***Investigating fatigue in primary care***

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Tiredness is a common presentation in general practice, but how useful are investigations, and what tests should be done and how soon?

**Learning points**

* Tiredness is a common complaint, reported in 5-7% of general practice encounters
* Investigations may exclude diagnosis and reassure the patient, but they have a low rate of identifying any underlying disease
* Investigations are warranted in those who have not recovered after one month or whose initial presentation is atypical or is associated with “red flag” symptoms
* Be alert for important but easily missed conditions such as carbon monoxide poisoning, coeliac disease, pregnancy, and sleep apnoea
* Further evidence is needed to establish best practice in the investigation of the tired patient

A 48 year old teacher with a two month history of continuing tiredness visits her general practitioner. She has an unremarkable medical history and no history of recent infection, and she denies unusual stress. She has not lost any weight. Clinical examination is normal with a blood pressure of 130/75 mm Hg, a regular pulse at 70 beats per minute, and no lymphadenopathy.

**The problem**

Fatigue is a normal part of life, but it can also be a symptom of disease, including serious illnesses. It is a common complaint in primary care, exceeded only by complaints of cough.[1](http://www.bmj.com/content/341/bmj.c4259#ref-1) Five to seven per cent of patients attending primary care have a primary complaint of fatigue, with this proportion being remarkably consistent across Western countries[2](http://www.bmj.com/content/341/bmj.c4259#ref-2) [3](http://www.bmj.com/content/341/bmj.c4259#ref-3) [4](http://www.bmj.com/content/341/bmj.c4259#ref-4) [5](http://www.bmj.com/content/341/bmj.c4259#ref-5) and over time.[4](http://www.bmj.com/content/341/bmj.c4259#ref-4) The proportion of patients presenting with fatigue as an additional complaint is nearly three times as high.[3](http://www.bmj.com/content/341/bmj.c4259#ref-3) [6](http://www.bmj.com/content/341/bmj.c4259#ref-6) Almost three quarters of consultations for fatigue are isolated episodes, with no follow-up consultations on the subject.[5](http://www.bmj.com/content/341/bmj.c4259#ref-5) This is presumably because most patients’ fatigue improves,[7](http://www.bmj.com/content/341/bmj.c4259#ref-7) especially if there is a time limited explanation, such as a recent infection.[8](http://www.bmj.com/content/341/bmj.c4259#ref-8) [9](http://www.bmj.com/content/341/bmj.c4259#ref-9)

It is not surprising, therefore, that general practitioners perform investigations in only half of patients complaining of fatigue[10](http://www.bmj.com/content/341/bmj.c4259#ref-10) and that few of these tests yield abnormal results.[10](http://www.bmj.com/content/341/bmj.c4259#ref-10) [11](http://www.bmj.com/content/341/bmj.c4259#ref-11) Even so, the high incidence of the fatigue complaints means that laboratory tests for fatigue account for almost 5% of the total number of laboratory tests ordered by general practitioners.[12](http://www.bmj.com/content/341/bmj.c4259#ref-12)

**The likelihood of finding a diagnosis**

A diagnosis is made in less than half of patients with fatigue; furthermore, many of the diagnoses are descriptive, such as stress, or are one of the many synonyms for fatigue itself.[6](http://www.bmj.com/content/341/bmj.c4259#ref-6) Patients understand that an underlying identifiable disease may not be present,[6](http://www.bmj.com/content/341/bmj.c4259#ref-6) though patients’ and doctors’ beliefs are sometimes mismatched, with a higher proportion of doctors than patients considering the particular problem to be psychological.[13](http://www.bmj.com/content/341/bmj.c4259#ref-13)

Precipitating factors for consultation can be stressful life events (underlying about two thirds of fatigue complaints)—for example, work disputes, family problems, bereavement, or financial difficulties; or they can be illnesses such as respiratory tract infections. Hypothyroidism and anaemia are identified in under 3% of patients.[10](http://www.bmj.com/content/341/bmj.c4259#ref-10) Other conditions, such as Addison’s disease, renal failure, liver failure, carbon monoxide poisoning, coeliac disease, pregnancy, domestic abuse, and sleep apnoea are all rare, though each may (rarely) present with fatigue as a predominant complaint. Indeed, almost any condition can do so.

**History and examination**

After the initial history taking, ask questions about the main organ systems, particularly about bleeding (menorrhagia, gastrointestinal), gastrointestinal symptoms, urinary symptoms (including polyuria and polydipsia), quality and length of sleep (sleep apnoea being characterised by episodes of night-time breathlessness, daytime sleepiness, and often snoring), recent infections, joint pains or swelling, and mental health problems including concentration, motivation, stressful events, and mood. Review prescribed and over the counter medications for iatrogenic fatigue and ask specifically about alcohol consumption. Examine the patient, including urine analysis and blood pressure measurement. Patients with Addison’s disease may have postural hypotension, as well as increased pigmentation.

**What is the next investigation?**

Rational investigation aims to allow most patients to forgo testing and improve spontaneously, while identifying the few patients with underlying disease reasonably quickly. Younger patients are less likely to have underlying disease, as are patients who consult frequently.[1](http://www.bmj.com/content/341/bmj.c4259#ref-1) [10](http://www.bmj.com/content/341/bmj.c4259#ref-10) Recent infection or stressful events can justify deferral of testing. Time can be a diagnostician as well as a healer, although it is probably advisable to offer a specific time for review rather than a vague “return if you don’t improve.” Take action accordingly when red flag symptoms or signs are detected; most are obvious (box 1).

**Red flags\***

* Weight loss
* Lymphadenopathy (such as a lymph node that is non-tender, firm, hard, >2 cm in diameter, progressively enlarging, supraclavicular, or axillary)
* Any other features of malignancy (such as haemoptysis, dysphagia, rectal bleeding, breast lump, postmenopausal bleeding)
* Focal neurological signs
* Features of inflammatory arthritis, vasculitis, or connective tissue disease
* Features of cardiorespiratory disease
* Sleep apnoea
* \*All the above are supported by narrative reviews from cohort and/or case-control studies conducted in primary or secondary care or are population based (sleep apnoea).[14](http://www.bmj.com/content/341/bmj.c4259#ref-14)

Investigations are warranted in those who have not recovered at about four weeks,[15](http://www.bmj.com/content/341/bmj.c4259#ref-15) [16](http://www.bmj.com/content/341/bmj.c4259#ref-16) although they may be warranted at presentation if this is atypical (an older patient or a patient who consults infrequently)[17](http://www.bmj.com/content/341/bmj.c4259#ref-17) or if clinical features suggest a diagnosis (such as polyuria and polydipsia). Clinical intuition has also been shown to have a useful role: the “art of general practice” is in noting a slightly unusual presentation from knowledge of the individual.[18](http://www.bmj.com/content/341/bmj.c4259#ref-18)

First line investigations should be targeted at picking up the relatively common diagnoses. Evidence from one randomised trial suggests that a limited set of blood tests (haemoglobin, erythrocyte sedimentation rate, glucose, and thyroid stimulating hormone) is almost as useful diagnostically as a more extensive set of tests.[15](http://www.bmj.com/content/341/bmj.c4259#ref-15) Whether mild hyperglycaemia causes fatigue is not clear, but one study of fatigue complaints in primary care found abnormalities of blood glucose more often than anaemia or hypothyroidism.[15](http://www.bmj.com/content/341/bmj.c4259#ref-15) The National Institute for Health and Clinical Excellence also recommends testing for coeliac disease in people with persistent fatigue, even when no other suggestive symptoms are present.[19](http://www.bmj.com/content/341/bmj.c4259#ref-19) Depending on the circumstances, additional first line tests may be appropriate (table[⇓](http://www.bmj.com/content/341/bmj.c4259%22%20%5Cl%20%22T1)).

Investigations requested after four weeks for patients who presented to their general practitioner with fatigue

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If first line tests are normal, a period of watchful waiting can sensibly follow. If tiredness has persisted for three months or if further suggestive symptoms have developed, then a second line of testing is reasonable. If tiredness persists for at least four months without a clear explanation, a diagnosis of chronic fatigue syndrome should be considered.[20](http://www.bmj.com/content/341/bmj.c4259#ref-20) Referral may be indicated if the patient or doctor continues to be concerned.

**Outcome**

In this case, as the patient has no red flag or suggestive symptoms and no abnormal findings, the likely temporary nature of the fatigue is discussed, together with some of the possible common precipitating factors. She is happy with a plan to return after one month for routine blood tests (full blood count, thyroid function tests, and erythrocyte sedimentation rate and viscosity) if things have not improved. In fact, she attends a couple of months later for a different problem and comments that her fatigue has improved, probably as she has resolved a difficulty at work.

**Notes**

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