

MANAGEMENT OF CHRONIC FATIGUE SYNDROME/MYALGIC ENCEPHALOPATHY (CFS/ME)

J Harry Baumer

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Although estimates of the occurrence of chronic fatigue syndrome/myalgic encephalopathy (CFS/ME) vary and depend on the definition, studies of school absence suggest the UK prevalence is between 50–100 per 100 000 children, with the highest rates in adolescents. It is a condition that has the potential to generate conflict between patients and doctors, even to the extent of the most appropriate name for the condition. It has previously been the subject of a report to the Chief Medical Officer¹ and joint Royal College reports^{2–3} on management.

In 2003 the Royal College of Paediatrics and Child Health initiated an evidence based guideline based on a rigorous literature review, and using the Delphi consensus process where evidence was lacking. It was developed in partnership with the Association of Young People with ME (AYME). This guideline was published in December 2004,⁴ and aims to increase knowledge and understanding among paediatricians about CFS/ME in children and young people (up to the age of 18 years) and to optimise the management of CFS/ME in young patients.

Although the graded recommendations are reproduced here, the full text of the guideline contains a wealth of additional information, and paediatricians are strongly urged to refer to the full guideline.

KEY PRACTICE RECOMMENDATIONS

Making a diagnosis

Taking a clinical history

- ▶ When taking a clinical history in children presenting with symptoms of CFS/ME, sufficient time should be allowed to listen to and document carefully the patient's description of symptoms and any associated disability [grade GPP]
- ▶ When taking a clinical history the paediatrician should explore all symptoms described by the patient including asking about the severity, onset, and course, and about other symptoms which might suggest alternative diagnoses [grade D]
- ▶ An initial family history should include an enquiry into chronic illness, and in particular CFS/ME or similar conditions in any family member [grade D]
- ▶ When initially assessing a patient, the paediatrician should be alert to the potential emotional dimensions of the illness including family dynamics, which should be explored sensitively. However, unless there are immediate concerns regarding the psychological wellbeing of the patient, a detailed exploration of family dynamics or the taking of a full psychiatric/psychological history is not necessary at this point [grade D]
- ▶ The clinician should acknowledge the distress caused to the child/young person and the parent by the symptoms being suffered [grade GPP]

Physical examination and investigations

- ▶ Paediatricians should undertake a thorough physical examination of all children and young people presenting with symptoms of profound fatigue at the earliest opportunity [grade D]
- ▶ Particular components of the examination should include [grade D]:
 - general physical examination including height, weight and head circumference
 - a neurological examination (including ophthalmic fundal examination, gait, and signs of muscle wasting)
 - check for lymph node/liver/spleen/tonsillar enlargement; any abnormal clinical signs such as pronounced cervical lymphadenopathy need full investigation
 - palpation over frontal, ethmoid, and maxillary sinuses (to look for evidence of chronic sinusitis)
 - lying and standing blood pressure and heart rate (for evidence of postural orthostatic tachycardia syndrome (POTS) or postural hypotension)
- ▶ Routine tests on all patients should include a blood test and a urine test for the following investigations [grade D]:
 - full blood count (FBC) and film to exclude anaemia, iron deficiency, and leukaemia
 - erythrocyte sedimentation rate (or viscosity) (unlikely to be raised in CFS/ME) and C reactive protein (a high concentration could suggest autoimmune disease—for example, systemic lupus erythematosus—or chronic infection—for example, tuberculosis)

Correspondence to:
Dr J Harry Baumer, Derriford
Hospital, Plymouth, Devon PL6
8DH, UK; harry.baumer@
phnt.swest.nhs.uk

- blood glucose for diabetes mellitus
- blood biochemistry (Na, K, creatinine) to look for renal impairment or endocrine abnormality (for example, Addison's)
- creatine kinase for evidence of muscle disease
- thyroid function because early clinical signs of hypothyroidism may be very subtle
- liver function (transaminases: AST, ALP, and albumin) for hepatitis
- urine tested for protein, glucose/sugar, to exclude renal disease, diabetes mellitus; tested for blood leucocytes and nitrites to exclude urinary tract infection
- ▶ Viral titres or other viral tests to impute or exclude current viral infection are not recommended apart from Epstein-Barr (EB) virus IgM, IgG, and EB nuclear antigen (EBNA) [grade C]
- ▶ As with the routine investigations some second line and other investigations may be repeated when there is a change in symptoms or signs, as clinically indicated [grade GPP]

Assessment of psychological wellbeing

- ▶ Careful attention to psychological wellbeing is an important part of the assessment and management of CFS/ME in children and young people [grade C]
- ▶ Professionals managing CFS/ME in children and young people should be aware of the possible contribution of individual and family psychological mechanisms to perceptions of illness severity, illness presentation and to recovery [grade C]
- ▶ The patient and family should be told that CFS/ME is a possible diagnosis as soon as possible and given a full explanation of what investigations are being undertaken to exclude other possibilities and why [grade GPP]
- ▶ The reasons for making a positive diagnosis of CFS/ME should be shared with the patient and their family and documented carefully in the patient's clinical notes [grade GPP]
- ▶ Paediatricians should be prepared to ask an experienced colleague for a second opinion if they, the patient or the parents have concerns about the diagnosis of CFS/ME [grade GPP]
- ▶ Doctors should explore and acknowledge patients' and parents' beliefs and attributions about the illness as early as possible after a diagnosis of CFS/ME has been made while not endorsing possibly unfounded theories of aetiology [grade D]

Management

- ▶ When a positive diagnosis of CFS/ME is made the paediatrician should establish, together with the patient and family, and where appropriate other professionals/team members, a comprehensive management plan with the identification of a management plan coordinator [grade D]
- ▶ As a minimum for all children with CFS/ME the plan should include:
 - activity management advice including establishing a baseline of activity level and gradual increases as appropriate
 - advice and symptomatic treatment as required
 - regular review of progress
- ▶ Early engagement of the family, as well as maintaining a therapeutic alliance throughout the illness, is crucial for successful implementation of the management plan [grade GPP]
- ▶ The member of the team coordinating the management plan should explain to the family the benefits of an activity diary to establish a baseline of activity, and help

the child or young person to get started and then review at regular, agreed intervals [grade D]

- ▶ Consistently used functional ability scales can help to determine the level of functioning alongside the plotting of activities in a diary, although sensitivity is advised in patients who are deteriorating [grade D]
- ▶ Once a stable baseline of activity has been established the patient, family, and the management plan coordinator should agree a cautious increase in activity that the patient feels is achievable [grade D]

Advice and symptomatic treatment

Diet

- ▶ The management team caring for children with CFS/ME should advise patients and families on the general importance of a well balanced diet while accepting that nausea and loss of appetite may make this hard for the patient to achieve. Restrictive diets are not recommended unless there is well founded evidence of specific food allergy or intolerance [grade D]
- ▶ In the minority of cases where patients have very unbalanced diets, are experiencing problems eating, or losing excessive amounts of weight, a referral to a paediatric dietician with understanding of the management plan may be helpful [grade D]
- ▶ In severe CFS/ME, dietetic assessment, especially where there is severe weight loss, is essential. A nutritional management plan should be developed involving both the patient and her/his parents [grade D]

Sleep

- ▶ A good history of the sleep pattern and sleep hygiene must be taken in patients with sleep problems before any interventions are started [grade GPP]
- ▶ The first line treatment for sleep problems in children with CFS/ME should be behavioural and cognitive interventions to promote a revision of the sleep regime [grade D]
- ▶ Medication could be considered for continued sleep problems that have not resolved with non-pharmacological approaches. Caution with dosing should be applied when prescribing medication to children as they can be more sensitive to effects and side effects of drugs [grade D]

Pain management

- ▶ Simple analgesics such as paracetamol and ibuprofen and non-pharmacological measures are first line treatments in the management of pain in children and young people with CFS/ME [grade GPP]
- ▶ If simple analgesics and other non-pharmacological measures do not work alone then referral to a psychologist may help with the perception and management of pain [grade D]
- ▶ If low dose amitriptyline or nortriptyline are considered these should only be prescribed after consultation with a colleague experienced in their use and side effects in children and young people. An initial dose of amitriptyline of 10 mg daily can be gradually increased up to 1 mg/kg (maximum 50 mg) daily, depending on effect and patient tolerance [grade D]
- ▶ When simple analgesics and cognitive behavioural techniques are ineffective, children and young people with severe and persistent pain may be referred to a suitable local pain management clinic, where available [grade NC]

Treatment for depression and mood disorders

- ▶ Antidepressant drugs should only be prescribed for children and young people with CFS/ME who have a severe mood disorder, in consultation with a colleague who has experience of their use and possible adverse effects in children and young people [grade D]

- ▶ If antidepressant treatment is considered appropriate, findings from adult studies suggest that fluoxetine should be considered as the treatment of first choice. If the initial (4–6 weeks) response is favourable it should be continued for a further six months [grade D]

Regular paediatric review

- ▶ If there has been a relapse the baseline should be reassessed and the paediatrician should reassure the patient and their family that a return to the previous level of functioning is possible [grade D]
- ▶ Paediatricians should reassess the management plan in all children and young people who have not made significant progress after six months, making it clear that this is not the fault of the child/young person. A significant deterioration in functional ability is an indication for earlier reassessment [grade D]

Further information for families

- ▶ Patients wishing to find out more about their condition should be supported in doing so but cautioned about the quality of some of the information in the public domain [grade GPP]
- ▶ Patients wishing to contact patient support groups should be encouraged to discuss the information provided by the group with their paediatrician or multidisciplinary team [grade D]

Inpatient care

- ▶ The majority of children and young people with CFS/ME can be managed at home with appropriate support from the GP and the local paediatric team [grade D]
- ▶ The majority of children with CFS/ME will not need hospital admission. However, there may be some circumstances when an admission is helpful such as, for example, for assessment or initiation of a management plan when the expertise is not available on an outpatient basis. In these circumstances it is preferable that admission is to a local unit with a multidisciplinary team experienced in managing CFS/ME in children and young people [grade D]
- ▶ Admission to an inpatient unit should be planned and presented as an option to patients and families with a day case admission offered if appropriate [grade GPP]
- ▶ If admitted to hospital, children and young people with CFS/ME should be admitted to a child/young person friendly environment where their special needs can be met [grade GPP]

Interventions for CFS/ME

Behavioural interventions

- ▶ Extrapolated evidence from adult studies suggests that cognitive behaviour therapy (CBT) is likely to be a beneficial management strategy for some children and young people with CFS/ME [grade B]
- ▶ Children and young people with CFS/ME should be considered for graded exercise or activity programmes supervised by an experienced therapist [grade B]
- ▶ Prolonged bed rest or complete inactivity should be avoided, where possible, as physical deconditioning is likely to exacerbate the fatigue and muscle weakness associated with CFS/ME [grade D]

Pharmacological interventions

- ▶ Although there is limited evidence of acute benefit after administration of immunoglobulin in the treatment of CFS/ME in children and young people, due to current concerns over the safety of blood products, immunoglobulin cannot be recommended for routine treatment [grade C]

- ▶ Given the inconclusive evidence for the efficacy of magnesium in adults with CFS/ME, the lack of studies on children and young people and concerns regarding toxicity, side effects, and the pain associated with the intervention, intramuscular magnesium injections are not recommended for children and young people with CFS/ME [grade D]
- ▶ The use of essential fatty acids, high dose vitamin B12 supplements, steroids, anticholinergic drugs, staphylococcus toxoid, or antiviral therapies are not recommended for the treatment of children and young people with CFS/ME [grade D]

Complementary therapies

- ▶ If patients and families express an interest in trying complementary therapies, they should not be discouraged, providing this does not interfere with current treatment [grade D]

Referrals to other health professionals

Psychiatry/psychology

- ▶ A referral to psychology/psychiatry is not necessary in every case. However, when assessment of psychological wellbeing suggests that clinically important psychological symptoms are present or if family focused treatments are being considered, a referral should be made if the multidisciplinary team does not include expertise in this area [grade D]
- ▶ Any child or young person with CFS/ME with suicidal ideation or who is considered at risk of self harm should be referred to a psychiatry/psychology team [grade D]
- ▶ When making a referral to the psychiatry/psychology services the reasons for the referral should be clearly explained [grade GPP]

Physiotherapy/occupational therapy

- ▶ When a young person's mobility and daily living is affected by CFS/ME, a referral could be considered to occupational therapists and physiotherapists experienced in treating the condition in children and young people for the assessment and appropriate treatment of mobility problems [grade D]

General practice

- ▶ If a paediatrician is responsible for the ongoing clinical care of a child or young person with CFS/ME, the child's general practitioner must be kept informed about the patient's progress on a regular basis [grade GPP]

Management of severe cases

- ▶ In severe cases, it is very important that the paediatrician, patient, and family should agree a member of the team who is responsible for coordinating secondary or tertiary key services. This individual should be able to establish a positive therapeutic alliance with the family [grade D]
- ▶ Referral to the Child & Adolescent Mental Health Services should be based on the clinical situation, local availability of expertise, and family agreement [grade D]
- ▶ Children and young people with severe CFS/ME should rarely be admitted to hospital. Where the child/young person is too ill to attend outpatient clinics the member of the team coordinating services should offer regular home visits to ensure that the young person's condition is being appropriately assessed and managed [grade D]
- ▶ Although inpatient care for children and young people with severe CFS/ME is rarely indicated, there may be some circumstances where it may be appropriate such as to carry out specific tasks which cannot be undertaken on an outpatient basis [grade D]

- ▶ Where inpatient care is indicated, the referral for admission should, as in all other clinical situations, be on the basis of informed consent and the purpose of the admission, whether for assessment, initiation of treatment or for particular procedures, explained to the patient and family [grade GPP]
- ▶ Where inpatient care is indicated it should be provided in a unit with a multidisciplinary team experienced in the care of children and young people with severe CFS/ME. In cases where a bed in such a unit is not available, and admission is considered by the team and the family to be essential, the child/young person should be admitted to a local unit after consultation with a colleague experienced in providing inpatient care for children and young people with CFS/ME [grade D]
- ▶ When admission for a child or young person with severe CFS/ME is indicated, a pre-hospital assessment of the individual needs of the child/young person must be undertaken [grade D]
- ▶ Where the doctor–patient/family relationship breaks down and cannot be reconciled, a second opinion should be actively recommended and sought. In these circumstances, the parental and family's choice should be taken into account with regards of which colleague to refer to [grade GPP]
- ▶ Paediatricians should familiarise themselves with sections 17 and 47 of the Children Act 1989 and the appropriate sections of the acts as they apply in Scotland and Northern Ireland [grade D]
- ▶ Referral under the Act should be made only when it is reasonable to do so and with the child's/young person's knowledge and consent. The latter may be dispensed with only when failing to refer would place the child/young person at greater risk or hinder enquiries already being made under the Children Act provisions [grade GPP]

Education and CFS/ME

- ▶ Paediatricians should be aware of the guidance from the Department for Education and Skills on education for children and young people with medical needs or equivalent statutory guidance [grade GPP]
- ▶ Paediatricians or management plan coordinators should liaise closely with schools, within existing guidelines on confidentiality, as soon as a diagnosis of CFS/ME has been made to ensure that education forms a part of a comprehensive management plan [grade D]
- ▶ The paediatrician should be responsible for the early identification of patients whose condition prevents or is likely to prevent them from attending school full time [grade GPP]
- ▶ For these patients the paediatrician should liaise with the school, the family, and other educational professionals to initiate an early referral to the Educational Welfare System and to ensure an appropriate individualised educational plan is implemented and monitored [grade GPP]
- ▶ Anxiety around returning to school should be identified and addressed [grade GPP]

Transition to adult services

- ▶ Paediatricians should ensure that their clinic or hospital has a transition policy for the transition of care of adolescents with chronic illness. This policy needs to be flexible enough to be adapted to meet the individual requirements of adolescents with CFS/ME [grade GPP]
- ▶ Paediatricians, in consultation with general practitioners, should identify an appropriate health care professional to take over the care of the older adolescent with CFS/ME and make sure that appropriate handover

Recommendation grades and levels of evidence

Grade	Evidence
A	At least one high quality meta-analysis, systematic review or RCT with a very low risk of bias and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias, directly applicable to the target population and demonstrating overall consistency of results
B	A body of evidence including high quality systematic reviews of case-control or cohort studies, or high quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from high quality meta-analysis, systematic review, or RCT with a very low risk of bias, or a body of evidence consisting principally of well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias, and demonstrating overall consistency of results
C	A body of evidence including well conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a high probability that the relationship is causal, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from high quality systematic reviews of case-control or cohort studies, or high quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
D	Recommendations agreed by Delphi consensus process (based on case-control studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal, or on non-analytic studies (for example, case reports, case series, or expert opinion)
GPP	Good practice point based on the clinical experience of the guideline development group, and not specific to CFS/ME
NC	A recommendation considered by the Delphi panel but did not reach consensus in two rounds

RCT, randomised controlled trial.

arrangements are in place before discharging their young adults [grade D]

COMMENTARY

The guideline addresses an important and controversial topic, and for the first time provides guidance that is evidence based. The scope is comprehensive, and covers those aspects relevant to paediatricians including the epidemiology, prognosis, diagnosis, and management options. Theories about the aetiology, and the management of co-morbidities, in primary care, are not included. The guideline also includes a young person's guide, and lists of national CFS/ME organisations and of Department of Health CFS/ME clinical network coordinating centres.

A parent and a representative of AYME were on the guideline development group. The web version includes a list of the organisations consulted on the draft guideline.

Only six of the 45 recommendations are graded A to C, demonstrating the lack of relevant research. A long list of research priorities is included. It is important to appreciate that the evidence for benefit from CBT and graded exercise comes from studies in ambulant adults. These treatments should not be assumed to be of benefit in all children in all situations and again paediatricians are urged to refer to the full text for guidance.

A formal Delphi consensus process was used for those recommendations where evidence was lacking. The Delphi panel included paediatricians, parents, and young people with CFS/ME, and a number of mental health professionals.

In summary, this evidence based guideline provides comprehensive practical guidance to paediatricians on the diagnosis and management of CFS/ME.

REFERENCE

- 1 **Hutchinson A (chair).** *A report of the CFS/ME working group: report to the Chief Medical Officer of an independent working group.* London: Department of Health, 2002:1–81.
- 2 **Royal College of Physicians, Psychiatrists and General Practitioners.** *Chronic fatigue syndrome. Report of a joint working group of the Royal Colleges of Physicians, Psychiatrists and General Practitioners,* 1996.
- 3 **Royal College of Paediatrics and Child Health.** RCPCH statement on chronic fatigue syndrome. London; RCPCH, 1998.
- 4 **Royal College of Paediatrics and Child Health.** *Evidence based guideline for the management of CFS/ME (chronic fatigue syndrome/ myalgic encephalopathy) in children and young people.* London: RCPCH, December 2004, http://www.rcpch.ac.uk/publications/recent_publications.html.

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Ataxia and autism

Non-progressive congenital ataxia is of two types: ataxia diplegia (with lower limb spasticity) and simple ataxia (without spasticity). Simple ataxia may be subdivided into “congenital cerebellar ataxia” (with uncoordination of voluntary movements) and “the dysequilibrium syndrome” (with lack of a sense of equilibrium or maintenance of body position in space). Studies have shown cerebellar abnormalities on imaging in only a minority of children with simple nonprogressive ataxia and only half of a series of children with cerebellar hypoplasia were ataxic. It has been suggested that there may be a link between congenital ataxia and autistic features. A study in Sweden (Ingegerd Åhsgren and colleagues. *Developmental Medicine and Child Neurology* 2005;**47**:193-8; see also commentary, *ibid*: 148) has confirmed the association.

The research team assessed 32 people aged 6–21 years (mean 12 years, 17 females), with a clinical diagnosis of nonprogressive congenital ataxia. Twelve had simple ataxia, eight ataxic diplegia, and 12 “borderline” ataxia. (The latter group had all had a diagnosis of either simple ataxia or ataxic diplegia at some time but did not fulfil the diagnostic criteria at the time of the study.) All 12 subjects with simple ataxia, seven of the eight with ataxic diplegia, and nine of the 12 with “borderline” ataxia had learning disability, which varied from mild to profound. An autistic spectrum diagnosis was made for 16 subjects (atypical autism, 7; autistic features, 4; autistic disorder, 2; Asperger syndrome, 2; “congenital” Rett syndrome, 1). Eight subjects (four in the “borderline” group) had attention deficit hyperactivity disorder. Five subjects in the simple ataxia group had cerebellar abnormalities on imaging. No cerebellar abnormality was demonstrated in subjects in either of the other two groups. Learning disability and autistic spectrum disorder were strongly associated with simple or “borderline” ataxia but no association was demonstrated between cerebellar abnormality on imaging and autistic spectrum disorder. There was only a weak association between ataxic diplegia and neuropsychiatric disorders.

The authors of this paper suggest that congenital ataxia may be one result of prenatally determined complex neurodevelopmental disorder that may also lead to autism and learning disability. It may not be an indicator of cerebellar disease.