograph
Sleep apnea	Snoring, interrupted breathing during sleep	Obesity, hypertension	Sleep study
Endocrinologic/metabolic			
Hypothyroidism	Cold intolerance, weight gain, constipation, dry skin	Bradycardia, goiter, slow deep tendon reflex relaxation phase	Thyroid function tests
Hyperthyroidism	Heat intolerance, weight loss, diarrhea, moist skin	Tachycardia, goiter, ophthalmopathy	Thyroid function tests

Chronic renal disease	Nausea/vomiting, mental status changes, decreased urine	Hypertension, peripheral edema	Renal function tests/ serum electrolytes
Chronic hepatic disease	Abdominal distention, gastrointestinal bleeding	Jaundice, palmar erythema, gynecomastia, splenomegaly, evidence of ascites	Hepatic function tests
Adrenal insufficiency	Weight loss, salt craving, gastrointestinal complaints	Hypotension, hyperpigmentation, vitiligo	Morning cortisol/ACTH, ACTH stimulation test
Electrolyte abnormalities			
Hyponatremia	Nausea, malaise, cognitive dysfunction	Generally normal exam	Serum sodium level
Hypercalcemia	Anorexia, polydipsia/polyuria, nausea	Generally normal exam	Serum calcium/albumin levels
Hematologic/neoplastic			
Anemia	Dizziness, weakness, palpitations, dyspnea	Tachycardia, pallor	Complete blood count
Occult malignancy	Weight loss, localized symptoms may be present depending upon type	Variable	Variable depending upon type
Infectious diseases			
Mononucleosis syndrome	Fever, sore throat, tender lymph nodes	Fever, exudate pharyngitis, tender cervical adenopathy	Complete blood/differential count, monospot
Viral hepatitis	Fever, nausea/vomiting, abdominal discomfort	Fever, jaundice, tender hepatomegaly	Hepatic function tests, viral hepatitis serologies
HIV infection	Weight loss, variable localized complaints	Variable physical findings	HIV serology
Subacute bacterial endocarditis	Fever/chills, night sweats, myalgias	Fever, new (regurgitant) murmur, peripheral manifestations	Blood cultures, echocardiogram
Tuberculosis	Fever/chills, night sweats, fatigue, weight loss	Cough, chest pain, dyspnea, hemoptysis	PPD/gamma-interferon assay, chest radiograph
Rheumatologic			
Fibromyalgia	Chronic diffuse muscle pain	Multiple "tender points" on palpation	None
Polymyalgia rheumatica	Aching/morning stiffness of shoulders, neck, and hips	Decreased range of motion of shoulders, neck, and hips	Erythrocyte sedimentation rate
Psychological			
Depression	Sad mood, anhedonia, altered sleep, cognitive dysfunction	Generally normal exam	Screening test (eg, PHQ-2, PHQ-9)

Anxiety disorder	Generalized nervousness, panic attacks, phobias	Tachycardia, muscle tension	Screening test (eg, GAD-7)
Somatization disorder	Multiple chronic constitutional and localized complaints	Generally normal exam	Screening test (eg, SSS-8)
Medication toxicity*			
	Variable	Generally normal exam	None
Substance use¶			
	Variable	Generally normal exam	None

* Benzodiazepines, antidepressants, muscle relaxants, first-generation antihistamines, beta-blockers, opioids, GABA analogues (note that those with renal or hepatic impairment are also more likely to have medication side effects)

¶ Alcohol, marijuana, opioids, cocaine/other stimulants

Investigations

Note that your physical exam and history should guide the investigations, don't order unnecessary tests.

Everyone should, however, be up to date on regular age-specific cancer screening and medical screening tests:

- FIT
- Mammograms
- Pap's
- A1C
- Renal function
- Lipids

Consider viral tests i.e. HBV, HIV, HCV if they have risk factors or have never had them done before (Note: HIV testing is now recommended q5 years for everyone)

There is poor evidence to suggest that ordering all the tests for everyone with help with a diagnosis. Labs only help clarify the diagnosis or change management in 5-8% of patients.

A Systematic Review in 2016 in BMC Family Practice found that a presenting complaint of tiredness led to a diagnosis of:

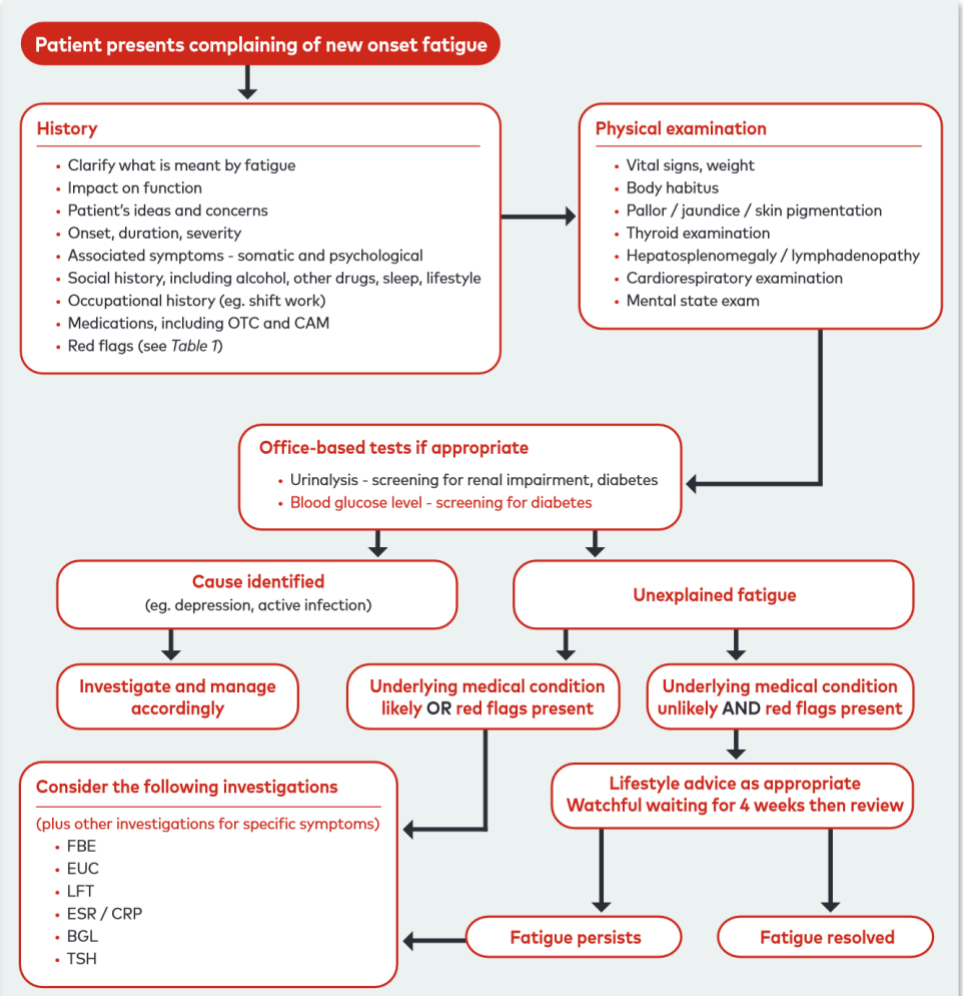
- Anemia in 2.8% of cases
- Malignancy in 0.6% of cases
- Serious somatic disease in 4.3% of cases
- Bepression in **18.5%** of cases.

But it is reasonable to consider the following in most patients

- CBC
- Electrolytes including calcium
- A1C
- Renal and hepatic function tests
- TSH

Tests like ANA, lyme serologies, and vitamin D levels are very low yield and should not be ordered unless you have a clinical reason to.

***Figure 1.* Guidelines for the investigation of fatigue†**



Chronic Fatigue Syndrome

If fatigue becomes chronic, it make be chronic fatigue syndrome, denied as pathological fatigue and post-exertional malaise that is out of proportion to the level of exertion, and that takes more than 24 hours to recover.

Criteria:

1. A 6-month history (3 months in children) of the following:
    a. Fatigue
    b. Post-exertional malaise or fatigue
    c. Sleep dysfunction and pain
2. Two or more categories of neurological or cognitive manifestations:
    a. Confusion
    b. Impaired concentration
    c. Information processing difficulties or word finding issues,
    d. Disorientation
    e. Perceptual and sensory disturbance
3. At least one symptom from at least two other categories of symptoms (these include autonomic, immune and neuroendocrine symptoms)

Typically, the physical exam is normal. Patients often feel febrile, but rarely have an elevated temperature. Painful lymph nodes, especially cervical lymph nodes, are also common, but there is rarely true lymphadenopathy. And

although patients often experience sore joints and muscles, on exam there is not typically any swelling or erythema, and studies like biopsies and EMGs are normal.

Treatment

1. Treat the cause of fatigue which is usually identifiable in 2/3 of cases
    a. Manage chronic diseases i.e. heart failure, COPD, cancer, diabetes
    b. Antidepressants
    c. CBT
    d. Exercise
2. 1/3 of cases will not receive a specific diagnosis to explain it. It is important to
    - Explore psychological factors that contribute to this
    - Improve their sleep using sleep hygiene and possibly CBTi
    - Explore stressors in their life such as work, relationships, finances, caregiver responsibilities, and domestic violence

Resources

1. TOP (toward's optimized practice) 2016 guidelines for myalgic encephalomyelitis / chronic fatigue syndrome: https://actt.albertadoctors.org/CPGs/Pages/Myalgic-Encephalomyelitis-Chronic-Fatigue-Syndrome.aspx
2. UpToDate: approach to the adult patient with fatigue . https://www.uptodate.com/contents/approach-to-the-adult-patient-with-fatigue
3. Rosenthal TC, Majeroni BA, Pretorius R, Malik K. Fatigue: an overview. Am Fam Physician. 2008 Nov 15;78(10):1173-9. PMID: 19035066.
4.Sugarman JR, Berg AO. Evaluation of fatigue in a family practice. *J Fam Pract*. 1984;19(5):643–647.
5.Jacques Cornuz, Idris Guessous and Bernard Favrat
6.CMAJ March 14, 2006 174 (6) 765-767; DOI: https://doi.org/10.1503/cmaj.1031153