

Remembering Tiredness.....

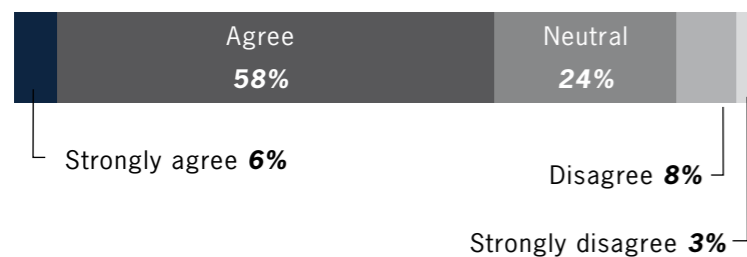
In February 2006, bpac distributed a programme on the laboratory investigation of tiredness. Many patients present to their GP each year with generalised symptoms of tiredness. This may result in multiple tests being performed to investigate the many possible causes of the symptoms. The bpac programme encouraged GPs to focus on a clinical approach to investigating tiredness and limiting laboratory investigation to a focused range of tests depending on clinical findings.

To investigate the impact of the programme, a random sample of GPs were surveyed (n = 68, response rate 34%) on what they recalled from the programme one month after its conclusion, and what changes they had made to their practice as a result.

Almost all GPs (87%) remembered at least one key message from the programme. The most frequently recalled message was that laboratory investigations should be focused - determined by patient demographics, risk factors and duration of symptoms.

Just over half of the GPs (54%) made at least one change to their clinical practice as a result of the programme. The most common changes were reducing the number of laboratory investigations requested for tiredness and changing the type of test requested. Other changes included assessing lifestyle issues as a cause of tiredness, tailoring laboratory investigations based on age groups, and delaying laboratory investigation. Of those who did not make changes, the most frequent reason given was "already carrying out programme recommendations".

"The bpac"z campaign has improved my knowledge of investigating tiredness"



Many of the GPs commented on the usefulness and high quality of the programme material. However, when following the recommendations, GPs may encounter patients who are not satisfied if they do not receive a full laboratory work-up. GPs need to find a balance between satisfying the needs of their patients and following guidelines for evidence based medicine. Communicating an investigation action plan to the patient may assist in allaying their concerns that their symptoms are not being fully considered.

The Laboratory Investigation of Tiredness

The investigation of tiredness is a clinical rather than laboratory task:

- Patients present with tiredness due to lifestyle, psychosocial, and physical causes: these often overlap and interrelate
- The key role of laboratory tests is in the diagnosis or exclusion of physical causes of tiredness

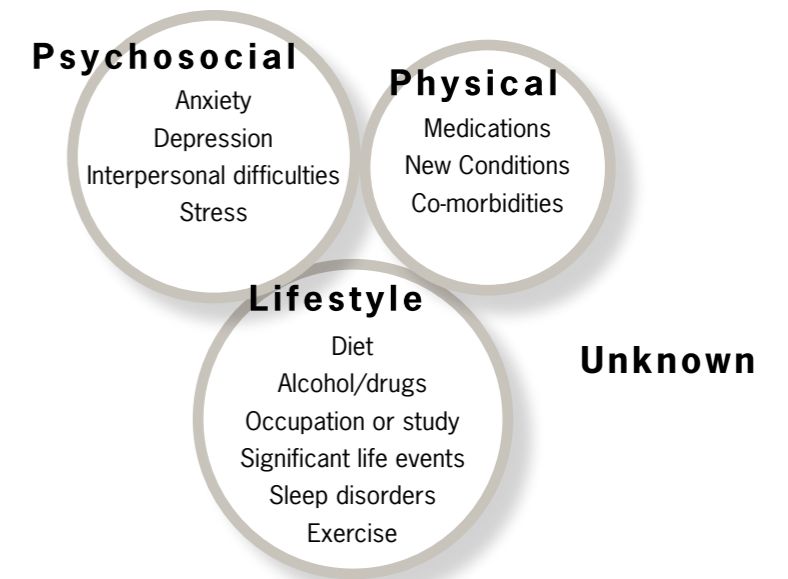
A focused approach to laboratory investigation of tiredness is usually determined by clinical findings:

- Problem definition from the patient's viewpoint
- Focused symptom review: especially looking for red flags
- Focused examination considering patient demographics and history
- Focused laboratory tests determined by clinical findings

Below is a consensus approach that has been suggested for investigating tiredness. There are few clinical trials that assess laboratory testing using patient benefits as outcomes.

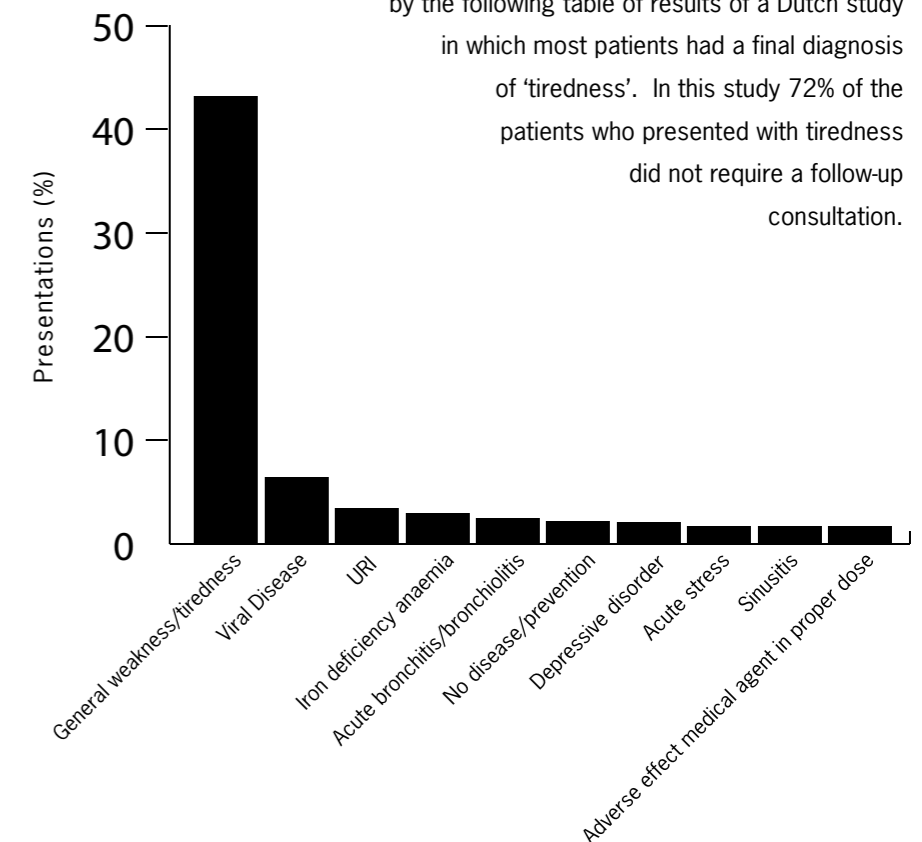
Patients under 50 years without other risk factors:	
Tests: CBC, Ferritin	
Comments: Searching for iron deficiency, macrocytosis, significant infections and leukaemias.	
Patients under 50 years with risk factors for the following conditions may require extra tests:	
Type II diabetes	Fasting glucose
Liver disorders	Liver function tests
Thyroid dysfunction	TSH
Renal impairment	Creatinine and eGFR, Electrolytes, Urinalysis
Body fluid transfer	HIV, Hepatitis B & C serology
Patients over 50 years OR tiredness lasting over one month	
Tests: CBC, CRP, Ferritin, Iron saturation, LFT, Creatinine and eGFR, Electrolytes, Calcium, Phosphate, TSH, Fasting Glucose, Urinalysis	
Comments: This wide range of tests reflects the increased risk that older people have of many diseases and the difficulty of reaching a diagnosis in chronic tiredness.	

Causes of tiredness Causes of tiredness can be usefully divided into three overlapping groups. Many presentations will not fit into these groups and the cause will remain unknown. It is useful to explain to patients during the first consultation that you are considering these three groups as possible causes of their tiredness.



Tiredness is a common presentation

Tiredness is a common presentation that is usually self limiting but may, on occasions, have more sinister causes. This is demonstrated by the following table of results of a Dutch study in which most patients had a final diagnosis of 'tiredness'. In this study 72% of the patients who presented with tiredness did not require a follow-up consultation.



For tired elite athletes, blood tests have a similar yield as the general public

Reference: Fallon KE. Clinical utility of blood tests in elite athletes with short term fatigue. *Br J Sports Med* 2006;40:541-544.

An analysis of pathology tests performed in 50 athletes presenting with fatigue found that only 1.2% of the results assisted in clinical decisions. The authors concluded that a “battery of blood tests did not contribute to the diagnosis in fatigued athletes”.

The primary aim of this prospective study was to determine, in a population of elite athletes, whether a set of haematological and biochemical investigations performed at their initial presentation with tiredness or fatigue, would enhance the diagnostic process over and above the information gained from clinical history and examination.

A range of tests were performed including: FBC, iron studies, electrolytes, urea, creatinine, total protein, albumin, CK, AST, ALT, alkaline phosphatase, γ -GT, total bilirubin, Hs-CRP, and TSH.

The findings of this study which focused on elite athletes presenting with predominantly short term fatigue, are similar to those found in a general practice population and patients with long term fatigue. In only one patient did the test results (raised total white cell count and neutrophilia) alter the diagnosis.

The authors commented that coaches and elite athletes often expect a test to be performed, however the clinical history is the most important factor of the consultation. They say that although routine ordering of blood tests should be discouraged, this may not convince the athlete or coach. Despite these recommendations and the cost savings that may flow from them, issues of athlete and coach reassurance and expectation need to be considered when the question is: to test or not to test?

Bottom line:

Although this study does not support routine blood testing for athletes with short term fatigue, the author recognises there are a wide range of other issues to consider. Clinicians in primary care are well aware of these issues and make testing decisions on a case-by-case basis.

Iron supplementation for non-anaemic fatigued women

Reference: Verdon F, Burnand B, Stubi CL, et al. Iron supplementation for unexplained fatigue in non-anaemic women: double blind randomised placebo controlled trial. *BMJ* 2003;326:1124.

Although fatigue is associated with iron deficiency anaemia, evidence is lacking for an association between iron deficiency and tiredness in the absence of anaemia.

In this study, the authors designed a randomised controlled trial to determine the effect of iron therapy in women with unexplained fatigue in the absence of anaemia. 136 women, aged 18 to 55, were included if their main reason for consulting was fatigue. Although some studies have previously been performed, this is believed to be the first randomised study to determine if iron supplementation was helpful in decreasing fatigue or tiredness in non-anaemic women. Other studies have measured other outcomes.

The study determined a mean decrease in the overall intensity of fatigue from baseline to one month was greater in the iron supplementation group than in the placebo group.

Further subgroup analysis showed the significant decrease in fatigue occurred only in women with baseline ferritin concentrations $\leq 50\mu\text{g/L}$.

This study supports others that have also indicated women with ferritin levels $\leq 50\mu\text{g/L}$ may benefit from iron supplementation even if haematological indices are normal.

Bottom line:

This study supports the anecdotal evidence from GPs that giving iron supplementation to women with ferritin $\leq 50\mu\text{g/L}$ often improves fatigue.

Because ferritin levels may be normal in women with haemochromatosis, it is worth testing iron saturation as well as ferritin in women with ongoing fatigue or other clinical features suggesting haemochromatosis.

The Laboratory Investigation of Tiredness

REMINDER