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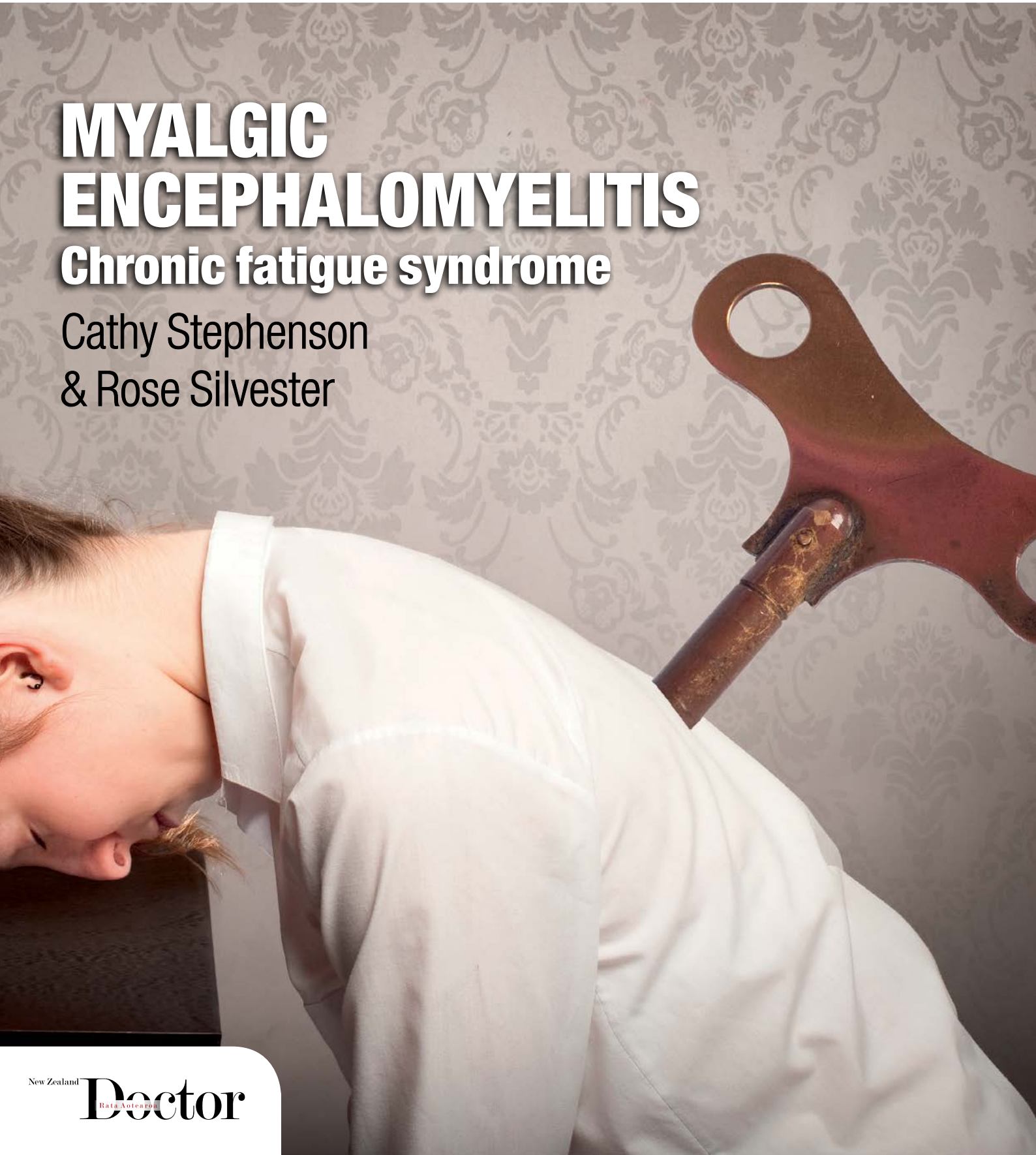
# How to Treat

# MYALGIC ENCEPHALOMYELITIS

## Chronic fatigue syndrome

Cathy Stephenson
& Rose Silvester



New Zealand Doctor
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### How much do you already know?

**Try this quiz**

1. There is a biomarker currently available that can confirm or refute a diagnosis of ME/CFS. True/False
2. Post-exertional malaise is an increase in symptoms resulting from the patient exceeding their energy envelope. True/False
3. Deconditioning is a significant contributor to the severity of symptoms in ME/CFS. True/False
4. ME/CFS is a leading cause of long-term school absence. True/False
5. Approximately 95 per cent of children with ME/CFS are undiagnosed. True/False
6. In order to diagnose ME/CFS, a viral illness must precede the onset of fatigue. True/False

Answers on page 7

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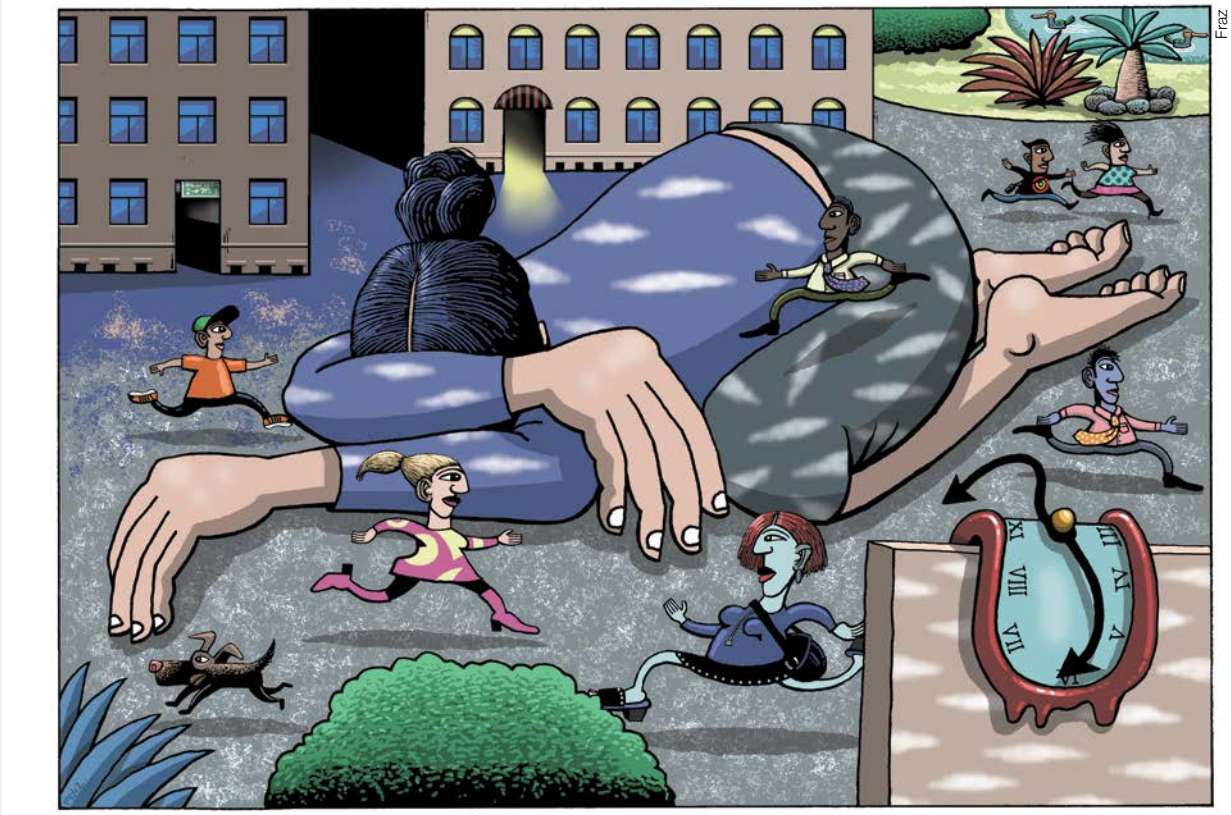
# Myalgic encephalomyelitis/ chronic fatigue syndrome




**Myalgic encephalomyelitis/chronic fatigue syndrome is a common, debilitating and costly disease. Diagnosing and managing complex chronic conditions such as this is not easy with a 15-minute consultation, but this article, by Cathy Stephenson and Rose Silvester, provides a framework of evidence-based information for GPs working with patients with ME/CFS**

Myalgic encephalomyelitis/chronic fatigue syndrome is a debilitating, chronic, multisystem disease that affects the neurological, autonomic, immune, endocrine, cardiac and energy metabolism systems. It is diagnosed with clinical criteria in the absence of alternative diagnoses.

Though chronic fatigue is a symptom of ME/CFS, it is by no means the only one. Core symptoms also include post-exertional malaise (PEM), cognitive impairment, orthostatic intolerance (OI) and unrefreshing sleep. Importantly, most people who present to general practice with the symptom of chronic fatigue do not fit the definition of ME/CFS.

The disease is known to occur both as individual cases and in outbreaks. It first came to Aotearoa's attention in the early 1980s as the "Tapanui flu". After an initial flurry of research, and concern for the fate of the New Zealanders who became unwell, interest waned. However, many of these people remain unwell today, over 30 years on.

Although ME has been included in the International Classification of Diseases since the late 1960s, in 1988, the Centers for Disease Control and Prevention (CDC) renamed it chronic fatigue syndrome. Unfortunately, this name erroneously elevated fatigue to be the defining symptom and labelled it a syndrome rather than a disease. The supposition that aligned with this was that CFS was a psychological issue, not a physical one.

This idea was compounded by the absence of a biomarker, the variable nature of the multisystem symptoms and the predominance of autonomic nervous system abnormalities. ME/CFS became a marginalised and neglected disease with dramatic underfunding of research

*Continued on page 4*

**Cathy Stephenson is a GP in Wellington and a health columnist. She has had the privilege of learning about ME/CFS from her patients, and is grateful to one of them for sharing their story here.**

**Rose Silvester is a clinical psychologist and carer of a person with ME/CFS. She is on the steering group of M.E. Awareness NZ**

# A wide range of seemingly unconnected symptoms that vary by day or week

I first met Amber a few years ago. She was a 19-year-old student nearing the end of her first year at university. At our initial appointment, there were no obvious clues as to what was going on with her: there was nothing in the way she greeted me, or in the way she walked or looked, to indicate how unwell she was feeling.

She gave a two-year history of a wide range of symptoms, covering just about every part of her body, without any obvious pattern to them. She talked about:

- fatigue ranging from mild to severe (sometimes so extreme she was bedbound)
- "brain fog" or cognitive impairment
- sleep problems – unrefreshing sleep and insomnia
- muscle pains, aches and leg cramps – "as if I had run a marathon"
- frequent cold and flu-like symptoms with chills
- dizziness and weakness on standing
- food sensitivities
- urinary symptoms, including frequency, urgency and pain
- gastrointestinal problems.

Amber was worried because it was becoming increasingly difficult for her to attend her classes, and despite seeing a range of doctors over the past two years, she was gradually getting worse. She described feeling like her body was a clock that could not be wound up and was ticking more slowly each day.

She reminded me of a few patients I had met before who had similar experiences – they all described a collection of seemingly unconnected symptoms clustered around a central experience of variability and a feeling of deep and ongoing fatigue. I wondered whether Amber, like them, might be experiencing ME/CFS, and we discussed the steps we could take to explore this possibility.

## Investigations

While there are clinical criteria that can help diagnose ME/CFS, it is important to exclude other differentials – these are numerous and range from common things we come across all the time in primary care, to obscure conditions we may have barely heard of (Panel 1, see page 5).[2]

After an unremarkable physical examination, including standing and lying blood pressure and pulse, and a neurological screen, I sent Amber for some blood tests. Of course, investigations will vary from patient to patient, but a basic screen would include:

**Routine blood tests** – complete blood count, C-reactive protein, ferritin, electrolytes, renal and liver function tests, calcium, magnesium, blood glucose, thyroid function tests, vitamin B12, folate, vitamin D and coeliac antibodies (unless patient is on a gluten-free diet).

**Other tests if clinically indicated** – immunoglobulins, antinuclear antibodies, rheumatoid titres, creatinine kinase and cortisol.

**If associated with a viral illness, consider** – Epstein-Barr virus, cytomegalovirus and HIV testing. Also consider testing for Lyme disease in patients who have travelled outside New Zealand, if symptoms indicate.

Amber returned the following week to the news that all her blood tests were normal, apart from a couple that were mildly, but not significantly, out of range. She did not look as well as she had the previous week – she was pale, slow and a little unsteady on her feet, and she reported feeling exhausted. When I remarked that she didn't look well, she told me this was how it was for her – the symptoms varied hugely throughout the day and over the week.

**She was pale, slow and a little unsteady on her feet, and reported feeling exhausted**

We discussed what she had done since the previous appointment. She described spending a night away with some friends, and then being so shattered she was barely able to get out of bed for two days.

I wondered if she was depressed, but although she described low energy, impaired concentration, poor sleep, altered appetite and (on that day at least) had quite marked slowing of speech and movement, she did not describe low mood.

Also, she demonstrated a clear drive to do more, be in class and engage with people around her. She was clearly worried, but objectively, her mood did not suggest depression. Furthermore, depression wouldn't adequately explain the other symptoms she was describing (Table 1).[3]

*It was as if my D-sized battery had been taken out and replaced with a very inadequate AA*

*Continued from page 3*

and lack of accurate training for medical professionals. This vacuum of knowledge allowed a proliferation of speculation that ME/CFS is a somatic symptom disorder. There is no evidence for this, however, and multiple pathophysiological changes across multiple systems invalidate any suggestion of malingering.

Research studies describe the following pathophysiological changes, although it is not known whether these occur before the onset of the illness or because of it:[1]

**Immune system abnormalities** – impaired natural killer cell function and/or T cell function, chronic increased production of inflammatory cytokines and, in some cases, slightly elevated levels of some autoantibodies (rheumatic factor, antithyroid antibodies, anti-gliadin antibodies, anti-smooth muscle antibodies and cold agglutinins).

**Cellular metabolism abnormalities** – impaired ability of cells to produce energy from the usual "fuel" they use. Impaired oxygen consumption and activation of anaerobic metabolic pathways in the early stages of exercise have been revealed in adults with ME/CFS.

**Neuroendocrine disturbances** – dysregulation of the hypothalamic–pituitary–adrenal axis. Some patients have flattened diurnal cortisol profiles compared with healthy people, despite normal cortisol levels.

**Blood pressure or heart rate regulation abnormalities** – many patients with ME/CFS, particularly adolescents, experience symptoms of OI – symptoms typically worsen when in an upright posture and improve with recumbency.

Many promising studies are currently underway and will likely see our understanding of pathophysiology substantially expanded in the next year. Focus is on establishing a biomarker, to specifically test for ME/CFS, and sub typing of the condition – things that would certainly make life easier for health providers and patients alike.

Table 1 **Symptom comparison between depression/anxiety disorders and ME/CFS in children and adolescents[3]**

| Symptoms | Depression/ anxiety disorders | ME/CFS | Comments |
|---|---|---|---|
| Fatigue, lack of energy, difficulty sleeping, cognitive problems, weight gain or loss | Yes | Yes | In ME/CFS, fatigue tends to fluctuate during the day and from day to day |
| Absence from school | Yes | Yes | ME/CFS is the most common medical cause of prolonged absence from school |
| Depression, feeling sad for no apparent reason | Yes | Sometimes | Patients with ME/CFS might be sad, discouraged and fed up. Clinical depression is more likely in those who encounter disbelief in the reality of their illness |
| Anxiety | Yes | Sometimes | In ME/CFS, anxiety can be associated with having an undiagnosed illness, ignorance about ME/CFS, and/or scepticism about the reality of the illness from family members, physicians or school staff. Panic attacks are occasionally seen. There is a higher degree of anxiety in patients with comorbid OI and joint hypermobility |
| Feelings of worthlessness, guilt, low self-esteem | Yes | No | Occasionally, young patients with ME/CFS feel guilty because the illness has caused family disruption. These feelings are secondary to the illness |
| Anhedonia (lack of interest and/or pleasure in activities previously enjoyed) | Yes | No | Patients with ME/CFS often wish to engage in, and still enjoy, previous activities but are limited by their energy levels. Patients with depressive illness do not wish to engage in previous activities but are physically able to do so |
| Severe depression with suicidal thinking | Yes | No | Severe depression with suicidal thinking is not present in ME/CFS without comorbid major depressive disorder |
| Lack of interest in friendships/ relationships | Yes | No | Patients with ME/CFS often want to socialise but are physically and cognitively unable to do so. Patients with depressive illness often do not wish to socialise |
| Post-exertional symptom worsening | No | Yes | A hallmark of ME/CFS. Patients with depression/anxiety often feel better after exertion |
| Orthostatic intolerance | Occasionally | Sometimes | Much more common in patients with ME/CFS |
| Hypersensitivities to light, noise, odours and medications | No | Sometimes | Common in patients with ME/CFS. Can contribute to feeling anxious and overwhelmed |
| Difficulty with thermoregulation, low body temperature, intolerance to heat and cold | No | Sometimes | Common in young patients with ME/CFS |

Panel 1
**Differential diagnosis[2]**

**Active medical conditions:**
- hypothyroidism/ hyperthyroidism
- primary adrenal insufficiency
- diabetes
- iron deficiency anaemia
- vitamin B12 deficiency
- iron overload syndrome
- Cushing syndrome
- coeliac disease
- depression
- infectious diseases (HIV, *Epstein–Barr virus, cytomegalovirus, Lyme disease*).

**Rheumatological conditions:**
- rheumatoid arthritis
- polymyalgia rheumatica
- systemic lupus
- Sjögren syndrome.

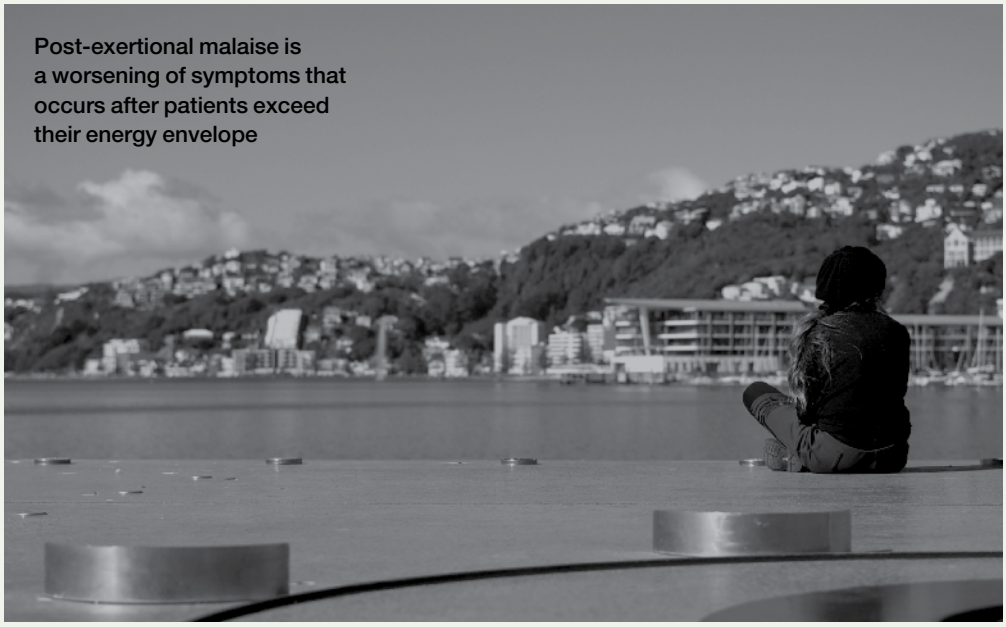
**Other conditions:**
- *fibromyalgia*
- *mast cell activation syndrome*
- *orthostatic intolerance*
- *small fibre polyneuropathy*
- *food intolerances*
- *complex regional pain syndrome*
- *Ehlers–Danlos syndrome (hypermobility or vascular type)*
- underlying conditions causing dysautonomias
- connective tissue conditions (eg, Marfan syndrome)
- multiple sclerosis
- cardiovascular conditions
- inflammatory bowel disease
- sleep disorders (eg, obstructive sleep apnoea, narcolepsy)
- craniospinal instability
- spinal stenosis
- cervical spinal fluid leak
- Chiari malformation
- toxic substance exposure
- malignancy
- iatrogenic conditions such as medication side effects or interactions.

*Italicised conditions are commonly comorbid*

# An evidence-based approach to diagnosis and classification is not easy

Until other methods of diagnosing ME/CFS become available, we rely, to a large degree, on the history we gain from our patients. In my conversations with Amber, it became clear that she, like many others, was wary of the ME/CFS label. This is not only because of the historical stigma but also because of the uncertainty around impact and prognosis.

Considering this, I think it's incredibly important that, as doctors, we take a thoughtful, considered and, where possible, evidence-based approach to diagnosis. In practice, this isn't easy, with inconsistencies between documents and guidelines, and a plethora of other obstacles getting in the way (Panel 2, see page 7).



Post-exertional malaise is a worsening of symptoms that occurs after patients exceed their energy envelope

## Diagnostic criteria

When researching how best to proceed with Amber, I came across the Institute of Medicine's (now the National Academy of Medicine) 2015 revision of evidence and proposal of diagnostic criteria. While this document has not been without its critics (some saying it oversimplifies a very complex problem), it has at least provided a point from which ME/CFS can be discussed, diagnosed and managed.[4]

If you want to look in more detail a diagnostic criteria, the CDC has published a useful summary of the symptom-based case definitions that have been used in clinical practice and research since 1994 (https://bit.ly/39juMwa).

While the Institute of Medicine's diagnostic criteria form the core features of ME/CFS (Panel 3, see page 7), patients will often have a multitude of additional symptoms and recognisable syndromes that may require attention. These may represent underlying conditions that initially drove the patient towards ME/CFS, be contributing conditions that perpetuate the problem, and/or be part of the muddy downstream effect of the illness and of living with a chronic condition.

If we highlight the diagnostic criteria among the multitude of other symptoms that sometimes cloud our vision, it can be easier to understand:

*Perceptual and sensory disturbance, ataxia, muscle weakness, fasciculations, visual disturbance,* ***cognitive impairment (brain fog),*** *extreme pallor, nausea and gastrointestinal symptoms, urinary frequency/bladder dysfunction, palpitations with or without cardiac arrhythmia, dyspnoea, sleep disturbance (hypersomnia, insomnia, sleep/wake reversal), small fibre neuropathy,* ***OI,*** *loss of thermostatic stability, sweating episodes, feverishness, acrocyanosis, chest pain, hypoglycaemia,* ***PEM,*** *recurrent sore throat, flu-like symptoms, new sensitivities to food/medications/chemicals,food allergy, other allergic reactions/mast cell activation syndrome, widespread muscle pain, pelvic pain, allodynia, chest pain, joint pain, headaches,* ***unrefreshing sleep,*** *swollen or tender lymph nodes, depression, anxiety/panic, joint hypermobility, cold extremities and* ***severe fatigue.***

**Patients will often have a multitude of additional symptoms**

## What is post-exertional malaise?

While fatigue is often thought of as the defining symptom, it is obviously not unique to ME/CFS. What is unique to ME/CFS is PEM.

PEM describes the unique energy production deficit of people with ME/CFS. It is defined by a marked worsening of symptoms (not just fatigue) in the period following physical, mental or emotional exertion. A delay of 24 to 72 hours after exertion is usual, and symptom exacerbation may last days, weeks or much longer. For more information about PEM, refer to the M.E. Awareness NZ website (https://bit.ly/2JcqYlb and https://bit.ly/3alBPoC).

Note that the exertion required to trigger PEM can be mental or emotional, not just physical – for people at the severe end of the spectrum, it could be as "minor" as brushing their teeth or having a conversation with a friend.

PEM is the symptom responsible for the "push–crash" cycle: on a good day, a person may push themselves to do a little more, then crash afterwards, experiencing a worsening of symptoms as a result. This was exactly what Amber described after she spent a night with friends. Some people report that this cycle results in an ever-lowering baseline with each crash (stepwise decline). While the mechanisms of PEM are not well understood, exercise physiology researchers (some here in New Zealand) have shown that ME/CFS patients have marked abnormalities on two-day cardiopulmonary exercise testing. When two sets of tests are performed two days apart, patients with ME/CFS show a characteristic deterioration in exercise capacity on the second day. This has helped to debunk any notion that ME/CFS is caused by deconditioning.[5,6]

***Some days, I would have little-to-no energy and be confined to the sofa or bed. Other days, I had a decent amount of energy. I used to think, wow, I have energy today – I must make the most of it! I'd go out and get things done, but then the next day, I would crash big time***

# Prevalence, onset and course of the disease – ME/CFS does not discriminate

Prior to meeting Amber, I had encountered only a handful of patients with ME/CFS, yet it's not a rare disease. While prevalence estimates vary, ME/CFS is thought to affect 0.85 per cent of the population, and around 60 per cent of those affected are women. We know that many people affected never get a diagnosis (some estimates put this as high as 91 per cent), which means many thousands of people are deprived of interventions that may help and, sadly, are frequently recommended interventions that can cause real harm.[4]

Children are not spared, with adolescence being one of the two peak times of onset (the other being in the 30s). A rigorous 2020 study in the US found prevalence rates of 0.75 per cent for children aged five to 17. Less than 5 per cent of these young people had been diagnosed.[7] ME/CFS is a leading cause of long-term school absence, yet this is often misread by parents and authorities as school refusal.

On further discussion with Amber, she described a fairly typical onset. She was an active, healthy student in high school when she contracted a viral illness. While she did gradually recover from this virus, a subsequent mild upper respiratory tract infection saw her largely confined to bed for many months. The respiratory symptoms were gone, but concomitant symptoms of malaise, body aches, chills and dizziness on standing persisted.

Though Amber's viral illness was never identified, common illnesses that correlate with an acute onset of ME/CFS include herpesviruses (Epstein–Barr, cytomegalovirus, human herpesvirus 6 and 7), enteroviral infections (eg, Coxsackie B) and influenza. Less common triggers include non-infectious immune provocations (eg, anaesthetics), physical or psychological trauma, and chemical or toxin exposure.

Around 25 per cent of people will describe a gradual or stepwise onset with no obvious trigger. Although no gene has yet been identified, genetics does play a role. Twenty-seven per cent of people with ME/CFS have first-degree relatives diagnosed with ME/CFS or chronic fatigue of unknown etiology.[8]

**ME/CFS is a spectrum disorder**

Patients at the mild end of the spectrum can continue with their lives, albeit with significant curtailing of usual activity. Patients who are moderately impaired have difficulty maintaining study or work, or standing or sitting for prolonged periods.

The approximately 20 per cent of ME/CFS patients who are severely affected are generally wheelchair-dependent, house or bed-bound and in need of full care. This level of severity can persist for months or even years. Those with severe ME/CFS may require home visits and/or Skype/telephone contact to enable them to access healthcare. Read more about the care of severely ill patients on the CDC website (https://bit.ly/3akjXKu).

It surprised me that, although Amber had been on a reduced schedule of study and had all but eliminated other interests, her presentation was considered mild because she was still able to "function" most of the time. However, she did describe periods of more severe exacerbations when study had not been possible and she spent prolonged periods in bed.

She commented that the doctors she had seen previously appeared to minimise her reports of the severity of her symptoms. Yet at her worst, she had been too unwell to leave the house. Her symptoms during these times were invisible, as they are for many others with ME/CFS.

Similar to many chronic conditions, recovery is possible for some patients (around 5–10 per cent). Others improve and are able to manage their illness to a point of minimal impact. The largest group, however, remains functionally disabled and significantly restricted by their symptoms. A further group do not improve or may worsen over time. While there is little research evidence, most experts agree children have a slightly better outcome.[1]

The impact of this condition should not be underestimated. Studies have shown that patients with ME/CFS are typically more impaired in their functioning than those with other chronic and disabling illnesses, including congestive heart failure, depression, multiple sclerosis and end-stage renal disease (Figure 1, see page 8).[4,9]

## Quiz answers

**1.** False **2.** True **3.** False **4.** True **5.** True **6.** False

*At my worst, I remember being bedridden, having my flatmates bring me dinner, and attempting to eat while still lying down because I didn't have the energy to sit up – the plate centimetres from my face, struggling to lift the fork the short distance from the plate to my mouth*

### Panel 2
### Obstacles to diagnosis[1]

**For healthcare providers, diagnosing ME/CFS can be complicated by the following factors:**

- As yet, there is no lab test or biomarker for ME/CFS.
- Fatigue and other symptoms of ME/CFS are common to many illnesses.
- For some patients, it may not be obvious to healthcare providers that they are ill.
- ME/CFS has an unpredictable pattern of remission and relapse.
- Symptoms vary from person to person in both frequency and severity – the most severely affected may not seek care because they are too ill to go to a clinic.
- The complexity and duration of the illness or prior healthcare experiences can contribute to communication difficulties between patients and healthcare providers.
- There is a lack of adequate education about, and acceptance of, ME/CFS in the medical community.

### Panel 3
### Diagnostic criteria for ME/CFS[4]

**Diagnosis requires the following three symptoms:**

1. a substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social or personal activities, which persists for more than six months and is accompanied by fatigue (often profound, of new or definite onset, not the result of ongoing excessive exertion and not substantially alleviated by rest)
2. post-exertional malaise*
3. unrefreshing sleep.*

**At least one of the two following manifestations is also required:**

1. cognitive impairment*
2. orthostatic intolerance.

** Frequency and severity of symptoms should be assessed – the diagnosis of ME/CFS should be questioned if patients do not have these symptoms at least half of the time with moderate, substantial or severe intensity.*

# Targeted management when no pharmacological solutions are available



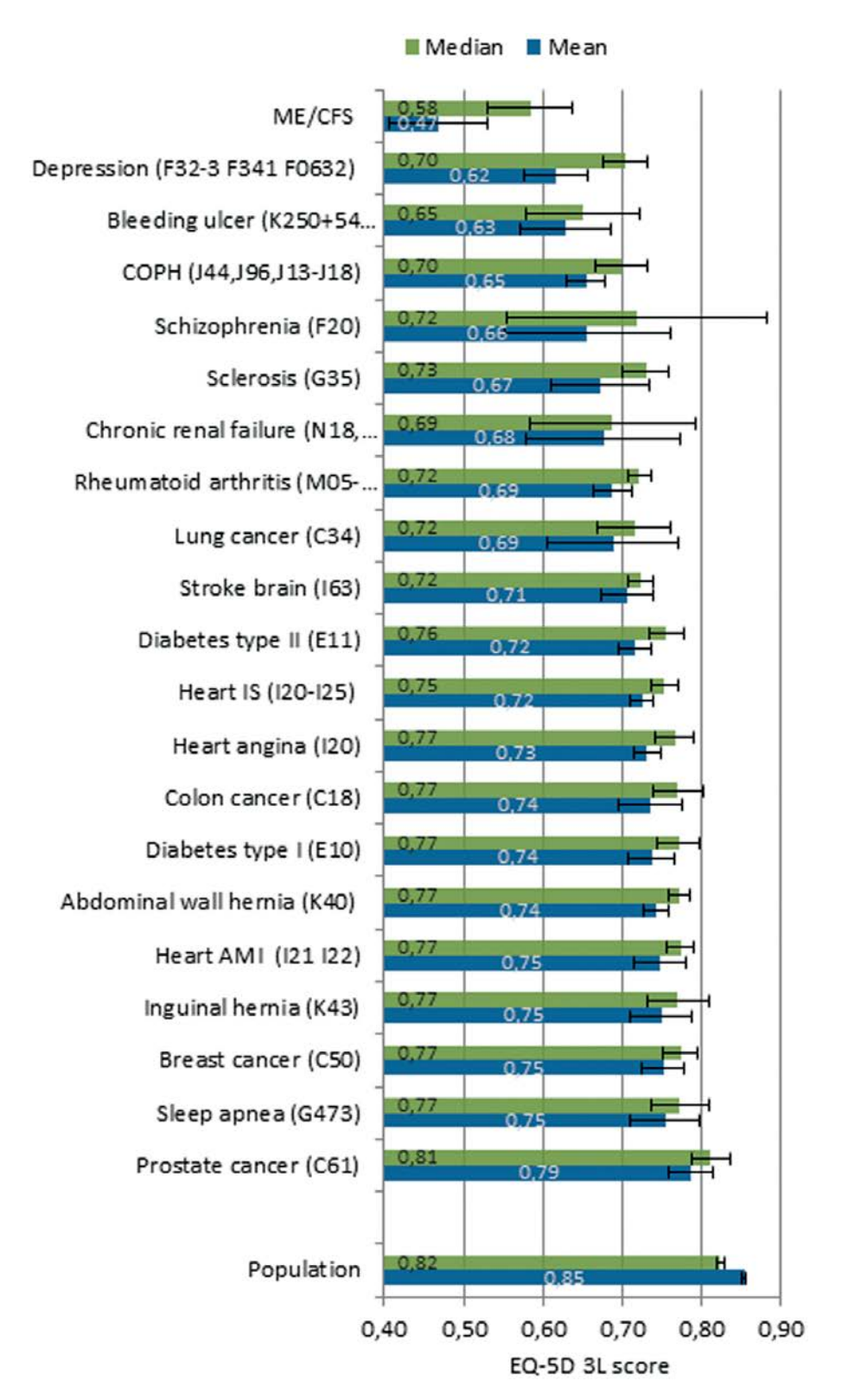



**Figure 1. A study by Falk Hvidberg and colleagues in 2015 reported that patients with ME/CFS have the lowest unadjusted EQ-5D-3L-based health-related quality of life compared with 20 other conditions, including multiple sclerosis and stroke[9]**

It was hard to know where to start to help Amber. As health professionals, we are trained to "treat", yet there are no pharmacological solutions for ME/CFS. However, there are a range of management strategies that are supportive for patients with ME/CFS. There is both evidence and experience to show that patients do better when their diagnosis and management is timely and appropriate.

### Validate the patient's experience

Amber commented a few months after we first met that the most helpful thing I did for her was to validate and affirm her experience. This may sound simple, but like many people with ME/CFS, Amber had found it difficult to be heard. It had been suggested to her that she was depressed, overly focused on her symptoms, and that she needed to "push through" the fatigue. It felt important to partner with Amber, and support her as best I could – together, we would figure out what might work for her.

### Pacing

During the first few months after meeting Amber, there remained considerable uncertainty about what was causing her symptoms. There was a lot to investigate, and it was important to be thorough. My hunch that this was ME/CFS was sufficient to advise her to *begin pacing immediately*. Over the past few years, there has been a fair amount of misunderstanding about the role of pacing, largely due to the popularity of a now debunked strategy for managing ME/CFS called graded exercise therapy.

Pacing is a strategy that reduces the frequency and severity of PEM and potentially mitigates longer term deterioration. It involves determining the threshold at which exertion (physical or cognitive) elicits PEM, and then ensuring the sum of all daily activities stays well beneath that threshold (for more information: https://bit.ly/3du3vJT).

As opposed to graded exercise therapy (which promotes a rigid incremental increase in exercise and is now known to be harmful for those with ME/CFS), levels of activity should only be very cautiously increased if the patient experiences improvement in energy levels. It is important to note that energy increase may

Patients with severe ME/CFS may rely on a wheelchair and carers for months or even years


**Figure 2. Amber's stepwise symptom management**

never occur and should not be the goal.

The variability of ME/CFS within a day and across days/weeks, and the delay between activity and the appearance of PEM (up to three days), can make establishing the pacing threshold difficult. For Amber, keeping a diary was helpful, as was a heart rate monitor. Amber found maintaining her heart rate below 120 beats per minute was a useful way to minimise PEM.

*Since getting ME/CFS, I have had to adapt small things in my daily life, to save energy where I can. Examples include using light cutlery, wearing clothes that are not too heavy or restrictive and wearing incredibly comfortable shoes (to avoid muscle aches). I also have short hair, so it's easy to maintain and doesn't take too much energy to wash*

### Stepwise symptom hierarchy

Together, Amber and I agreed on a stepwise symptom hierarchy. This hierarchy simply lists symptoms from most to least troubling (Figure 2, above), which can be a really helpful way to prioritise an approach when managing multiple symptoms.

Sleep, pain and cognitive issues are common problems in general practice populations, and GPs are well versed in how to manage them. We should approach our symptom management for ME/CFS patients in the same way we would for anyone else, although these symptoms tend to be more persistent and resistant to treatment in this group.

As many people with ME/CFS find, Amber was very sensitive to medications, so the rule of "go low and slow" had to be carefully applied. As with other complex, multisystem conditions, it was tempting to prescribe medications for all her problems, but polypharmacy may have further complicated her situation. We stuck to tackling one thing at a time, in line with the symptom hierarchy.

One of Amber's more troubling symptoms was that of orthostatic intolerance (Panel 4). She described a cluster of symptoms when standing still, which tended to worsen on getting up from sitting or lying. She felt light-headed, puffed, weak

**Energy increase may never occur and should not be the goal**

## Panel 4
## Symptoms and signs of orthostatic intolerance

OI presents as a worsening of symptoms on becoming upright (in severe cases, this may be just moving from fully to partially recumbent) and on prolonged standing.

Symptoms include:

- dizziness/light-headedness
- tachycardia
- changes in vision
- headache
- breathlessness
- syncope or presyncope
- pain, tingling or numbness in feet (primarily), but also in hands and face
- chest discomfort/pain
- acrocyanosis (discoloured extremities due to blood pooling)
- nausea
- distress/agitation
- loss of cognitive acuity.

Screen for OI using the NASA Lean Test (https://bit.ly/38irsQK). This requires 30 minutes or longer to carry out, a bed for the patient to lie on and repeated measurements of blood pressure and heart rate, so needs planning if to be done in a busy clinic. OI can be highly variable and may require multiple assessments to understand the pattern. Patients may be able to conduct lean tests at home, at different times of day over several days, by recording heart rate with a fitness tracker or heart rate and blood pressure using a home device.

In adults, postural orthostatic tachycardia syndrome (POTS) is defined by an increase in heart rate of 30 beats per minute or more within the first 10 minutes of standing, in the absence of hypotension. In children and adolescents, an increase of 40 beats per minute or more is used.

Orthostatic hypotension is defined by a decrease in systolic blood pressure of 20mmHg or a decrease in diastolic blood pressure of 10mmHg within three minutes of standing.

Patients should be referred for a tilt table test if results are well outside these limits or if symptoms are unclear or severely disabling.

and muddled, with tingling/aching in her feet.

OI is an abnormal autonomic nervous system response to orthostatic challenge, and it is thought to be the most overlooked, yet potentially manageable, feature of ME/CFS. While OI does occur in adults with ME/CFS, it is almost universal in adolescents, with >90 per cent of young people experiencing it. Common variants of OI are orthostatic hypotension, neurally mediated hypotension and postural orthostatic tachycardia syndrome.

## Panel 5
## Managing orthostatic intolerance

**Advise the patient that they may benefit from:**

- Being out of bed, as tolerated by fatigue (lying down for long periods will exacerbate postural symtoms), and raising the head of the bed by 20cm.
- Avoiding weight loss, but having regular, small meals with smaller portions of carbohydrate.
- Increasing fluid intake – begin with 2L per day and assess response. This may be increased to up to 4L per day. Water is best. Avoid caffeine drinks or drinks with high sugar content as these may cause further dehydration. Drink a glass of water (at least 400ml) to stimulate blood pressure control before any orthostatic challenge, such as getting up in the morning, going shopping or showering.
- Increasing salt intake if blood pressure is normal or low (in combination with increased fluid intake). Dose–response is individual but, as a guide, 5g salt per day is commonly required. Salt can be added to food or salty snacks can be introduced. Salt capsules (eg, SaltStick) can provide a useful supplement and minimise nausea associated with high salt. These are costly, so consider including them in a disability allowance. Electrolyte drinks can substitute for some salt. Enerlyte can be obtained on prescription and combined with a little lemon juice, or similar, to enhance taste. Sport shops stock electrolyte tablets that can be added to water. Avoid electrolytes containing high levels of sugar (eg, Powerade).
- Performing counter manoeuvres on standing/prolonged standing – these are manoeuvres that increase muscle action in the legs and pelvis to enhance blood flow against gravity (eg, walking on the spot, foot raises prior to standing, crossing legs in scissor fashion).
- Avoiding overly long or hot showers, or standing or sitting for prolonged periods.
- Wearing pressure garments – over-the-counter garments can be trialled (ideally, toe to waist) or medical-grade garments can be obtained on prescription.
- Encouraging recumbent exercise within limits of pacing (eg, swimming, recumbent cycling).
- Reducing or stopping relevant medications.

If the above strategies are ineffective, consider secondary referral where fludrocortisone, midodrine, beta-blockers and pyridostigmine may be considered.

While Amber did not meet the threshold for a diagnosis of POTS, she did experience mild tachycardia on the NASA Lean Test (she had a sustained increase of 25 beats per minute with stable blood pressure) and reported that her symptoms improved on resuming a recumbent position.

The standard first-line strategy for managing OI is to increase daily fluid intake (to 2–4L), and increase salt if blood pressure is normal (Panel 5). This is often enough to moderate the symptoms.

### Advocacy and support

Although getting diagnostic clarity can be helpful as it enables us to use a targeted, evidence-based approach to management, ME/CFS is a diagnosis that carries an uncertain prognosis and has no definitive treatment. Understandably, it is often very difficult for our patients to accept. Patients with ME/CFS need the triad of support to optimise stability: clinical, emotional and practical.

Most major centres have support networks or groups for people with ME/CFS. These groups provide invaluable opportunities to connect with, and learn from, others with ME/CFS. Some centres also have field workers who can support and advocate for patients. Information about these organisations can be found on the M.E. Awareness NZ website (m.e.awareness.nz) or the Associated New Zealand ME Society website (anzmes.org.nz).

NZcare4ME is an online, closed network of carers of young people with ME/CFS. Entry to the group is via Facebook (www.facebook.com/NZcare4ME).

In terms of financial support, because ME/CFS is long-term, many people over age 16 will be entitled to the Supported Living Payment (https://bit.ly/2uP5Eyn). Eligibility is not means tested, and the applicant can be in part-time study or work to qualify. Care Plus, a programme that supports GPs and people with chronic health conditions, caters for higher needs (https://bit.ly/2TEOYC2).

As Amber was functioning reasonably well, she didn't require home help or equipment. For patients who do, access is via the somewhat convoluted Long Term Support-Chronic Health Conditions pathway, rather than through Disability Support Services. This LTS-CHC funding is administered by DHBs and accessed through Needs Assessment Service Coordination agencies. Unfortunately, availability is limited to patients with "very high needs".

Young people with ME/CFS will usually require some support in their learning. For mildly affected children, school accommodations may suffice.[10] For those unable to attend full-time, support for learning can come from the Regional Health Schools (regionalhealth.school.nz). Strong advocacy from a GP can support families and can assist the RHS to understand the capabilities and limitations of the child.

I am aware that this is coming last, which is ironic given its importance – mental health. Adjusting to the losses that came with ME/CFS was hard for Amber, and depression and anxiety sat alongside her at times, as they often do with chronic conditions. We worked to adapt the things she enjoyed – to bring them within her "energy envelope" – and to find value in other manageable things. It will be an ongoing adaptation – although Amber's condition has stabilised and she is able to predict and rely upon her health a lot more, there are constant reminders that some things are simply out of reach.

*Before the onset of ME/CFS, I had never struggled with mental health issues, but suddenly my ability to carry out everyday tasks was reduced and my life was impacted in so many ways. It's like losing a limb – you have to learn how to live within your new limitations and to cope with the strain it puts on your mental health*

### Referral for specialty assessment and intervention

ME/CFS is complex and there is so much yet to be discovered about this disease. Making things more difficult for practitioners is that we receive remarkably little training about it, given it is a condition that is so prevalent and disabling. The need to make differential diagnoses and to clarify comorbid conditions can certainly stretch our capacity (particularly in a 15-minute consultation), so referral to secondary care is almost certainly going to be required.

Ideally, there would be multidisciplinary teams of specialists to refer to – ones that are able to integrate the complexity of the multiple body systems involved – but the reality in New Zealand is that this is currently rarely, if ever, available. The best advice I can give is to check your local HealthPathways, to see if the pathway for ME/CFS has been localised. If it has, refer according to their advice. If it hasn't, discuss with your colleagues or at your peer review group, and find out if there is a local specialist (physician, paediatrician or rheumatologist) who has a special

interest in these patients.

All too often, upon entering secondary health services, patients with ME/CFS report being passed from specialty to specialty and being reassessed through a lens of doubt, speculation or minimisation. Others report being told there is no help to be had. Add to that the infrequency of appointments, as well as patients being unable to be seen in their own home by secondary specialists, and it is easy to see how many patients can find it confusing, frustrating and unrewarding.

As GPs, we have the privilege of knowing our patients well, and we have the opportunity to support and advocate for them as they navigate this system – ensuring their concerns are well represented, that myths or misunderstanding about the condition are not perpetuated and that plans are progressing in a timely manner. At this stage, this may be the most valuable thing we can offer.

**Final thoughts**

This exploration of ME/CFS may have thrown up more questions than it has answered, but hopefully it can provide a framework for working with this community of patients. It is a challenging diagnosis.

Our obligation is to steer our patients away from interventions that have clear harm and towards an understanding that is based on evidence. However, we need to remain mindful that research has been scant, and the recommendations of experienced clinicians and researchers may precede the published evidence by as much as 10 years.

It is likely that patients with ME/CFS will be immersed in this emerging information. From walking alongside Amber over the years, I have learnt a huge amount – not only about my approach to the diagnosis and management of this condition but also about the strength and resilience of those whose lives are so affected by it. ■

**There is both evidence and experience to show that patients do better when their diagnosis and management is timely and appropriate**

## Useful resources

- Centres for Disease Control and Prevention. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. January 2020. www.cdc.gov/me-cfs
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- Rowe PC, Underhill RA, Friedman KJ, et al. Myalgic encephalomyelitis/chronic fatigue syndrome diagnosis and management in young people: A primer. *Front Pediatr* 2017;5:121.
- Two RNZCGP-endorsed education modules on ME/CFS have been created by ThinkGP: thinkgp.com.au/education

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M.E. Awareness NZ

This publication has been reprinted by M.E. Awareness NZ to provide an update on the diagnosis and management of myalgic encephalomyelitis/chronic fatigue syndrome. The content is entirely independent and based on published studies and the author's opinion.

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New Zealand Doctor Rata Aotearoa


M.E. Awareness NZ provides health professionals, patients and the general public with evidence-based information about Myalgic Encephalomyelitis /Chronic Fatigue Syndrome.

## LOOKING FOR SUPPORT WITH ASSESSMENT AND MANAGEMENT OF PATIENTS WITH ME/CFS?

### WE RECOMMEND THESE RESOURCES

**HEALTH PATHWAYS**

- Refer to your local DHB's pathways; most have recently updated their guidance for ME/CFS.

**ONLINE CME**

From Australia's ThinkGP
Accredited by RNZCGP (1 point each)

- Module 1 -**Busting The Myths And Redefining ME/CFS**
  thinkgp.com.au/education/mecfs
- Module 2 - **Ensuring A Patient-Centred Approach To Care For People Living With ME/CFS**
  thinkgp.com.au/education/mecfs-part-2

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**RESOURCE LISTS**

- Clinical Primers
- International CMEs
- Research Summaries
- Documentaries

**KEY RESOURCES**

- Guidance On Post-Exertional Malaise (PEM) for Clinicians
- The Art and Science of Pacing for ME

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