

A 12 year old boy called John presents to his general practitioner (GP) with a two week history of sore throat and headaches. The GP examines John and notes that he is pale, has some tender lymphadenopathy, and a red throat.

The GP thinks this is either a viral sore throat, glandular fever, or maybe just a virus. He is concerned however as John doesn't look well and is worried something else is going on. He explains that he thinks this is probably something like glandular fever but he would like to do some blood tests and would like to see John early next week. He takes blood for full blood count (FBC) and monospot, checks his liver function tests (LFTs) at the same time, and does a throat swab.

Next week John sees the GP again and nothing has changed very much. He thinks the headaches have got a bit worse. His back has started to hurt. There is nothing new to find on examination but the GP notes that the throat still looks red, and he still has cervical lymphadenopathy. This time the GP examines John's optic discs, which are normal. He looks at his back, which has a full range of movement and no tender points.

The GP is not sure what is going on and still thinks John looks unwell. He suspects this is viral but is concerned as it has now been going on for three weeks. He reviews the blood tests which are: haemoglobin 11.9 g/l, mean corpuscular volume (MCV) 75 fl, total white cell count $6.5 \times 10^9/l$, normal differential; platelets $312 \times 10^9/l$, monospot negative, throat swab negative. The GP says that the blood tests are reassuring and that he thinks John has just had a nasty virus like glandular fever. He suggests John take another week off school and come back to see him if things have not improved.

A week later the parents bring John back. They are frustrated because he has now been unwell for four weeks. They tell the GP there is a family history of diabetes and they wonder if this is what is wrong with John.

The GP examines John again and thinks that nothing has changed much, although the throat looks a bit better. He tests John's urine which is clear. The GP still thinks this is probably viral and reassures John's parents. He also refers John to the paediatric outpatient department and asks for him to be seen quickly.

Four weeks later John is seen in the paediatric outpatient clinic by the paediatric specialist registrar. John is now finding it difficult to get out of bed and describes that he feels unwell all the time and is experiencing quite a lot of pain in his back, and knees and ankles. He says that his legs feel "like lead". John says he is too unwell to read and is spending most of the day watching television in his bed. He is sleeping a lot in the day because he is uncomfortable with the aches and pains and feels quite restless at night. John's parents tell the registrar that he sometimes seems to have a low grade temperature, but they have not measured it. They also say that he complains of headaches about once or twice a week. The headaches seem to be across the front of the head and he sometimes feels nauseated with them. On examination John looks pale and tired. His throat is very slightly red and there is some cervical lymphadenopathy. The registrar checks his fundi and his discs are normal. His blood pressure is not raised. The registrar does not find anything else after a careful examination, but notes that John seems to find moving quite difficult as he says that his back hurts.

The registrar is not sure what is going on. He notes that John has now been unwell for eight weeks and appears to have deteriorated over the last two weeks. He is reassured by the normal first blood tests, but is concerned that this could be an inflammatory disorder. He thinks of a list of possibilities (table 1) and plans the necessary investigations. Although he thinks about chronic fatigue syndrome or myalgic encephalopathy (CFS/ME), he thinks that eight weeks is not long enough to make that diagnosis. In addition to the diagnostic investigations, he also decides to

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Table 1 Differential diagnosis considered and the investigations requested

Diagnosis	Investigation
Leukaemia	FBC and film
Dermatomyositis	CPK
JIA	ESR, CRP, FBC
Glandular fever	EBV serology
Hepatitis	LFT
Renal impairment	U&E and creatinine
Endocrine disease, e.g. Addison's or hypothyroidism	U&E and thyroid function
Diabetes	Random glucose

CPK, creatine phosphokinase; CRP, C reactive protein; EBV, Epstein-Barr virus; ESR, erythrocyte sedimentation rate; FBC, full blood count; JIA, juvenile idiopathic arthritis; LFT, liver function test; U&E, urea and electrolytes.

Table 2 Adult criteria for diagnosis of chronic fatigue syndrome/myalgic encephalopathy (CFS/ME)²

- ▶ Debilitating persistent or relapsing fatigue for at least 6 months which is not life long and is severe enough to cause substantial reduction in previous levels of occupational, educational, social, or personal activities
- ▶ Not the result of ongoing exertion and not substantially alleviated by rest
- ▶ Four or more of the following symptoms persisting or recurring during 6 or more consecutive months of illness and did not predate the fatigue: impaired memory or concentration, sore throat, tender lymph nodes (symptom), muscle pain, pain in several joints without swelling or redness, headache, unrefreshing sleep, feeling ill after exertion
- ▶ No clinical evidence of other causes of fatigue

check John's ferritin as he notes the MCV from the GP was low. He also decides to repeat John's Epstein-Barr virus (EBV) titres.

COMMENT

- ▶ Until recently, paediatricians have had to use adult criteria for chronic fatigue syndrome which require persistent or relapsing fatigue for six months (table 2). The recent publication from the Royal College of Paediatrics and Child Health (RCPCH) *Evidence based guideline for the management of CFS/ME* do not give a minimum time for fatigue and therefore a diagnosis can be made once other causes for fatigue have been excluded (table 3 for further information). In practice, the exclusion of other causes of fatigue takes several weeks and therefore it is unlikely that a diagnosis will be made before six weeks.
- ▶ There is some evidence that systolic blood pressure is lower in adolescents with CFS/ME than in controls.¹ The RCPCH guidelines recommend that blood pressure and pulse are checked both lying and standing to exclude postural orthostatic tachycardia syndrome (POTS) or postural hypotension which can be helpful in explaining to young people what is happening to them.

A week later the parents phone the hospital leaving a message for the registrar saying they are very concerned about John as he is still no better. They wonder about the blood results. They are also not sure what they should say to the school because John has now been off school for nine weeks and the education welfare officer has contacted them about John.

The registrar looks up the blood results and discusses John with his consultant. The consultant decides that she will review John when he comes to the clinic the following week.

In the clinic next week the consultant reviews what has happened with John and his parents. She notes that John was completely well until 10 weeks ago. John's main complaints at the moment are that he feels exhausted, finds it hard to concentrate on anything, and aches all over. The consultant asks carefully about what John is and is not able to do and finds out that John has tried to do various things when he has felt "well", such as going for a walk, but that this always makes him feel much worse afterwards so he has given up. The consultant then asks about John's sleep and notes that he feels tired but cannot get off to sleep. He thinks this is because his back hurts and he feels restless. He sometimes doesn't drop off until

Table 3 Royal College of Paediatrics and Child Health definition for CFS/ME (2004)

RCPCH definition	Generalised fatigue persisting after routine tests and investigations have failed to identify an obvious underlying "cause". In CFS/ME the fatigue is likely to be associated with other classical symptoms and is classically exacerbated by effort (both mental and physical)
Other classical symptoms	Severe malaise, headaches, sleep disturbances, concentration difficulties, memory impairment, depressed mood, myalgia/muscle pain at rest and on exercise, nausea, sore throat, tender lymph nodes, abdominal pain and arthralgia/joint pain
Symptoms reported less often	Feeling too hot or cold, dizziness, cough, eye pain/increased sensitivity to light (photophobia), vision or hearing disturbances (hyperacusis), weight loss or gain, muscle weakness, lack of energy for usual activities and diarrhoea

about 2 am which is why he is sleeping in until about midday on most days. John's parents say that they are woken by John frequently in the night, because they can hear him getting in and out of bed, but they haven't noticed him snoring. He always used to sleep well before this illness. John has tried to go to school a few times over the last few weeks as his parents thought it would be good for him, but the school have phoned the parents each time after about an hour and asked them to pick him up. His parents say that John has always done fairly well in school and has always had several good friends. He denies being bullied and said that school was "OK" before he became unwell. The consultant examines John again carefully and looks at his discs but can see no abnormality. His throat now looks normal.

The consultant reviews all the test results and notes that the only abnormality is a slightly low ferritin. She is reassured that all his inflammatory markers are normal. She notes that John's EBV titres did not suggest a recent EBV infection. She realises that John is frustrated and a bit low, but feels this is in keeping with how unwell he is feeling and does not think his mood is a cause for his symptoms. She doesn't feel this is a primary problem with school avoidance and therefore thinks the most likely diagnosis is chronic fatigue syndrome or ME (CFS/ME). Luckily she had recently read the RCPCH guidelines for the management of CFS/ME. She has also seen the National Service Framework (NSF) exemplar for CFS/ME which had been published recently (see recommended reading list).

Table 4 Routine tests on all patients (RCPCH guidelines 2004)

Test	To exclude
FBC and film	Anaemia, iron deficiency, and leukaemia
ESR or viscosity and CRP	Autoimmune disease or chronic infection
Blood glucose	Diabetes mellitus
Blood biochemistry (Na, K, creatinine)	Renal impairment or endocrine abnormality, e.g. Addison's
CK	Muscle disease or myositis
Thyroid function	Hypothyroidism
AST, ALP, and albumin	Hepatitis
Urine glucose, leucocytes and protein	Urine infection, renal disease, diabetes mellitus

ALP, alkaline phosphatase; AST, aspartate transaminase; CK, creatine kinase.

COMMENT

- ▶ When considering a diagnosis of CFS/ME it is important to make sure that other primary causes of fatigue have been excluded. This includes medical and psychological diagnosis (the main one being primary depression), but also includes primary sleep problems and behavioural problems such as school refusal. Although it is important to exclude primary diagnosis masquerading as CFS/ME, it is also important to consider secondary mood disorders which are relatively common. Some cohorts of young people seen in specialist centres report that up to 25–50% present with associated problems of depression, anxiety, and somatisation.^{3–5}
- ▶ The RCPCH recommend a minimum list of screening investigations to exclude other relatively common causes of fatigue and a more extended list of investigations if symptoms or signs suggest an alternative diagnosis (tables 4 and 5).
- ▶ Low ferritin concentrations have been described as a cause for fatigue in adults and are easily treatable.⁶
- ▶ There is some evidence that recovery in EBV associated CFS/ME may be quicker than with other forms of CFS/ME and so confirmation of recent glandular fever may be helpful to the young person and their family.⁷ Other viral serological tests are not indicated as they are unlikely to be helpful in clinical management (RCPCH guidelines).

The consultant explains the diagnosis to John and his parents, who are relieved and say that they had been wondering about ME as John's mother had ME five years previously and thought that some of John's symptoms were similar. The consultant asks John's mother about her symptoms and then reassures John that even though he has a similar condition to his mother, the outcome in young people is better. The consultant explains what CFS/ME is and that the management plan will include careful and gentle activity management and symptom management, and the approach will be a rehabilitative approach to give

Table 5 Examples of second line investigations only to be undertaken if symptoms/signs or first line investigations suggest an alternative diagnosis

Blood tests	Antinuclear antibody, immunoglobulins, celiac serology, Lyme disease, toxoplasma, brucellosis antibodies, copper and caeruloplasmin, cortisol and synaethen test, B12, folate, ferritin, blood carboxyhaemoglobin
Urinalysis	Organic acids, amino acids, toxicology screen
Imaging	Chest x ray, MRI, CT or USS

CT, computed tomography, MRI, magnetic resonance imaging; USS, ultrasound scanning.

John a better quality of life and improve his activity level. She has a discussion about what John would like to achieve in the short and medium term. She then explains about helping him to find his baseline in activity and asks him to keep a computer colour coded diary of activity levels over two weeks. The consultant discusses John's sleep pattern and gives him some basic advice on how to manage his sleep (table 6). She also tells him that if these methods do not help there is some treatment she can offer which may improve things. The consultant suggests that John may like a wheelchair to help him get out of the house, which John and his parents think is a good idea. They also make a plan to start some home tuition while John is not attending school, and she explains that she will liaise with John's school, the home tutoring unit, and John's education welfare officer to devise a sustainable plan for education. This will ultimately include a plan for re-integration back into school as this is one of John's primary goals.

The consultant arranges to see the family in six weeks to review progress but asks them to call her if he should deteriorate. She gives John and his family a pack which contains the RCPCH leaflet about CFS/ME, contact information for the Association for Young people with ME (AYME), and leaflets on pacing, graded activity, sleep, and dietary advice. She reassures John and his family that most young people his age get better.

COMMENT

- ▶ It is important to reassure young people and their parents that the prognosis is much better in young people than in adults.⁸ In addition these figures are based on young people referred to tertiary centres which may represent the severe end of the spectrum. It is possible that the prognosis for young people seen in general paediatric clinics is better than this.
- ▶ Basic advice on sleep can be very helpful for young people with CFS/ME and should be tackled early (table 6).

Table 6 Suggestions to the patient to improve sleep quality

Action	
Make sure you only sleep in your bedroom	If possible, do not watch television or do computer work in bedroom or close to your bed If you need to rest during the day, try and rest on a day bed which is different to your night bed and if possible in a different room
Have a sleep routine	Have a routine before going to bed, e.g. bath, warm drink which will cue your brain that it is now time to get ready to sleep
Try not to stimulate yourself just before bed	Try to reduce physical or mental stimulation (television or reading for some people) just before bedtime
Avoid day/night reversal	Watch out for day/night reversal. Be consistent about the time you wake up and go to sleep. Try and expose your brain to as much sunlight during the day as feasible. Some young people have tried light boxes in the winter
Do not sleep too much and correct day/night reversal	Long sleeps decrease sleep quality so keep hours of sleep at night only slightly more than age appropriate levels. Work this out from peers. If day/night reversal is a problem, start getting up a few minutes earlier each day to reverse this (max 15–60 minutes a week)
Limit daytime sleeps	Try to rest, not sleep, during the day If you have to sleep keep it to less than 40 minutes before 3 pm

- ▶ Home tuition should be offered to those that are missing a significant amount of school as with other illnesses. As young people with CFS/ME need to manage their energy levels we would recommend that young people have their home tuition spread throughout the week in hourly blocks if possible. A rehabilitation programme needs to explore both previous problems with schooling as well as current problems with both cognition and memory. This may be done effectively with liaison between paediatrician and home tutor.
- ▶ Aids such as wheelchairs are often useful in the context of a rehabilitation programme as they allow young people the chance to do more without expending too much energy. They are particularly useful in helping children get to school, although most children do not like to use them in school as they do not want to be different to their friends.
- ▶ Evidence is now emerging that CFS/ME is heritable. Twin studies report consistently higher concordance rates in monozygotic (MZ) twins compared to dizygotic (DZ) twins for both adult (MZ = 0.55, DZ = 0.19)^{9, 10} and paediatric cohorts (0.81 v 0.59 for one week, 0.75 v 0.47 for one month).¹¹ These studies suggest that part of the heritability in fatigue and CFS/ME, such as that described by Bell 10 years ago,^{12, 13} is caused by genetic susceptibility.
- ▶ Symptomatic treatment should be offered when appropriate and the few medical options available are listed in table 7.

CHRONIC FATIGUE SYNDROME/MYALGIC ENCEPHALOPATHY

How common is CFS/ME in young people?

There is currently no information in the literature on incidence of CFS/ME in young people. The prevalence is reported to be between 0.19–2% based on telephone surveys in the UK and the USA.^{5, 14, 15} Lifetime prevalence (up to 30 years old) of self reported CFS/ME, uncorroborated by a physician, of 0.8% has been reported from the 1970 British birth cohort.¹⁶ Lifetime prevalence (age 8–17 years) of disabling fatigue of three months and six months of 2.34% and 1.29% has been reported from a longitudinal cohort of twins.¹¹

Who is affected?

Reports on cohorts of cases attending specialist clinics usually observe higher rates in girls than in boys and a predominance of high socioeconomic backgrounds,¹⁷ which is consistent with self reported CFS/ME from the 1970 British birth cohort.¹⁶ However two community studies using telephone administered questionnaires report equal rates of affected males and females,^{5, 14} and Jordan *et al* report no socioeconomic

class gradient.¹⁴ It seems that boys are more likely to present with cognitive problems and fatigue and less likely to have the physical symptoms, which may mean they are less likely to present to health services.^{2, 14}

Diagnosis

Until recently paediatricians have used adult definitions for CFS/ME which have required six months of fatigue and a variety of other symptoms (table 2). The RCPCH recommends using “disabling fatigue without another cause”. This requires that clinicians are assiduous in excluding other causes of disabling fatigue. There are screening tests that should be carried out on every young person with suspected CFS/ME (table 4) and then a longer list of investigations which may be necessary (table 5).

Management

Initial steps in managing this condition include basic advice about sleep, diet, and energy management.

Sleep

All young people with CFS/ME should be given information about sleep hygiene (table 6). In addition we encourage young people to work on correcting their day/night reversal and to avoid sleeping excessively long hours. Many young people report an improvement in symptoms with this approach but this has not been formally studied in this age group.

Diet

Young people and their families invariably want to know about diet. It seems to be helpful to: avoid sugar bursts during the day, keep meals small and frequent, avoid caffeine and alcohol, and maintain reasonable levels of iron intake.

Pacing and graded activity

The RCPCH guideline (2004) describes pacing in some detail but a brief description is “a means by which a person with CFS/ME balances their daily activity, working from an established baseline of functional ability”. A young person’s baseline is the level of activity they can do consistently on good days and bad days without payback. Once a young person has found their baseline they will naturally want to increase their activity levels. We try and limit this increase to approximately 15% a week to avoid a flare (fig 1). This gradual increase in activity which is very slow is called graded activity.

Activity levels must include all activity the young person is doing such as watching television, texting friends, and

Table 7 Medical management of symptoms

Symptom	Treatment	Notes
Pain	Amitriptyline	Can be very effective for pain which does not respond to analgesics. Drowsy side effect can help with sleep problems (see below)
Poor sleep with pain	Amitriptyline	Although most young people tolerate 20–30 mg once a day easily, some need to start at 5 mg and work upwards. If they do not have benefit after a six week trial at 30 mg once a day then stop treatment
Difficulty getting off to sleep	Melatonin	Not so helpful if the problem is a restless night, but can help if it is difficulty getting off to sleep. Adult practitioners suggest that the effect wears off if it is used every night and suggest using it on alternate nights
Pain	NSAIDs	Reported to be helpful by adult practitioners for pain

NSAIDs, non-steroidal anti-inflammatory drugs.

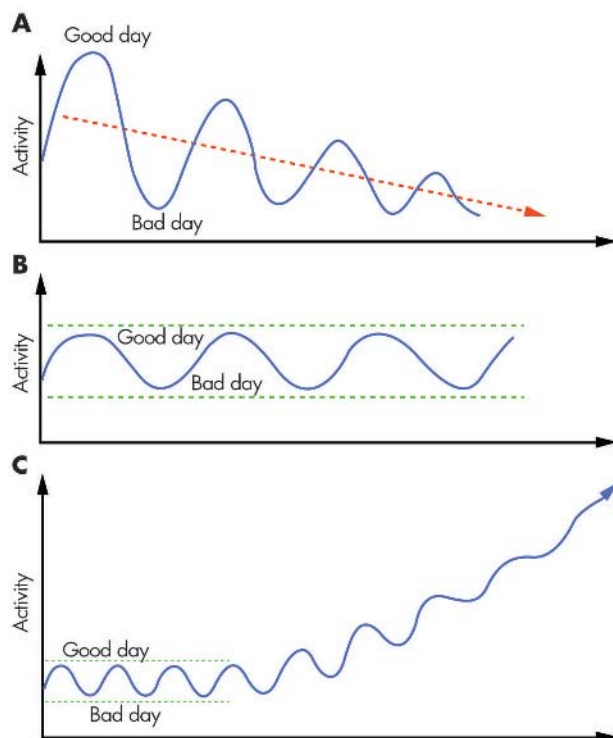


Figure 1 Diagram used to explain to young people about: (A) the boom bust approach and the resulting decreasing overall level of activity; (B) finding a baseline with small changes in activity level even on good days and bad days; and (C) the gradual increase in activity once the baseline has been found.

playing computer games. In devising a rehabilitation strategy for young people, it is important that the goal setting is defined around the young person's aims and needs and not ours. For example, if a young person's goal is to increase time with their friends, a rehabilitation programme designed around increasing school work is likely to fail.

Graded activity programmes for young people have been designed assuming that results from the adult literature can be transferred to young people. There are no trials looking at effectiveness in young people. A recent pilot study of 13 young people with CFS/ME in York who were able to attend some school suggested that graded rehabilitation (and pacing) are generally acceptable, with a drop out rate of one in seven and one in six of each treatment arm, respectively.¹⁸

Cognitive behavioural therapy

Cognitive behavioural therapy (CBT) has both a cognitive element (which focuses on the identification and modification of thoughts, beliefs, and assumptions) and a behavioural element which aims to gradually and consistently introduce a change in behaviour such as an increase in activity. It is usually provided by psychologists, but other therapists can be very good at providing a service. It can be provided in groups or on a one to one basis.

Although CBT is frequently offered as treatment for adults there is only one randomised controlled trial in adolescents ($n = 61$). This trial compared CBT with remaining on the waiting list and showed an improvement in fatigue severity, functional impairment, and school attendance.¹⁹ However, the study design suggests that the treatment arm may have

CSF/ME: clinical message

- ▶ CFS/ME in young people is relatively common although the prognosis is generally good
- ▶ A positive diagnosis of CFS/ME should be made as soon as possible. There is no minimum time required but other causes must be excluded
- ▶ Exclusion of other causes of fatigue does require screening blood tests and possibly more investigations as well as thorough history and physical examination
- ▶ Young people with CFS/ME should be able to access a rehabilitation programme which looks at sleep, energy management, diet, education, and socialising with goals set by themselves

more graded activity than CBT and it has been argued that the control group should be receiving another form of therapy for comparison.

Medical management

Medical treatments can be effective for some of the symptoms of CFS/ME, especially pain and sleep problems. One of the most commonly used treatments for pain is amitriptyline which is used at a much lower dosage (5–30 mg once a day) than when it is used to treat depression. The main "side effect" of amitriptyline at this dosage is drowsiness, but this can be used to advantage if the young person has difficulty getting off to sleep. Adult practitioners report that some adults with CFS/ME are sensitive to drug treatment and therefore start at 5 mg a day and increase up to 30 mg for a trial period before deciding on effectiveness. This does not seem to be such a problem in the adolescent group, but some young people do describe feeling unwell at doses of 20–30 mg and are fine when it is started at a lower dose.

Low ferritin values should be treated with oral iron and this often results in a rapid (2–3 days) improvement in symptomatic fatigue.

Other symptoms should be treated as in any other young person (constipation/period problems being relatively common) but be aware that some young people are very sensitive to medication and lower doses may be necessary.

Education

Young people with CFS/ME not only find it difficult to get to school and sit for prolonged periods of time in the classroom, but they also describe difficulties with concentration and short term memory. Subjective memory impairment is a common problem in adults and is part of the US Centers for Disease Control and Prevention (CDC) definition for CFS/ME in adults.² Boys may be more likely to complain of cognitive or memory problems compared to girls.¹⁴

Education and the return of young people to school needs to be tackled within a holistic rehabilitation programme for the child or young person using the principles of pacing and graded activity described above. Home tuition is useful while the young person is out of school and helps them continue with education while they regain the level of fitness required to go to school. We normally advise that young people should be able to manage an hour of school work at home daily plus at least an hour of other activity before attempting a return to school. We usually arrange transport for the young person if the parents are unable to drive them. We normally advise that initial return to school should be at lunch time (if this is

what the young person wants) to increase socialisation while continuing education at home. We then suggest that the child returns to the classroom just for an hour initially before increasing in the context of graded activity. Some children choose to start with lessons that they love and are “easy” for them such as art or history, while continuing core subjects (which may be harder) at home with home tuition. It is important that the young person goal sets their return to school. Ayme has information packs for schools which may be helpful.

Alternative health practice

Many families ask about the benefit of alternative health strategies. Our personal practice is to recommend they start with treatment which has an evidence base and not try too many different things at once. Some alternative treatments may help symptom relief such as acupuncture for headaches. It is important to discuss potential benefits and side effects (including financial and travel) with all families.

Severely affected young people

Although there are few if any studies in this group of young people because of the problems of recruitment, there is extensive literature from patients about their experience (see further reading). Many of these children are too unwell to attend clinics or hospital and therefore should be offered a package of care based around their needs in the home. This will involve close working between all health professionals, education staff, and the family and may require input from social services for aids such as stair lifts and adaptations to the house. Nursing input may be important for feeding, self care, etc.

We still encourage a goal orientated rehabilitation programme at home based on established models of rehabilitation. Care must be taken in establishing goals with the patients as in many cases young people (and professionals) try and set goals which are unrealistic. If the model of finding a baseline as described above is used then goal setting is likely to be realistic. Severely affected young people often battle with boredom and need low energy expenditure ideas to keep them going. There are particularly good ideas described in a booklet written by young people called *Surviving severe ME* (see further reading).

Further support

We all need to recognise that having CFS/ME and caring for a child with CFS/ME can be physically, emotionally, and financially draining. Parents often need more support and find contact with other parents helpful. Benefits such as the Disability Living Allowance (DLA) can improve a young person's quality of life and should be applied for. When completing the DLA mention any cognitive or organisational problems such as preparing a meal in addition to the physical problems.

FURTHER READING

- ▶ 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. This includes a patient information leaflet.

- ▶ Department of Health. *National Service Framework exemplar: chronic fatigue syndrome/myalgic encephalopathy (CFS/ME). Change for children: every child matters.* Obtainable from DoH publications, order line 08701 555 455.
- ▶ Jill Moss. *Somebody help me.* ISBN 0-9525-783-01 or Ayme as below
- ▶ *Surviving severe ME* by Claire Wade. Obtainable from Ayme by email: info@ayme.org.uk
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Competing interest: Esther Crawley is a medical advisor for Association for Young people with ME (AYME)

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