

Scottish Good Practice Statement on ME-CFS

Quick Reference Clinical Guide

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QUICK REFERENCE CLINICAL GUIDE TO THE SCOTTISH GOOD PRACTICE STATEMENT ON ADULTS WITH ME-CFS

Purpose

The purpose of this Quick Reference Clinical Guide to the Scottish Good Practice Statement on ME-CFS is to provide general practitioners with summary guidance, to assist with the differential diagnosis and clinical management in primary care of **adults with ME-CFS**. The Statement is primarily based on a synthesis of best available current evidence.¹ It is therefore a 'living' document and will be subject to periodic review as the evidence base evolves. It should be noted the Statement offers guidance and should not be regarded as prescriptive; such general advice will always require to be modified in line with needs of any individual patient and experience. A summary '*Patient Guide for Adults*' and a more detailed reference document entitled '*Scottish Good Practice Statement on ME-CFS*,' have been prepared along with this document (including interim advice on children, young people and those severely affected). Copies of all three documents are available at:

<http://www.show.scot.nhs.uk/GoodPracticeStatementonME-CFSforGeneralPractitioners>

Prevalence and classification

The condition has an estimated prevalence of at least 0.2-0.4%. It can affect anyone, at any age, from any ethnic group. It is more common in women and in patients aged from 35-55 years. WHO has classified Benign Myalgic Encephalomyelitis (ME), including post viral fatigue syndrome, under disorders of the nervous system (neurological diseases) - ICD 10 G93.3.

CLINICAL EVALUATION OF ME-CFS

Diagnostic criteria

No one set of criteria for the diagnosis of ME-CFS has been universally agreed. These include: the Oxford (1991), US Centers for Disease Control (1994), Canadian Consensus Document (2003) and NICE Guideline (2007) definitions. (A copy of the Canadian Consensus Document definition is included in the full Scottish Good Practice Statement document, where diagnostic criteria are discussed further.)

Initial presentation

The onset of ME-CFS may be sudden or gradual, following viral infections, other physical illnesses, stressful events or without precipitant. The illness usually presents with a combination of persistent or recurrent fatigue, myalgic and/or joint pain (in the absence of joint swelling or redness), that can be widespread and migratory. Pain, rather than fatigue may often be the patient's worst symptom. The symptoms may be present at rest and are provoked by physical or mental exertion. Post-exertional malaise lasting more than 24 hours is commonplace. There is a substantial reduction in activity levels.

As with any long term condition, early and accurate diagnosis of ME-CFS brings significant benefits. The aim should be to make a provisional diagnosis by 3-4 months into the illness.

It is helpful to create a list of all current symptoms as 'polysymptomatology' is a significant diagnostic clue. Recurrent 'flu-like' symptoms, sore throats, painful swollen lymph nodes, sleep disturbance (hypersomnia, insomnia and unrefreshing sleep) and headaches (tension or migraine type) are common associated symptoms. Neurological symptoms of muscle twitches, spasms and muscle weakness are common occurrences. Cognitive symptoms are almost always present – particularly sluggish or 'fogging' of thinking, poor attention and forgetfulness. Other symptoms include: peri-oral and peripheral paraesthesia, postural light headedness, sensitivity to light and noise, dizziness, palpitations, pallor, nausea, irritable bowel symptoms, alcohol intolerance, urinary frequency and urgency, feelings of fever and shivering, and altered appetite and weight.

Exclude: other possible causes of fatigue, enquire about travel, tick/insect bites, unusual infections, drug and alcohol use. **Review:** current prescribed medications.

To exclude psychiatric morbidity in the differential diagnosis, mental state examination should be undertaken on all patients with fatigue. Major depressive disorder and panic disorder with agoraphobia can be the sole cause of persistent fatigue or present, as for other diseases, as important, and reversible, co-morbid disorders in ME-CFS. Questions should be tailored, enquiring about the ability to enjoy anything (including those activities the patient *is* physically capable of) and 'situationally-specific' somatic symptoms of panic (ie chest pain, palpitations, dizziness, weakness after a typical time gap on leaving the house).

Some patients presenting with complaints of persistent fatigue and/or pain will have somatisation disorder; review previous frequency and history of medical contact.

Examination: a full physical examination should be performed including:

- height & weight (Severe obesity is commonly associated with chronic fatigue. *Very* small stature can raise the possibility of rare mitochondrial diseases).
- Erect+supine blood pressure and pulse rate (to exclude significant postural hypotension which can resemble some of the symptoms of ME-CFS or be a sign of Addison's. An increase in heart rate of over 30 bpm on standing may suggest Postural Orthostatic Tachycardia Syndrome (POTS), a recognised co-morbid finding in ME-CFS - consider cardiology referral for further assessment);
- general medical examination, including looking for signs of anaemia, tanning in unusual sites (for Addison's), enlarged or tender lymph nodes and organomegaly;
- skin and joints for evidence of systemic inflammatory diseases. Note any peri-articular tenderness typical of fibromyalgia;

- a neurological examination to exclude specific neurological abnormalities such as obvious muscle wasting, ptosis, upper motor neurone signs, ataxia, fasciculations, absent reflexes. *If any of these abnormalities are present, neurological specialist referral is indicated.* Note: Muscle twitches and spasms are common occurrences in ME-CFS and some 'give-way' weakness is also common (because of pain or fatigue) but normal power is usually possible even if only for a few seconds with encouragement.

Features suggestive of other disorders or requiring further investigation

Fatigue is a symptom of many diseases and therefore a definitive list is not possible. The following should be regarded as '*red flags*' for alternative diagnostic explanations, as part of the process of differential diagnosis:

- Substantive unexplained weight loss
- Objective neurological signs
- Symptoms or signs of inflammatory arthritis or connective tissue disease
- Symptoms or signs of cardio-respiratory disease
- Symptoms of sleep apnoea
- Clinically significant lymphadenopathy

Investigations to exclude alternative diagnoses

All patients

Blood tests: FBC, U&Es and creatinine, LFTs (including albumin), TFTs, glucose (random), ESR, C reactive protein, calcium, creatine kinase, ferritin. **Other:** urinalysis.

When indicated by history or examination

Blood tests: AMA (if minor alterations in LFTs), ANA, CMV, coeliac serology (*if diarrhoea/altered bowel habit, weight loss or history of auto-immune disorders and positive family history of coeliac disease*), EBV, ENA, HIV, Hepatitis B&C, Lyme, serology for chronic bacterial infections, Toxoplasma. **Other:** ECG (*if any cardiological symptoms*).

Investigations not currently indicated in clinical practice

Laboratory tests: B12 & folate (where normal FBC), candida albicans, fibrinogen, lactate dehydrogenase, mitochondrial testing, platelet activation, protein electrophoresis, prothrombin fragment 1&2, soluble fibre monomer, thrombin-antithrombin complexes, XMRV serology. **Other:** MRI brain scan (*in the absence of objective neurological signs*), Tilt table testing (*in the absence of unexplained syncope or other clinical indications*), auditory brainstem responses, EEG, electrodermal activity, PET imaging, SPECT imaging.

INTERVENTIONS, MANAGEMENT and REHABILITATION

Guiding principles - all patients will benefit from the general skills of good medical practice including being treated with respect, being listened to with empathy, and having the opportunity to build a rapport with their general practitioner. All

treatment should be collaborative and tailored to the needs of the individual patient. Present evidence levels for specific interventions that have been tried in ME-CFS are summarised at the end of this section.

Treatment for associated clinical conditions and symptoms - such as headache, irritable bowel syndrome, dizziness or depression should follow standard clinical practice. Pain symptoms are often problematic. Simple analgesics should be tried first – paracetamol or NSAIDs (oral or topical), escalating to co-codamol or co-dydramol if required. Avoid high doses of opiate analgesics and consider ‘atypical’ analgesics like tricyclics (low dose), gabapentin, pregabalin and duloxetine. For pain, a TENS machine, gentle massage, local heat treatment, or acupuncture may be useful for some patients (acupuncture may also be helpful for headache). For sleep disturbance, a low dose of a tricyclic antidepressant or trazodone should be considered to help re-establish normal sleep rhythm. As for their use in pain control, careful explanation should be given that these drugs are not being used in these situations as antidepressants. If clinically indicated, hypnotic drugs should be used in the short term only.

Medicines management - it is usually beneficial to start with very low doses of medicines and then steadily increase dosage over time. Liquid formulations may be helpful, if available. Side effects are often particularly bad during the first few weeks of exposure so try to avoid frequent changes to medication particularly between drugs in the same therapeutic class. Be alert to the problems of polypharmacy and stop medications that are not producing substantive benefits. Patients with ME-CFS are often very sensitive to the side-effects of medications (eg beta blockers and some antidepressants may be poorly tolerated).

Dietary advice - research into the efficacy of individual dietary regimens has been inconclusive. Some patients report intolerances to various foods as contributory to their gastrointestinal problems. A healthy diet should be encouraged. Many patients have reported that use of supplements may be helpful as part of a self-management strategy for their symptoms such as: vitamin B12, vitamin C, coenzyme Q, multivitamins and minerals, although the evidence base is lacking to support their routine use. As vitamin D levels have been found to be low in many patients with ME-CFS, foods high in vitamin D and adequate sunlight exposure are encouraged.

Rehabilitation - in most cases the aim for management will be rehabilitation or re-enablement, for regaining function, according to the patient’s needs and circumstances. Re-enablement should encompass cognitive, emotional and social aspects as well as physical aspects. Any rehabilitation or increase in activity should start from an agreed, stable and possibly very low baseline and should be gradual. Keep goals small and achievable. Patients should be counselled to engage in activity within their limits and regularly. Specific enquiry should be made about a ‘boom and bust’ approach of doing everything on a good day then ‘paying for it’ and this should be strongly discouraged.

Pacing - activity management or 'pacing' is a way of self-managing the reduced 'energy envelope' of people with ME-CFS. *Patient experience indicates that adequate and good quality rest is important, especially in early stages and during relapses.* Gaining the optimal balance between activity and rest can be difficult. It will vary from patient to patient and also during the course of the illness in any patient. A safe, consistent and often low baseline of activity (mental as well as physical) should be established which avoids setbacks (including delayed reaction). A diary may help to establish patterns of activity. Pacing is widely considered by patients to be the most helpful intervention. The clinical effectiveness of this strategy is presently being tested in a large RCT. A description of this approach for patients and a booklet on pacing is available at: <http://www.afme.org.uk>

Graded exercise therapy (GET) - is intended to redress decline in physical fitness due to inactivity. *GET has proved to be a particularly controversial form of treatment – which many patients have concerns about and some patients have indicated that GET has worsened their symptoms.* GET makes use of an exercise programme involving a gradual increase in exercise/activity. It must be delivered by a suitably trained GET therapist with experience in ME-CFS, ideally on a one-to-one basis. Where fibromyalgia is also present, supervised aerobic exercise therapy may help physical capacity and relieve pain symptoms.

Counselling – although it lacks a robust evidence base, as with any chronic illness, counselling from a trained counsellor/nurse may be helpful for some, particularly in the early stages of the illness, in supporting patients as they learn to manage the consequences of ME-CFS.

Cognitive behavioural therapy (CBT) - can be used, as in other chronic physical medical conditions, as a tool to aid people develop better ways of coping with symptoms such as fatigue, pain and sleep disturbance. CBT may be of particular value to patients when their symptoms have led to a psychological response that has compounded their problems.

Evidence levels for interventions

The grading of level of evidence has been made in accordance with the SIGN Guidelines approach. When coming to a decision about specific treatments for individual patients, and in keeping with recent SIGN developments, due weight must also be given to people's experience of living with ME-CFS. Research evidence continues to evolve and further details of evidence grading are available at:

<http://www.sign.ac.uk/guidelines/fulltext/50/annexb.html>

Interventions that benefit some, but not all (Level 1+):

- Duloxetine or pregabalin (where neuropathic pain and/or fibromyalgia present)
- Cognitive Behavioural Therapy (when delivered in centres with specific expertise in treating ME-CFS)
- Graded Exercise Therapy (when delivered in centres with specific expertise in treating ME-CFS – may also be helpful if fibromyalgia is present)

Interventions that benefit some, but not all (Level 4):

- Acupuncture (particularly for headache)
- Gabapentin
- Pacing
- 'Step 1' analgesics
- TENS
- Tricyclic antidepressant drugs (starting with low dose)

Interventions that possibly work and are unlikely to do harm (Level 2-):

- Acetyl-L-carnitine and propionyl-L-carnitine supplements
- Essential fatty acid supplements
- Massage therapy
- Melatonin

Interventions for which trials have shown a lack of benefit (Level 2- and above):

Acyclovir, acyclidine, alpha interferon, amino acids, ampligen, clonidine, dexamphetamine, fludrocortisones, fluoxetine, galantamine, ganciclovir, general dietary supplements, growth hormone, homeopathy, hydrocortisone, inosine pranobex, interferon, liver extract, low sugar/low yeast diet, magnesium, medicinal mushrooms, moclobemide, ondansetron, osteopathy, phenelzine, pollen extracts, selegiline, sulbutiamine, terfenadine, topical nasal corticosteroids.

Interventions that may do more harm than good (Level 4):

Amantidine, antifungal drugs, baclofen, benzodiazepines, methylphenidate, naltrexone, nimodipine, thyroxine (*except where patients have a diagnosis of hypothyroidism*), non specific advice on activity (eg 'go to the gym and do some exercise').

Interventions that do more harm than good (Level 2-):

Immunoglobulins, oral NADH, Staphylococcus toxoid.

Referral

Referrals may need to be made to designated clinical services, for assistance with the management of patients, in those whom the diagnosis has been made, or to the appropriate medical specialty in situations where there is diagnostic doubt. A generic diagnostic, management and referral algorithm (care pathway) is included in this guidance below - and will need to be modified appropriately by NHS Boards, to take account of local service development and provision.

Prognosis

The prognosis is variable. The majority of patients will show some degree of improvement over time, especially with treatment, although many will pursue a fluctuating course with periods of relative remission and relapse. Patients in primary care also present with milder fatigue states that have a much more favourable prognosis. However there is a significant minority, who are severely affected for many years and in extreme cases, for decades.

Other key aspects

A good understanding of support and entitlements for patients with ME-CFS and their carers, is essential - including statutory benefits, assistance from charities and the availability of self-help groups. Adults may also not be able to undertake their original job and may need careers advice and re-training. Please refer to the full Scottish Good Practice Statement on ME-CFS, for additional advice and sources of further assistance, including information on: **children and young people, people who are more severely affected, and research & development.** See:

<http://www.show.scot.nhs.uk/GoodPracticeStatementonME-CFSforGeneralPractitioners>

Reference 1 Bagnall AB, Hempel S, Chambers D, Orton V, Forbes C. *The treatment and management of chronic fatigue syndrome/myalgic encephalomyelitis in adults and children.* Centre for Reviews and Dissemination, University of York. February 2007. http://www.york.ac.uk/inst/crd/CRD_Reports/crdreport35.pdf

GENERIC CARE PATHWAY

Key Guiding Principles:

- **WORK IN PARTNERSHIP WITH THE PATIENT**
- **MUTUALLY AGREE ALL TREATMENTS**

Reassessment and interim advice

- Remain vigilant for newly emerging symptoms suggestive of alternative diagnoses.
- Maintain relationship and encourage discussion of mood state.
- Manage symptoms as required. Encourage early rehabilitation as appropriate. Encourage activity based on rehabilitation principles. Agree the appropriate balance of activity and rest. Suggest use of a diary & planned activity, *within abilities*, setting achievable goals. Be alert for, and caution against, a 'boom and bust' approach such as doing all the week's housework on a 'good day' then collapsing the next day.

Patient presents with symptoms that may indicate ME-CFS

Do an initial assessment

- Take history (including exacerbating and relieving factors, sleep disturbance, inter-current stressors)
- Conduct physical examination
- Check for symptoms of psychiatric morbidity

Arrange Investigations

- FBC, U&Es, creatinine, LFTs (inc albumin), TFTs, ESR, CRP, calcium, creatine kinase, random glucose, ferritin, urinalysis
- Consider whether any other investigations are indicated by history

Make provisional diagnosis

- In adults if symptoms have lasted 4 months and other diagnoses have been excluded
- Reconsider diagnosis if any 'red flag' symptoms/signs are present

ME-CFS diagnosis not supported at this stage: Consider referral to appropriate medical or psychiatric clinic

- If specific diagnostic query (such as possible MS)
- If substantial pre-existent co-morbidity

If ME-CFS suspected -

- and symptoms have lasted more than four months and not improving
- or presentation is severe -

consider referral to Specialist Clinic/ Treatment Centre for:

- assessment
- further investigation as appropriate
- management advice
- referral for specific treatments if appropriate
- an expert intervention package tailored to the needs of each individual patient.

Maintain general practice involvement after specialist referral and follow general principles of good medical care

Review management plans and progress

- Remember to seek out positive features, such as goals met and achievements

Help manage setbacks and relapses



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