



# Fatigue – a general diagnostic approach

**BACKGROUND** Fatigue or excessive tiredness of body or mind is a common presenting problem in general practice.

**OBJECTIVE** This article provides a diagnostic model for the diagnosis of fatigue in general practice.

**DISCUSSION** Fatigue is not a diagnosis but rather a symptom. Fatigue is interchangeable with terms such as tiredness, weariness, loss of energy, listlessness and exhaustion. It can be a difficult and frustrating symptom for the general practitioner to evaluate.

In a survey of morbidity and treatment in general practice in Australia, 2.6% of all patients presented with weakness or tiredness.<sup>1</sup> However, fatigue is often 'hidden' or is a secondary symptom when the patient asks their general practitioner for a 'check up', or 'a tonic', or complains of sleep disturbance.<sup>2</sup> Shires and Hennen estimated that one in 10 patients in family practice in the United States presented with fatigue as a primary complaint.<sup>3</sup>

Fatigue has been implicated as a major cause of occupational and motor vehicle accidents. It leads to impaired performance and limitations of daily functioning, especially in the elderly. Tiredness can be a symptom of many serious and uncommon diseases including malignant disease. The challenge for the GP is to diagnose such disorders quickly without over investigation.

## Causes and associations of fatigue

Common causes of tiredness/fatigue are listed in Table 1 and include the obvious lifestyle and social and psychological factors in addition to the chronic, malignant infectious and endocrine disorders that we strive to identify. Despite its frequency, there has been relatively little study of the causes of fatigue. In a United Kingdom general practice, Jerrett found no physical cause of fatigue in 62% of his patients;<sup>4</sup> it was usually associated with sleep disturbance or stress. Many patients

were suffering from psychological problems or psychiatric illness, including depression or anxiety or bereavement. Obstructive sleep disorder is an important cause of day time fatigue, occurring in 2% of patients attending general practice and 10% of middle aged men.<sup>4</sup>

## The diagnostic approach

A summary of the 'safety' diagnostic model is presented in Table 2. The most probable diagnoses to consider are those related to psychological distress including anxiety, stress, depression, somatisation disorder and sleep disorders.

Studies have reported that over 50% (and in some cases as many as 80%) of reported cases of fatigue have been of psychological causation.<sup>5</sup> Overwork is a common cause of fatigue and is often obvious to everyone but the patient. General practitioners are invariably concerned about misdiagnosing a serious disorder presenting as fatigue. Such disorders include anaemia and its causes, malignant disease and subacute or chronic infections such as hepatitis; especially hepatitis C, bacterial endocarditis and tuberculosis which can be 'hidden' or masked in the initial stages of disease and not readily apparent.

The symptom of fatigue is fraught with pitfalls. Classic examples include incipient congestive cardiac failure (CCF), haemochromatosis, coeliac disease, Addison disease, Parkinson disease, meta-

**John Murtagh**



*John Murtagh, AM, MD, BSc, FRACGP, DipObstRCOG, is Adjunct Professor of General Practice, Monash University Professorial Fellow of General Practice, University of Melbourne, and Adjunct Professor, Graduate School of Integrative Medicine, Swinburne University, Victoria.*

**Table 1. Common factors/causes associated with fatigue**

**Lifestyle**

- drug and alcohol abuse
- sleep deprivation
- over work/‘burnout’
- sedentary lifestyle
- inappropriate diet

**Social**

- bereavement
- occupational stress including bullying
- unemployment

**Psychological**

- anxiety
- depression
- post-traumatic stress disorder
- sleep disorders

**Physical**

- drug therapy, eg. antihypertensives
- infectious disorders, eg. Epstein-Barr virus (EBV)
- anaemia
- cardiac failure
- chronic disease, eg. COPD
- malignancy
- hypothyroidism

**Unknown**

- chronic fatigue syndrome
- fibromyalgia

**Table 2. Diagnostic model<sup>6</sup>**

**Question 1**

What are probability diagnoses?

**Answer 1**

Stress and anxiety  
 Depression  
 Viral/postviral infection, eg. EBV  
 Sleep related disorders, eg. sleep apnoea

**Question 2**

What are serious disorders not to be missed?

**Answer 2**

Malignant disease  
 Cardiac arrhythmia, eg. sick sinus syndrome  
 Cardiomyopathy  
 Anaemia  
 HIV infection  
 Hepatitis especially, hepatitis C  
 Haemochromatosis

**Question 3**

What are the pitfalls?

**Answer 3**

‘Masked’ depression  
 Coeliac disease  
 Food intolerance  
 Chronic infection, eg. tuberculosis  
 Incipient CCF  
 Fibromyalgia  
 Lack of fitness  
 Drugs: alcohol, prescribed, withdrawal

Menopause syndrome  
 Pregnancy  
 Neurological disorders, eg. cerebral ischaemia  
 Renal failure  
 Metabolic, eg. hypokalaemia, hypomagnesaemia  
 Chemical exposure, eg. occupational  
 Rarities  
 Hyperparathyroidism  
 Addison disease  
 Cushing disease  
 Narcolepsy  
 Multiple sclerosis/myasthenia gravis  
 Connective tissue disorders, eg. rheumatoid arthritis, systemic lupus erythematosus

**Question 4**

Seven masquerades checklist

**Answer 4**

Depression  
 Diabetes  
 Drugs  
 Anaemia  
 Thyroid disease  
 Spinal dysfunction  
 Urinary tract infection (UTI)

**Question 5**

Is the patient trying to tell me something?

**Answer 5**

Highly likely. Psychogenic and lifestyle disorders are very common in this presentation in general practice

bolic disturbances such as hypokalaemia, chronic renal failure and drugs, whether self administered or iatrogenic. Drug withdrawal, especially from illicit drugs such as amphetamines, marijuana, cocaine and heroin, also has to be considered. Fatigue is a symptom that may represent a ‘ticket of entry’; a plea for help in a stressed, anxious or depressed patient. Any of the primary psychiatric disorders can present as fatigue.

**History**

In routine history taking, it is mandatory that questions be asked about the following:

- sleep patterns (it is not uncommon for patients

to say they sleep well and yet on questioning it is found they have initial insomnia, middle insomnia, or both, with or without early morning waking). It is most relevant to talk to any sleeping partners to obtain a history of sleep disturbance

- weight fluctuations
- energy – performance, ability to cope
- sexual activity
- suicidal ideas
- self medication – over-the-counter preparations, eg. bromides, stimulants, analgesics, alcohol, cigarettes, other drugs. This is particularly important in the drug addiction prone

group (doctors, pharmacists, nurses, liquor industry workers, truck drivers)

- fears (including phobic symptoms, hypochondriasis)
- precipitating factors (present in over 50% of patients with depressive illness)
  - postpartum
  - postoperative
  - associated with chronic physical illness
  - bereavement
  - chronic pain conditions
  - retirement
  - medication
  - post-trauma, eg. motor vehicle accident
  - postviral infections, especially hepatitis, mononucleosis, influenza
  - work history – determine whether the patient is a workaholic
  - dietary history – determine pattern, including fad diets or skipped meals
  - menstrual history and symptoms related to menopause
  - self question: ‘Is this patient depressed?’

**Physical examination**

A routine physical examination is important, followed by a more detailed specific examination relevant to the individual patient. It is wise to take time and have a good look at the patient especially the facial features for signs of physical disease or mental distress. Check the mucous membranes for pallor, the sclera for jaundice and also the pulse.

In particular it is important to ascertain the presence of hepatosplenomegaly and lymphadenopathy. In general, the physical examination is unrewarding. In chronic fatigue syndrome (CFS) the relevant abnormal findings are muscle tenderness, mild pharyngitis and tender, slightly enlarged cervical lymph nodes. When an alternative underlying medical illness is responsible for the tiredness there will usually be evidence for this on physical examination, eg. positive Babinski reflex in multiple sclerosis, postural hypotension in Addison disease, right ventricular lift with an atrial septal defect. Routine office urinalysis should be performed. A mental state assessment should also be considered.

**Investigations**

Investigations should be selected judiciously from the list in Table 3. The key screening investigations

**Table 3. Investigations for fatigue**

- Haemoglobin, blood count and film\*
- ESR\*
- ECG and Holter monitor
- Thyroid stimulating hormone (TSH)\*
- Liver function tests\*
- Urea/renal function tests\*
- Serum electrolytes (including calcium and magnesium)\*
- Blood sugar\*
- Plasma cortisol
- Serum iron, ferritin, transferrin saturation\*
- Micro and culture of urine\*
- Tests for autoimmune disorders – antinuclear antibodies, rheumatoid factor
- HIV screening
- Chest X-ray and spirometry
- Chronic infection screening (consider): hepatitis A, B, C, D, E, cytomegalovirus, EBV, Ross River virus, Lyme disease, brucellosis, Q fever, tuberculosis, malaria, infective endocarditis, toxoplasmosis
- Primary neuromuscular disorders – muscle enzyme assay, electromyography
- Tissue markers for malignancy
- Referral to a sleep disorder laboratory for sleep apnoea study

\* Tests most patients should have when examination is completely normal

are full blood count (FBE) and erythrocyte sedimentation rate (ESR), urea and electrolytes, blood glucose, liver function tests, thyroid function tests and urinalysis. Despite this, a recent study on investigation of tiredness revealed that only 3% of patients who had a pathology test ordered in this setting had a significant clinical diagnosis based on an abnormal result.<sup>7</sup>

The diagnosis of CFS can only be made when the minimum investigations have been shown to be normal or to demonstrate minor abnormalities in liver function or blood film (atypical lymphocytes).

**Conclusion**

Analysing the symptom and reaching a diagnosis demands considerable clinical skill as fatigue may indicate the first subtle manifestation of a serious physical disease or, more commonly, may represent a patient’s struggle to cope with the problems of

everyday life. Chronic fatigue is a feature of the ‘high pressure’ nature of many people’s lifestyles. Careful consideration must be given to the differentiation of the physiological tiredness that results from excessive physical activity from psychological tiredness.


Furthermore, before diagnosing tiredness as psychological, pathological as well as physical causes must be excluded. General practitioners should not over simplify their approach and categorise fatigue into either psychological or physical causes as these are often interrelated. They must be perceptive in their diagnostic approach without resorting to over investigation.

#### **SUMMARY OF IMPORTANT POINTS**

- When patients complain of fatigue, believe them.
- Always consider underlying psychological distress, especially depressive disorder.
- Take a searching history especially regarding lifestyle and drug intake.
- Keep in mind haemochromatosis – the key test is transferrin saturation.
- The key screening investigations are FBE, ESR, urea and electrolytes including calcium, blood sugar, liver function tests, thyroid function tests and urinalysis.

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#### **CORRESPONDENCE**

Email: [murtagh@bigpond.com](mailto:murtagh@bigpond.com)