

**Michael Harrison**

BSc(Med), MBBS, FRCPA is Managing Partner/CEO, Sullivan Nicolaides Pathology, Brisbane, Queensland.
michael_harrison@snp.com.au



Pathology testing in the tired patient

A rational approach

Background

Pathology tests are often ordered by general practitioners to investigate patients with nonspecific complaints such as malaise and tiredness.

Objective

This article looks at the tests ordered regularly by GPs to investigate tiredness, the value of these tests, and why these tests are ordered in general practice.

Discussion

General practitioners investigate about half of all tired patients, and most commonly on the first encounter. Tiredness accounts for 4.6% of pathology tests and 2.3% of the growth in pathology testing requested by GPs. Typical pathology tests requested in this circumstance are FBC, EUC, TSH, ferritin and LFTs. Investigations are usually performed to exclude diagnosis and reassure the patient. However, these tests have a low pick up rate of serious disease. More research is needed to establish best practice in the investigation of the tired patient. Future evidence based guidelines should be simple, evidence based and targeted at the general practice experience of patient care.

■ **Complaints of malaise and tiredness are common in the general practice setting. Most often tiredness is associated with psychological conditions; serious underlying physical disease is unusual. It is surprising how little research exists to inform general practitioner decisions about testing in a patient with tiredness or other nonspecific presentations. There are no Australian guidelines to guide GPs on this issue.**

How common is tiredness?

In the Bettering the Evaluation and Care of Health (BEACH) database for 2007–2008,¹ weakness and tiredness is ranked 48 in a list of 119 most common problems managed in general practice. With 0.6561 cases of tiredness per 100 encounters, this equates to 700 000 patients managed for tiredness in Australian general practice each year. However, BEACH may underestimate the problem. Data collection depends on GP recording of the main reason for the encounter. Tiredness is a vague symptom and GPs may not record it as the 'main reason' for the encounter if there are other associated features.

The first published work looking specifically at the investigation of patients with weakness and tiredness in Australia was undertaken by the Quality Use of Pathology Program (QUPP).^{2,3} The authors examined the electronic records of four group general practices. Of 60 000 patients, 21% reported tiredness.^{2,3} The world literature is similarly scant as other studies, however available reports show similar figures (Britain 18%,⁴ Texas 6.9%,⁵ and Canada 13.6%⁶).

The QUPP study showed a female predominance in the group (64 vs. 36%) and also in the likelihood that pathology was requested (57 vs. 46%).^{2,3} Other reports have also shown a female predominance.^{4–6} Most patients (55%) saw their GP only once, so not surprisingly, most (67%) had their pathology performed on the first visit. Other predictors of the likelihood of pathology being requested included: increasing



age (2.8 times in >60 years of age group, 95% confidence interval [CI]; adjusted odds ratio [OR]: 1.4–5.5), repeat visits to GP (7.2 times, OR: 4.2–12.5), and absence of comorbidity (four times, OR: 2.2–2.3).³

How often are tests ordered?

A considerable amount of pathology testing is committed to evaluating the problem of tiredness. BEACH data shows that 62% of tired patients will have pathology tests requested by the attending GP (sixth highest in BEACH). Tiredness is the third highest in BEACH for the number of tests requested for specific problems being managed with 235.8 tests per 100 encounters.

What tests are performed?

The BEACH program first looked at weakness/tiredness in 1998.⁷ At that time, it ranked third in a listing of problems for which pathology tests were frequently ordered and accounted for 4.6% of pathology tests requested by GPs. Almost half the patients with tiredness had pathology tests requested and, when the decision to investigate was made, an average of three tests were requested per testing episode.

Tests requested are consistent with a wide range of diseases with nonspecific presenting complaints or subtle signs (*Table 1*). Another test of interest, B12, was ranked thirteenth with a frequency of 5%.

Between 2004–2005 and 2007–2008, the total number of patients managed for weakness and tiredness has remained essentially the same (700 000), slipping from position 44 to 48.¹ However, over the same period of time, pathology testing by GPs in this setting has increased. The frequency that any pathology is requested on a patient with this problem has increased 11.3% from 56 to 62%, and the number of tests/test groups requested per patient has increased 3% from 3.67 to 3.78. The increase in the amount of testing on the same number of weakness and tiredness problems is responsible for 2.3% of the total increase in pathology requested by GPs.

What is the 'pick up rate' of serious disease?

Tests ordered in the QUPP^{2,3} study were similar to those reported by BEACH. The QUPP study looked at the rate of detected abnormality and what flowed from this, including test repeats and subsequent encounters. It showed that 166 (16%) of the 1046 tests/test groups (with approximately three tests/test groups per patient) were abnormal and this led to 12 patients (4%) having a 'significant clinical diagnosis'.

The QUPP study indicates that investigating patients complaining of tiredness without other significant history has a low rate of detection of significant disease. This mirrors findings of international studies (12% abnormality rate and 7.6% diagnoses,⁸ 33% abnormality rate and 9% diagnoses)⁹ (*Table 2*).

Why do GPs request tests to investigate tiredness?

At the time of the 1998 BEACH report on GP pathology use, another study by Mara and Vining¹⁰ looked at the link between weakness/tiredness and high pathology test use. General practitioners in the study felt that patients with nonspecific complaints were difficult

Table 1. Tests requested and abnormality rate

Test	Frequency %	Abnormal result* %
FBC	74	12.0
Thyroid tests	47	6.8
LFTs	34	9.7
EUC	23	10.9
Ferritin	20	9.1
Glucose	19	–
ESR	12	32.0
Heterophil Abs	7	–

* Abnormality rate in QUPP study⁴

Table 2. Diagnosis (no.)/% of test performed leading to this diagnosis

Anaemia (3)	1% of FBC
Diabetes mellitus (2)	2% of blood glucose
Renal failure (2)	1% of creatinine tests
Glandular fever (1)	Calculation not possible
Goiter (1)	Calculation not possible
Hepatitis (1)	1% of LFTs
HIV infection (1)	Calculation not possible
Hypokalaemia (1)	0.5% of K tests
Hypothyroidism (1)	0.7% of TFTs
Nephropathy (1)	Calculation not possible

to assess and were concerned that their investigations and follow up were consistent with their peers. They were concerned that overinvestigating may be occurring, but also that serious disease could be missed.

A number of other studies have looked at pathology use by Australian GPs and attempted to identify the reasons for requesting a test. The list in *Table 3* was developed by a GP focus group from a survey of GPs requesting pathology.¹¹ It highlights the multiple other issues faced by the GP when presented with a patient complaining of tiredness. These include: pressure to find a diagnosis, to reassure the patient, to ensure that the patient returns for follow up, and to answer their concerns.

Existing guidelines

In 2003, Gialamas et al³ noted that there were no guidelines in Australian general practice. In 2008 this is still the case. International guidelines are consensus rather than evidence based:

- The Dutch College of General Practitioners recommends postponing tests until patients are reviewed a month after initial presentation, and they recommend a restricted set of tests including full blood count (FBC), erythrocyte sedimentation rate (ESR), thyroid function tests (TFTs) and glucose¹²
- The Canadian Family Practice Guidelines Development Group recommends the following tests in adult patients with fatigue of less than 6 months duration:¹³ Hb, white cell count (WCC), ESR,



electrolytes, urea creatinine and urinalysis (EUC), glucose, thyroid stimulating hormone (TSH). They attach a complex list of tests to 'perform only in these situations'; in reality this is no different to the intuitive requesting performed by all GPs, albeit with some structure to it

- In 2006, bpac^{nz} issued this consensus statement:¹⁴
 'For patients with fatigue and: 1. <50 years old – FBC and ferritin. If there are 'risk factors', add glucose, EUC, LFTs, TSH, human immune deficiency (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) serology; 2. >50 years old or tiredness of more than 1 month duration – FBC, iron studies, c-reactive protein (CRP), glucose, EUC, calcium and phosphate, LFTs, TSH, urinalysis and antinuclear antibody (ANA).

Is there a better approach? Is there enough evidence available to develop evidence based guidelines? Unfortunately, not. In a 1998 JAMA editorial¹⁵ the rhetorical question: 'What constitutes good laboratory medicine?' was asked and answered thus, 'sadly the answer in 1998 is that we still do not know, not even in a research mode. We not only haven't gotten [sic] to first base, we haven't even picked (up) our bat'. A 2006 Bandolier review¹⁶ of diagnostic testing summarised current knowledge thus: 'We really don't know very much that's any use about almost any test'.

What is best practice?

Best practice in the investigation of the tired patient resists definition. We do know that patients without comorbidity presenting with tiredness are unlikely to have significant disease. Despite this, pathology testing in these patients is rising. General practitioners identify issues such as pressure to find a diagnosis, to reassure the patient, to ensure that the patient returns for follow up, and to answer their concerns. The question is, in an era of evidence based medicine, is pathology testing the best way to achieve these aims?

Table 3. Reasons for requesting pathology¹¹

Monitor illness	29.1%
Exclude diagnosis	23.0%
Screening	15.1%
Monitor drug	11.5%
Confirm diagnosis	4.4%
Make diagnosis	4.1%
Reassure patient	3.1%
Fishing	1.5%
Treatment response	1.4%
Repeat (previously abnormal)	1.2%
Target therapy	1.0%
Buy time	0.9%
Pre-operative	0.7%
Pressure	0.6%
Curiosity	0.6%

Guideline development in this setting is difficult as scant evidence is available, and guidelines which don't take into account routine behaviour are unlikely to be adopted. More research is needed to establish best practice in the investigation of the tired patient. Future guidelines should be simple, evidence based and targeted at the GP experience of patient care.

Summary of important points

- Tiredness is reported in 21% of patient encounters in general practice.
- Each year in Australia 700 000 patients are managed for tiredness.
- Tiredness problems are associated with 4.6% of total pathology investigations requested by GPs.
- Pathology testing in the tired patient is rising.
- Investigations are usually performed to exclude diagnosis and reassure the patient. However, these tests have a relatively 'low pick up rate'.
- More research is needed to establish best practice in the investigation of the tired patient.
- Future guidelines should be simple, evidence based and targeted at the GP experience of patient care.

Conflict of interest: none declared.

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