Evidence Based Guideline for the Management of CFS/ME (Chronic Fatigue Syndrome/ Myalgic Encephalopathy) in Children and Young People

December 2004

Royal College of Paediatrics and Child Health

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FOREWORD

CFS/ME is a challenge at any age but especially so when it occurs in children and young people. Growing up is difficult enough without having to cope with what can, in some cases, be a long and debilitating illness. The illness is a real challenge for patients and their families but also for those looking after them. The development of the guideline arose from the recognition of these difficulties and of the need to ensure that wherever children happen to live they have services available locally which are sympathetic to their particular needs.

The guideline is important for a number of other reasons. It marks the completion of a research project in collaboration with the Association of Young People with ME (AYME). This was funded by a grant from the National Lottery and has allowed a multidisciplinary group of professionals to come together with young people suffering from the condition and their families through their patient organisation. Much has been written about the management of CFS/ME yet little of the previous guidance is evidence based. The RCPCH, therefore, decided that an evidence based guideline was needed and this report represents the first such guideline fully developed by the College. All relevant papers were critically reviewed and graded according to the quality of the evidence and where evidence did not exist consensus panels were convened using a Delphi technique.

This then is an evidence based guideline developed between professionals and patients. It should empower those asked to care for such children as well as providing important guidance to children, young people and their families as to what does and does not work. In a chronic condition like this, which is of unknown aetiology and uncertain outcome, it is understandable that families will clutch at straws and take up any possibility that might make a difference. This guideline will help them to make the most of living whilst the enigmatic condition is running its course.

We are especially grateful to Linda Haines, Head of Research, for her tenacity in bringing this guideline to fruition. At various times she has been researcher, chair of the guideline development group, author, editor and at times mediator! It has been worth it. In addition we thank all of those listed on page 11 who were members of the guideline development group.

Alan Craft
President
Royal College of Paediatrics and Child Health

IMPORTANT NOTE:

This is the full, web-based version of this guideline.

The shorter print version of the document, published simultaneously, omits the appendices.
The web version is available at
http://www.rcpch.ac.uk/publications/recent_publications.html

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Use of the Guideline, Limitations and Local Implementation

This guideline has been developed according to accepted methodology which is outlined in section 1.3

It will be clear to the reader, from the small number of recommendations which are evidence based (6/45 are A-C grades), how limited the research evidence underpinning the management of children and young people with CFS/ME is. The majority of recommendations in the guideline have therefore been derived by consensus. Although this is accepted guideline methodology the limitations of this approach are discussed below.

The methodology used to develop the consensus recommendations has been described in detail. Although these recommendations achieved a consensus of the Delphi panel (>75% of the panel agreeing/ strongly agreeing) this does not necessarily mean that individual panel members or members of the Guideline Development Group not on the panel personally agree with the consensus recommendations.

Overall some of the strongest evidence found was for specific behavioural interventions. However, this was also the area that generated greatest controversy and discontent in responses to the consultation draft, particularly from patient groups. The evidence base for these interventions in children and young people is growing but at the time of writing the results of recent trials on this patient group were not available. Therefore the evidence for recommendations in these areas was extrapolated from systematic reviews concluding that cognitive behaviour therapy (CBT) and graded exercise therapy (GET) showed promising results in ambulant adults. Although extrapolating evidence from adult studies is an accepted methodology in terms of guideline development, it does mean the recommendations in these areas should be interpreted with some caution especially as there is currently little information about the similarities and/or differences between the condition in adults and children. There must also be caution in extrapolating results from studies on mild or ambulant patient to those who are more severely ill. Furthermore CBT and GET are very general therapies that have also been shown to be effective in patients with other chronic conditions. Although they may help some patients, they should not be interpreted as interventions to treat or "cure" all children and young people with CFS/ME. As the guideline points out, CFS/ME presents with a wide range of symptoms; just as individual children and young people may not have the same package of symptoms so they may also not react in the same way to the recommended interventions. It is important to accept that with the current paucity of knowledge of both the causation and management of CFS/ME, any treatment protocol should be used in collaboration with the

patient and their family and flexibly. The principle of informed consent is naturally paramount, as in all other areas of medicine.

In developing this guideline, the guideline development group were anxious that the document is seen as a practical way to improve the care of children and young people with CFS/ME with immediate impact. In several areas covered by the guideline, a decision had to be made between developing recommendations which identify a course of action in an aspirational health service or giving practical guidance for paediatricians managing children and young people with CFS/ME with the current environment where service provision may vary considerably between localities. In most cases the latter approach was taken but the guideline development group are also keen that the guideline is used locally to argue the case for improved services for children and young people with CFS/ME. The group are aware that there are serious deficiencies in services in many areas; these include a patchy availability or long waits for specialist services such as Children and Adolescent Mental Health Services (CAMHS) and pain management teams, a general shortage of multidisciplinary teams experienced in the management of children and young people with CFS/ME, and a lack of beds in suitable hospital environments. It is hoped that the establishment of the new Department of Health Clinical Network Coordinating Centres will be a driver for improved services for all children and young people with CFS/ME and form an infrastructure for future research into the condition.

1. Introduction and Guideline Methodology

1.1 Introduction

CFS/ME (Chronic Fatigue Syndrome/Myalgic Encephalopathy) is a condition, which, for a number of reasons, has caused more polarisation of views and more conflict between patients and their doctors than perhaps any other illness. To date there is no clear understanding of the aetiology of the condition and this has led not only to different approaches to its management but also to different terminologies. The World Health Organisation (WHO) ICD–10 classification uses the term Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis whereas in the recent Chief Medical Officer's (CMO) report (1), the term CFS/ME is used without an explicit definition of the abbreviations. Although CFS is the term used most consistently in the medical literature many patients' organisations prefer the term ME, although even here there has been considerable debate as to whether this should be myalgic encephalomyelitis or myalgic encephalopathy. The CMO's report acknowledged that, in relation to terminology, the important requirement is the need for patients and clinicians to agree a satisfactory term as a means of communication. With this advice in mind the guideline development group have decided that, for the purpose of this guideline, the composite term CFS/ME should be used as an abbreviation of Chronic Fatigue Syndrome/Myalgic Encephalopathy except when referring to specific studies when the term used in the paper has been adopted.

In 1996 a joint Royal Colleges report provided guidance on the management of CFS (2) and in response, the Royal College of Paediatrics and Child Health (RCPCH) published a statement on the management of CFS in children (3). This statement acknowledged that CFS/ME in children is a chronic disabling illness of uncertain and probably complex causation and highlighted the important role paediatricians have to play in supporting the child or young person and their family and in co-ordinating multidisciplinary management. This role was also endorsed in the CMO's report (1).

While it is clear that paediatricians have the same responsibilities towards patients with CFS/ME as towards those with other chronic illnesses, patient groups are continuing to hear distressing stories of young people profoundly disabled by CFS/ME who are being let down by health professionals. Although there are also examples of outstanding care being given by individual paediatricians, some patients, often those most severely affected, are having to travel substantial distances to access this.

The CMO, in his report, issued a challenge to the Royal Colleges to build on the deliberations of the Working Party. It is the College's view that the ability to recognise the

common presentation of CFS/ME in children and young people, and understand the impact chronic illnesses have on the family, should be part of the core competences of **all** paediatricians, with a smaller number of paediatricians developing a special interest in the management of CFS/ME who can take on referrals and provide a second opinion.

In order to develop the required competences paediatricians need knowledge about the condition and guidance on how to diagnose and manage CFS/ME, underpinned by the best available evidence. It is hoped that this evidence based guideline, developed as part of a RCPCH Research Division study on CFS/ME in young people funded by the Big Lottery Fund (formerly known as the Community Fund), will help to achieve this.

1.2 Guideline Aim and Scope

The aim of this guideline is to increase knowledge and understanding among paediatricians about CFS/ME in children and young people, to give paediatricians confidence in making a positive diagnosis, and to ensure that young patients with CFS/ME are managed optimally. To achieve these aims the guideline:

- Provides a background section on the epidemiology, clinical features and diagnostic criteria of CFS/ME in children and young people
- Provides evidence based recommendations for the diagnosis and management of children and young people referred to paediatricians with symptoms consistent with a diagnosis of CFS/ME
- Provides consensus-derived recommendations for areas of clinical importance with no or low quality evidence
- Highlights good practice points
- Defines the role of the paediatrician in caring for children and young people with CFS/ME as part of a multidisciplinary team
- Provides an information leaflet for patients and families

The guideline is primarily aimed at paediatricians managing children and young people with symptoms consistent with a diagnosis of CFS/ME. However it is acknowledged that for many patients the ideal model of management will be multidisciplinary and may also involve other health professionals such as the primary care team, members of the CAMHS team, physiotherapists and occupational therapists. The scope of the guideline therefore also covers the paediatrician's relationship to other professionals whose input might be necessary.

The patient population for the guideline is defined in the Guideline Definitions (page 27) but is in essence any child/young person up to the age of 18 referred to a paediatrician for assessment with debilitating fatigue.

The guideline does not cover the following clinical circumstances, patient groups or subject areas:

- The management of children and young people in primary care before referral to a paediatrician
- The long term inpatient management of patients (although the indications for inpatient admission are covered)
- The management of children and young people who may be chronically tired but who have a diagnosis of another medical or psychiatric illness which is causing the fatigue
- The management of co-morbid disorders
- Appraisal of the evidence underpinning theories of aetiology and biological/ immunological markers of CFS/ME or health economics of the condition

1.3 Guideline Methodology

The guideline has been developed by a multidisciplinary team whose members are listed on page 11. In developing the guideline the team have closely followed guidance on guideline development produced by the RCPCH Quality of Practice Committee (4).

The guideline development group met to agree the scope of the guideline. The pathway from the initial referral to a paediatrician of a patient with unexplained fatigue to the establishment of an appropriate management plan was then broken down into a series of clinical questions (Appendix 1) and a systematic literature search of the evidence underpinning these questions was conducted by the RCPCH clinical effectiveness co-ordinator. The search strategy used for the guideline was based on that used in the most recent evidence review undertaken by the Centre for Reviews and Dissemination (5) although the search was updated and restricted to papers on children and young people. Medline, Embase, Cinahl, PsychINFO and CLIP databases were searched from 1966 up until February 2004. Further details of the search strategy including MeSH terms are provided in Appendix 2.

The initial search identified 1049 potential papers which were then culled on the basis of either the abstracts or the full paper to those relevant to the guideline scope. Included papers were any relating to fatigue states (however defined and including post-viral fatigue) in children or adolescents up to 18 years of age. Excluded were papers reporting research on adults only or studies where there was no separate analysis of adult and child participants (but see below). Also excluded were annotations, letters not containing data, commentaries and editorials, primary studies on less than five individuals and studies on

participants diagnosed with fibromyalgia without a concurrent diagnosis of CFS/ME.

The literature search was supplemented by papers from the files of the guideline development team and by scanning reference lists of relevant summaries, overviews and other clinical practice guidelines.

A different approach was used in relation to the evidence for interventions for CFS/ME, where extrapolated evidence from adult studies was included. This is because there have been three recent high quality systematic reviews of interventions, a Cochrane review of RCTs of cognitive behavioural therapies in adults (6), a review by the NHS Centre for Reviews and Dissemination at York of RCTs and controlled trials of any intervention in adults and children (5), and most recently a review of the effects of treatments of CFS/ME (7). The York review has also been published as a summary (8), and combined with a similar review undertaken in the USA at around the same time (9). Given that these reviews involved a rigorous appraisal of the quality of studies it was felt unnecessary to duplicate this work. When appraising the evidence for interventions, the guideline reviewers were sent the summary of the York systematic review (8) and were not asked to reappraise the original studies cited although the original studies are referenced for completeness with an asterisk to indicate the paper was not reviewed in the development of this guideline. As the most recent search for these reviews was undertaken in March 2003, the guideline search strategy was re-run in February 2004 and any RCTs subsequently identified in either adults or children were sent to the development group for review.

The research evidence was allocated to the appropriate question and then critically appraised by at least two members of the guideline development team using the SIGN 50 (Scottish Intercollegiate Guideline Network) (10) grading hierarchy (page 21). Where the evidence was of a sufficiently good quality (2+ or above) a recommendation was derived with an evidence level attached. Recommendations based on evidence from adult studies were downgraded to reflect the extrapolation of this evidence for a child population. In the guideline text, recommendations based on good quality evidence (i.e. A, B or C) are marked with the evidence grade in a circle as shown.

The A-C recommendations were then reviewed by the RCPCH's QPC as part of the College's guideline appraisal process. The evidence was reviewed by a member of the Committee and the level of agreement with the quideline reviewers established. The QPC reviewed 7 recommendations originally graded as B & C. As a result of this review one recommendation was removed completely, one was downgraded from a B to a C, one downgraded from a B to a C with a change of wording and one where the grading

was unchanged but the wording was slightly modified. Three recommendations were unchanged. The full appraisal document can be downloaded from the RCPCH web-site (www.rcpch.ac.uk)

Where the evidence was classified as level 2- or less according to the SIGN grading hierarchy, the reviewers considered the evidence and then drafted a recommendation using this and their own clinical expertise. These draft recommendations were then agreed by a Delphi consensus methodology before being incorporated into the guideline (section 1.3.1 below). These recommendations are indicated by a 'D' in a circle alongside the recommendation as shown.

For the section on leaving the care of a paediatrician (section 3.9), no research evidence at all was identified and the reviewers drew on the experiences of a small number of patients who were accessed through the support group the Association of Young People with ME (AYME).

In addition to the recommendations, the guideline also contains a number of good practice statements. These are defined as statements which are not specific to the management of children and young people with CFS/ME and would be just as applicable to any child or young person referred to a paediatrician. These are marked in the guideline text with tick in a circle, as shown.

The evidence based guideline is preceded by a background section on the epidemiology, clinical features, diagnostic criteria, and differential diagnoses of CFS/ME in children and young people. The evidence in these areas was critically appraised but not graded and there are no clinical practice recommendations arising from this section. In the rest of the text the evidence levels are cited alongside the references for those studies graded as 2+ or above; if no evidence level is cited the grade of evidence was considered to be below this level.

1.3.1 Delphi Consensus

A modified Delphi method (11) was used to obtain a group consensual agreement for those recommendations not based on strong research evidence. In this methodology a panel of experts is asked to rank their agreement with selected statements. The Delphi panellists for the guideline were selected on the basis of their knowledge and experience of managing children and young people with CFS/ME and included both health professionals from a range of relevant disciplines, and lay members, including support group representatives and young adult patients. A full

list of the participants is provided in Appendix 3.

The Delphi panel were sent a questionnaire of the draft recommendations accompanied by background text which summarised the literature reviewed and the reviewers interpretations. The panel ranked their level of agreement with the recommendations on a Likert scale (1-9) with 1 as strongly disagree, 5 equipoise and 9 strongly agree. They were also asked to provide justification for any major disagreement. Panellists were given the option not to score recommendations outside their area of expertise. A consensus was pre-defined as 75% of the panellists ranking the recommendation at 7 or above i.e. the lower interquartile range was greater than or equal to a rank of 7.

Recommendations not reaching consensus after the first round were modified on the basis of the comments received and incorporated into a second questionnaire. These were supplemented with new recommendations developed as a result of panellists comments and recommendations reaching consensus in the first round but which had been reworded to improve clarity. Only the panellists who had returned a first round questionnaire were included in the second round. The second round Delphi generated 4 new recommendations which panellists were asked to score separately in a small third round.

93% (41/ 44) of panellists participated in the first round, 90% (37/41) in the second round and 73% (27/37) in the third round. Over the 3 rounds a total of 48 recommendations were considered by the panel, 10 of which did not achieve consensus. The level of consensus, comments from the panel and clinical importance were used to decide what to do with these recommendations. As a result, two recommendations in relation to routine tests and investigations were included as optional rather than for all patients, three were excluded completely, and four recommendations on other areas were removed but the main reasons for lack of consensus discussed in the text. One recommendation remains in the guideline marked as no consensus (‘NC’ in a circle as shown).

A draft of the guideline was sent to a large number of organisations and individuals who had expressed an interest. A list of organsiations consulted and those commenting on the guideline is provided in Appendix 7. The comments made were considered by the guideline development group and incorporated where appropriate.

1.3.2 Grades of Evidence/Derivation of Recommendations

Table 1: SIGN Levels of Evidence/Derivation of Grades of Recommendation

Levels of evidence

1++	High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1-	Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case-control or cohort or studiesHigh 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
2+	Well conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendation used in this guideline

A	At least one meta analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
D	Recommendations agreed by Delphi consensus process based on evidence levels 2-, 3 or 4
NC	Recommendation not agreed by a Delphi consensus process

Guideline Revision

The guideline will be updated within three years of the publication date unless new national evidence based guidelines in this area have been published in the intervening period.

Conflicts of Interest

Members of the guideline development group were asked to complete a conflict of interest form. A conflict on interest was defined very broadly as accepting in the last 5 years funds from an organisation which would gain or lose financially from the conclusions of the guideline. None were declared. Declarations considered not to be a conflict of interest include acting as an expert witness on the guideline topic, a fee for writing an article on the topic and accepting a paid honorarium as a clinical advisor to a patient support group. In addition ten members of the guideline development team were authors of papers included in the evidence review although no reviewer appraised their own papers.

2. Background to CFS/ME in Children and Young People

2.1 Epidemiology

2.1.1 Incidence/Prevalence

There are no published figures on the incidence of CFS/ME in children and young people but several studies have estimated the point or period prevalence. These estimates vary widely because of differing case definitions and ascertainment methods although when studies of similar design are compared the estimates are similar.

Two non-UK studies identified cases by local physician surveillance, confirming diagnosis with follow-up interviews or questionnaires, and should provide the most robust estimates, although both are based on small numbers. Prevalence estimates were 5.5/100,000 (CI 0.1-30.5) in under 10's and 48/100,000 (CI 22-91) in 10-19 year olds in Australia (12) and 2.7/100,000 in 12-17 year olds in the US although this study used a stricter case definition and only half the eligible physicians participated (13). A UK general practitioner survey of cases of medically unexplained disabling fatigue for more than 3 months (14), identified 410 cases, 51% of whom had CFS/ME, severe or chronic fatigue as a diagnosis, a prevalence of 62/100,000 (CI 56-69).

Population studies have given higher prevalence estimates probably because data were based on self- or parental- report, and used broader case definitions (13;15-17). Three studies (two USA and one UK) report 'lifetime' (before 18 years) prevalence rates of CFS-like symptoms of approximately 2% (15;18;19). Two English studies of school absences for CFS, showed prevalence rates of around 70/100,000 (20;21), while a USA study provided a slightly lower rate of 52.9/100,000 (13). Most studies focus on the prevalence of the condition in adolescence; those reporting prevalence in younger children show it to be markedly lower (12;13;15).

Few studies report age of onset; where they do this reflects the study population. For example in the Bell study (18) of cases 18 months-15 years mean age of onset was 10 years 6 months (median 11 years). Farmer, (19) in a study of children and young people from 8-17 years reported a mean age of onset of about 12 years. Studies on older children show a higher mean age of onset of 14.3 years (range 10.1-16.9 yrs) (22) and 13 years (range secondary school age) (20).

2.1.2 Gender, Social Class, Ethnicity and Geographical Variation

Two UK studies reported no significant gender difference (17;21) although there were very few cases, whereas four report a female excess of two thirds to a third (14;19;20;23), as do half the US studies (13;18) and the Australian study (12). The evidence for a gender difference in CFS/ME is therefore inconclusive. Where studies have reported a difference, girls outnumber boys 3:1.

There is no evidence from epidemiological studies, for varying prevalence rates in different patient groups, largely because the small number of cases precludes estimating variation by socio-economic class and ethnicity. Data on social class and ethnicity of those attending specialist clinics, particularly in the US, are likely to be confounded by social class differences in referral patterns and lack of a control group. Bell (18) showed no difference in the socioeconomic profile of cases compared with their age-, sex- and school district-matched controls.

There have been two reports of clusters of cases of CFS/ME in children and young people (18;20), although neither study provided an aetiological explanation for the clustering and both could have been explained by random variation. Other potential explanations for apparent clustering of cases include variations in case definition and/ or diagnostic criteria and reporting bias.

2.1.3 Prognosis

There are no population-based follow-up studies to provide evidence of prognosis. Information on prognosis and prognostic factors comes from longitudinal follow-up of case series, where it is difficult to determine the representative nature of the cases and the effect of responder bias. Most studies involve few cases, with a variable duration of follow-up both within and between studies, making correlation with care/treatment not possible. Studies with extended follow-up show 60-80% partial or complete recovery with an average duration of illness of 37.5-49 months (24-26) with a small group of about 20% of cases remaining incapacitated. Smaller studies, with variable or shorter follow-up times, also identified groups of young people remaining seriously impaired, ranging from 5% - 6% of patients (27;28), through 19% - 22% (23;29) to 40% - 47% (30;31). A systematic review (32) reported that 66% of young people made a full recovery, but that an estimated 5% had persistent debilitating illness. Hinds (33) found those under 20 years had a significantly better recovery rate (of 40%) than older people. No studies have reported any deaths from the condition.

2.2 Clinical features of CFS/ME

Clinical features of CFS/ME in children and young people have been described in a range of settings for patients presenting with varying severity, although not all studies have been restricted to patients with a diagnosis of CFS/ME. However there are a number of common features and symptoms reported in the literature which are summarised below.

2.2.1 Onset

Both gradual and sudden (i.e. new and definite) illness onset have been noted in children and young people, although new and definite are variably defined in the studies. In some of the studies reviewed, the majority of patients had a sudden illness onset (22;27;28;34), whereas in more recent studies a gradual illness onset was more common (23;26;35;36).

Some patients have reported a preceding acute illness, often of an infectious nature, such as a specific influenza like illness, streptococcal pharyngitis, acute EBV infection, gastroenteritis, glandular fever and sinusitis (22;28;31;34-37). However it should be noted that in some studies preceding illness information was patient-reported without corroborating laboratory investigations (35;37) and most studies lacked a comparative control group (28;34;37).

2.2.2 Clinical Symptoms

Debilitating fatigue (both physical and mental) is the most commonly reported symptom, (15;18;23;27;31;34;36;38;39), typically exacerbated by exercise or activity (31;40). Fluctuations in intensity of fatigue have been reported (28). In some patients fatigue is constant, in others intermittent over a period of weeks to months with brief episodes of remission (31;34).

One small study attempted to characterise the nature of the fatigue associated with CFS/ME compared with that associated with other chronic illness. This found that children and young people with CFS/ME reported higher levels of both physical and mental fatigue compared to patients with cystic fibrosis or controls (39).

Other frequently reported symptoms are 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 (18;22;23;27;28;34;37;39;38;41). Symptoms

reported less often include 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 (18;22;26-28;34;36;39;38).

There is clinical and research evidence of sleep disturbance in children and young people with CFS/ME with phase delay and interruptions being the commonest problems (42). Sleep disturbances also include non-refreshing sleep (18;28;31;43), excessive sleep (22;28;36;37), difficulty falling asleep (27;37;39), waking frequently during the night (27;37), difficulty waking in the morning (27), daytime drowsiness (39) and daytime napping (27;28).

One study suggested sex and age differences in reported symptoms, although symptoms were parent-reported (15). Eye pain or light sensitivity was more common in children under 12 years than in older adolescents, girls were more likely to report headaches, sore throat and lymph node pain and boys were more likely to suffer from school problems, impairment in memory or concentration and post-exertional malaise.

The number of symptoms reported seems to vary with stage and severity of illness; 94 primary care patients (34), reported a mean of 3 symptoms at first presentation whereas patients attending a tertiary clinic who had been ill for at least 6 months reported an average 8.3 symptoms (39).

2.2.3 Psychological Symptoms

Some children and young people with CFS/ME have symptoms and/or a diagnosis of depression and anxiety (24;44-48). Other psychological conditions and psychological co-morbidities reported in some children and young people with CFS/ME include school phobia or poor attendance (44;45;48;49) somatisation (45;47;49) social withdrawal (45;47;48;50) and personality features such as conscientiousness, vulnerability, a sense of worthlessness and emotional lability (24).

2.3 Diagnostic Criteria for CFS/ME

As there are no distinct markers for CFS/ME, its diagnosis has generated much discussion and debate. Diagnostic criteria have been defined for adults, although in the absence of clinical markers these have been based on expert opinion and their development driven by the need for consistent definitions for research rather than for clinical practice. These diagnostic research criteria include criteria from the Communicable Disease Centre (CDC)

USA (51) and the Oxford criteria (52). Appendix 4 summarises the published diagnostic criteria for CFS/ME . Although these criteria differ slightly, the principle features are unexplained fatigue as a predominant symptom with significant impairment of function and participation, the exclusion of other underlying causative disorders including psychological/psychiatric causes, a definite illness onset, a certain number of diverse non-specific symptoms and a minimum of 6 months fatigue duration. The term *idiopathic chronic fatigue* has been used to describe a condition where fatigue significantly impairs participation in normal activities, there is no clear clinical cause and fatigue has been present for 2 or 3 months or more with or without other non-specific symptoms, although it fails to meet the criteria for chronic fatigue (51). A distinction has also been made in adults between CFS/ME and post-infectious fatigue syndrome as a sub-type of CFS/ME, which requires definite evidence of infection at onset corroborated by laboratory evidence (52). A recent series of workshops has addressed some of the inconsistencies in these diagnostic criteria and their application (53).

There are currently no diagnostic criteria for CFS/ME in children and young people. Several authors have considered the applicability of the adult criteria to children and young people (2;54), generally concluding that six months of fatigue is too long given the potential for serious educational and social disruption. Recommended fatigue durations of 8 weeks (55) and 3 months (2) have been proposed.

2.3.1 Guideline Definitions

Given the lack of research evidence, particularly from epidemiological studies, to inform the development of diagnostic criteria for CFS/ME in children and young people, the development group have derived some operational definitions to define the patient population for the purpose of this guideline.

In formulating the definitions, the group considered that the requirement for a specific illness/fatigue duration or the presence of a pre-defined number of symptoms before diagnosis is not appropriate in children and young people with debilitating symptoms. Diagnostic delays can cause anxiety in the patient and family and delay the initiation of an appropriate management programme. Furthermore, in practice, many children and young people will have been unwell for a significant period before being referred to a paediatrician from primary care. It was also considered that a diagnosis of CFS/ME should be based on the impact of the condition on the patient.

Given these considerations, it was felt that when referred a patient with debilitating fatigue for assessment, an appropriate initial opinion is one of “generalised fatigue”.

The process of assessing the patient for differential causes of the fatigue should differentiate between this initial general fatigue, which may be caused by a number of conditions, and **CFS/ME** which will continue to cause functional impairment after alternative differential diagnosis have been excluded.

Generalised Fatigue

This is fatigue causing disruption of daily life. The child or young person tires unduly easily, compared with his or her pre-morbid state and may be unable to take part fully in school activity. Generalised fatigue may be caused by conditions such as anaemia and hypothyroidism or viral infection or may be going on to develop into CFS/ME.

An experienced paediatrician who has taken a careful history and undertaken a thorough physical examination can give a provisional diagnosis of generalised fatigue while awaiting the results of laboratory investigations, which may or may not identify an underlying cause for the fatigue. This opinion does not require a specific illness duration but requires that the fatigue is causing significant functional impairment**.**

CFS/ME

CFS/ME is defined as a 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 (page 25) such as difficulty in concentrating and disturbed sleep patterns and is classically exacerbated by effort (both mental and physical).

The CFS/ME may or may not be triggered by a virus but a diagnosis of post-viral fatigue as opposed to CFS/ME requires a history of an infection at onset/presentation corroborated by laboratory evidence of a viral infection. The possibility that the CFS/ ME was triggered by an unspecified viral infection not be picked up by laboratory investigations can be acknowledged in discussions with patients and families but it should be emphasised that viral infection does not have to be the trigger or the cause.

A positive diagnosis of CFS/ME should be made as soon as it becomes clear that, having excluded all other causes for the symptoms, the symptoms are continuing to cause significant functional impairment. However, the diagnosis should be seriously considered in <u>any</u> child or young person who has had generalised fatigue causing significant impairment for 6/12 months for which no alternative explanation has been found, even if tests for some differential diagnoses are still awaited.

Paediatricians should therefore be prepared to make a positive diagnosis of CFS/ME when a child or young person has characteristic symptoms supported by normal results and when the symptoms are causing significant functional impairment. This diagnosis does not depend on a specific time frame and a positive diagnosis of CFS/ ME is not a prerequisite for the initiation of an appropriate management plan.

2.3.2 Differential Diagnoses and Co-morbidities

Profound fatigue and the other symptoms associated with CFS/ME can also be symptoms of other medical, including psychiatric, conditions. The steps for making a diagnosis for CFS/ME as outlined in section 3.1 (page 32) should be sufficient to exclude the main differential diagnoses and an experienced practitioner will look for pointers to other diseases which will have characteristic patterns of history and examination. If the patient does not follow the expected illness course or develops new findings on examination, then these diagnoses and the tests needed to confirm them should be considered. Any of these conditions could co-exist with CFS/ME.

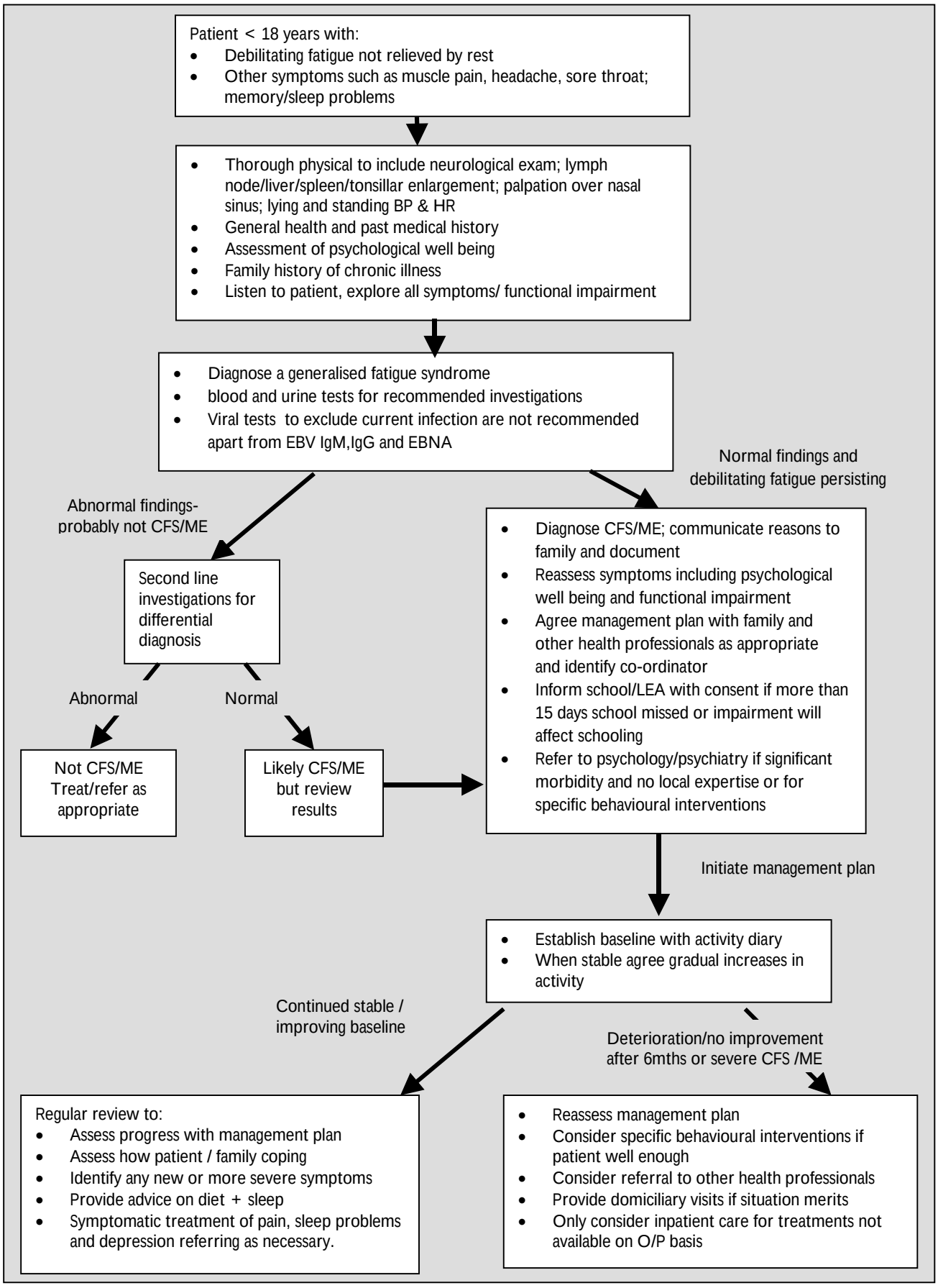
The table below identifies the main differential diagnoses and the tests needed to confirm or refute these. It should be noted that the list is presented in alphabetical order and is not exhaustive nor a checklist of investigations but is provided for information. Routine tests and investigations to aid making a diagnosis of CFS/ME are found in section 3.1.3.

Category	**Examples**	**Further tests**
Anaemia	Haematinic deficiency Leukaemia Autoimmune	Haematinics Bone marrow Direct Coombs Test
Auto-immune disease	Systemic Lupus Erythematosus Dermatomyositis Vasculitis Hepatitis	ANA Cardiac enzymes Muscle biopsy ASOT Test
Chronic Infection	Chronic tonsillitis Tuberculosis Hepatitis Brucellosis Lyme Disease Toxoplasmosis Cytomegalovirus Epstein Barr Virus	Throat swab, ASOT Chest X Ray, Mantoux Specific tests
Drug induced	Substance abuse Therapeutic drugs e.g. anti-epileptics, beta blockers	Toxicology Drug levels, Trial of withdrawal of medication.

Category	Examples	Further tests
Endocrine disorder	Diabetes mellitus Hypothyroidism Addison's	Covered in routine tests Cortisols a.m. & p.m. & Synacthen test
Gastro-Intestinal Disease	Coeliac Disease Inflammatory bowel disease	Coeliac Serology +/- Jejunal biopsy Endoscopy
Immunodeficiency (Symptoms preceding onset of fatigue)	Hypogammaglobulinaemia	Igs
Miscellaneous	Connective tissue disorder (e.g. Ehlers Danlos syndrome) Fibromyalgia Postural orthostatic tachycardia syndrome	Clinical assessment including Beighton score for joint hypermobility (EDS) or tender points score (FM) Lying & Standing BP and pulse
Neurological	Multiple Sclerosis Wilson's	MRI, VEP, CSF (Igs), copper & caeruloplasmin, slit lamp, liver biopsy
Neuromuscular disorder	Myasthenia Muscular dystrophy Glycogen Storage Disease	EMG, Ach Abs, Tensilon test, CK, Muscle biopsy
Occult Malignancy	Lymphoma Neuroblastoma Brain Tumour	Biopsies VMA MRI Brain
Psychiatric/psychological	Anxiety disorders bipolar disorder, major depressive disorder, school refusal/school phobia, eating disorders, Fabricated or induced illness	Mental state exam and screening questionnaire followed by psychiatric opinion
Sleep Disorder	Obstructive sleep apnoea Narcolepsy	Sleep study MSLT and polysomnography

3. Evidence Based Guidelines

Clinical Algorithm for Management of CFS/ME



3.1 Making a Diagnosis

CFS/ME in children and young people is diagnosed after taking a careful clinical and family history, making a thorough physical examination and excluding differential diagnoses by undertaking a minimum number of tests and investigations (page 35). This may take considerably longer than an average outpatient appointment and consideration should be given to providing a 'double slot' in the clinic for patients attending for the first time.

These steps will also identify any existing co-morbidities or underlying medical conditions. All co-morbidities require identification and management, whether they are differential diagnoses, causes, consequences or in a complex relationship with generalised fatigue or CFS/ME.

3.1.1 Taking a Clinical History

A thorough medical history is important in the initial assessment of children and young people presenting with symptoms of CFS/ME. The components of the medical history are as follows:

Identifying symptoms
The symptoms associated with CFS/ME in children and young people have already been described (page 25). As the condition can present with a wide range of symptoms across many systems it is important to identify them all (2) and gauge their severity as well as their onset and course. Exploring all symptoms reported may help with making a differential diagnosis and aid identification of conditions with overlapping symptoms such as fibromyalgia, irritable bowel syndrome and Ehlers Danlos Syndrome (EDS) (56).

In relation to the fatigue, it is important to explore whether it is physical and/or mental and establish if it is related temporally to exertion (57) and how it impacts on the patient's day-to-day activities. The use of visual analogue scales, validated questionnaires (40) or fatigue scores (58) may be helpful but are not essential before a diagnosis is made.

It is important to acknowledge the distress and disability associated with the symptoms. Listening carefully to a description of the symptoms aids the building of a therapeutic alliance, and gives the doctor an opportunity to understand the impact of the illness on the child or young person and their family. The child or young person who feels their condition is not understood or believed by their doctor can be left feeling very isolated

and unsupported and is unlikely to enter into a therapeutic alliance (59-65).

When taking a clinical history in children and young people 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.

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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.

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Other factors

As well as establishing the clinical symptoms and illness onset, the medical history should also explore the following:

- The patient's pre-morbid and general health
- Medication
- Past medical history, including experience of illness and psychiatric history and any history of joint dislocation
- Careful attention should be given to psychological state and enquiry made about emotional symptoms
- Any treatment to date, including contact with health practitioners both orthodox and complementary and how positive or negative that experience was for the patient and their family. It is also important to identify if there has been any previous adverse experience of doctors (2;58;62) as exploring previous experiences of "illness disconfirmation" may help to secure trust (66;67)
- The possibility of substance abuse
- A history of recent foreign travel

Additional factors suggested by the evidence review are:

- Diet and sleep patterns (58)
- How the patient is coping with the illness such as rest, pacing or graded exercise (62;66;68)
- The impact of condition (e.g. time spent in activities, changes in school grades, time off school) (38)
- Any significant social, family or academic stress or bullying at school (60)

Although paediatricians should be alert to the potential emotional dimensions of the illness, full psychiatric and psychological assessments are considered to be second-

line investigations and do not form part of the routine investigations recommended for all patients (section 3.1.3) unless there are immediate concerns about their psychological well being.

Initial Family History

An initial family history should include an enquiry into chronic illness, and in particular CFS/ME, fibromyalgia, EDS or similar conditions in any family member (2;68;60). The paediatrician also needs to be aware of the emotional contributors to any illness (not just CFS/ME), as well as the relevance of family dynamics, and to think about these, whilst not necessarily asking about them initially as exploring family dynamics too early by asking specific questions may be considered intrusive. A detailed exploration of family dynamics (69) should not be undertaken at this point and it is unhelpful to begin family psychiatric history taking until physical concerns have been discussed and appropriate test results are available (67), unless there are immediate concerns about psychotic illness or anorexia nervosa.

An initial family history should include an enquiry into chronic illness, and in particular CFS/ME or similar conditions in any family member.

When initially assessing a patient, the paediatrician should be alert to the potential emotional dimensions of the illness including family dynamics, which should be sensitively explored. However, unless there are immediate concerns regarding the psychological well being of the patient, a detailed exploration of family dynamics or the taking of a full psychiatric/psychological history is not necessary at this point.

It is also important to assess and acknowledge the impact of the illness on family functioning and adaptation, as well as the level of anxiety and the degree and nature of parental concerns about the child's/young person's symptoms (66;67).

The clinician should acknowledge the distress caused to the child/young person and the parent by the symptoms being suffered.

3.1.2 Physical Examination

A thorough physical examination of children and young people with symptoms of CFS/ME should be undertaken at the first consultation. This is an essential first step to excluding other underlying illnesses, and will also reassure patients and families that the illness is being taken seriously.

Paediatricians should undertake a thorough physical examination of all children and young people presenting with symptoms of profound fatigue at the earliest opportunity. D

The literature has largely focused on the physical examination of mild or moderately affected children and young people, in whom the physical examination is often normal with the exception of, on occasion, pharyngitis and tender lymphadenopathy (68;70). No studies were found which reported the findings of a physical examination in severely affected patients.

Particular components of the examination include:

- **General physical examination including height, weight and head circumference**
- **A neurological examination (including ophthalmic fundal examination, gait and signs of muscle wasting)**
- **Lymph node/liver/spleen/tonsillar enlargement. Any abnormal clinical signs such as marked cervical lymphadenopathy need full investigation (28;40;61)** D
- **Palpation over frontal, ethnoid and maxillary sinuses (to identify chronic sinusitis)**
- **Lying and standing BP and HR (for evidence of Postural Orthostatic Tachycardia Syndrome (POTS) or postural hypotension) (56;71), ((72;73) Level 2+)**

Additional non-invasive tests which may be undertaken in the initial physical examination and may help with making a differential diagnosis or identifying groups of symptoms needing symptomatic treatment include:

- Tenderness score at pressure points (FMS inventory ((56;74;75) Level 2+)) to help with differential diagnosis of fibromyalgia, which has overlapping symptoms with CFS/ME ((75) Level 2+), (76))
- Assessment of joint mobility and any cutaneous features (scarring or hyperextensibility) to help make a differential diagnosis of EDS (56)

3.1.3 Tests and Investigations

Many patients and their families are understandably concerned that the symptoms are a result of a potentially serious underlying illness or disease. However, investigations must be kept to the minimum needed to rule out any plausible alternative diagnosis.

Ideally all tests should be carried out over a short period of time, not protracted over months or years.

Many of the recommended tests will have already been carried out in primary care. The paediatrician should check which tests have already been done and ask for the results. It is not normally necessary to repeat these. It may be helpful to explain to the family the value of drawing a line under investigations and moving on to managing the condition.

Tests and investigations in patients with symptoms consistent with a diagnosis of CFS/ ME fall into three categories:

Routine Investigations - to be undertaken in all children and young people presenting with symptoms consistent with a possible diagnosis of CFS/ME unless there is a clear reason not to (e.g. if the child/young person or parents/guardian refused early on but agreed to continue medical follow-up).

Second Line Investigations - only to be undertaken when symptoms and or signs and or results of previous investigations suggested a particular differential diagnosis or set of diagnoses, e.g. ANA in presence of joint pain and swelling or a raised ESR.

Other Investigations - occasionally in very specific circumstances, other tests may be indicated. However, if a test is done to exclude a diagnosis (rather than as a clinically indicated investigation e.g. as part of the differential diagnosis), it should be borne in mind that while a negative result may be perceived as assisting in the management of the patient, the probability of not having the condition in the presence of a positive test is increased in rare conditions, and may create further problems.

Routine Investigations

Routine investigations are those which should be carried out on all patients. The purpose of the investigations should be explained to the patient and the family. These investigations should be completed quickly to facilitate making a diagnosis, although a change in symptoms and signs will require a clinical review and possibly reinvestigation.

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Routine tests on all patients should include a blood test and a urine test for the following investigations:

- **FBC & film to exclude anaemia, iron deficiency and leukaemia**
- **ESR (or viscosity) (unlikely to be elevated in CFS/ME (77;78)) and CRP (c-reactive protein) (a high level could suggest autoimmune disease, e.g.**

Systemic Lupus Erythematosus, or chronic infection, e.g. Tuberculosis)

- **Blood glucose for diabetes mellitus ((22) level 2+)**
- **Blood biochemistry (Na, K, creatinine) to look for renal impairment or endocrine abnormality (e.g. Addison's)**
- **CK 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 (22) level 2+); tested for blood leukocytes and nitrites to exclude urinary tract infection**

Viral titres

There is evidence from cohort and case controlled studies that some children and young people with CFS/ME have evidence of viral infection, e.g. EBV (79-83), ((22;30) level 2+). There a number of serological tests for EBV. These need to distinguish primary, reactivated or past infection, which is not always straightforward and expert (virological) advice may be required. Antibody tests for EBV viral capsid antigen (VCA), IgM, IgG and EBNA tests were used to identify current or recent EBV infection in a group of patients referred for assessment of fatigue ((22) level 2+), (2;84)). Confirmation of recent/current EBV infection may be helpful to the family as recovery in EBV associated CFS/ME may be quicker than with other forms of CFS/ME (22). A false positive can be obtained if the patient is positive for Rheumatoid factor (which can be checked by the laboratory). Unless there are specific clinical features such as persistent lymphadenopathy or biochemical hepatitis, other viral serological tests are not indicated as they are unlikely to be helpful in clinical management and interpretation of the results may be difficult.

Viral titres or other viral tests to impute or exclude current viral infection are not recommended apart from EBV IgM, IgG and EBNA. **C**

Second Line Investigations

The following tests should not be done as *routine* and should only be undertaken when symptoms and or signs and or results of previous investigations suggested a particular differential diagnosis or set of diagnoses. The list of potential investigations is exhaustive and the table on page 29 gives some indication of the wide range of possible tests. A few important examples are:

- **Blood tests** for antinuclear antibody, immunoglobulins, coeliac serology, Lyme disease, toxoplasma, brucellosis antibodies, copper & caeruloplasmin, cortisols

& Synacthen test, B12, folate, ferritin, carbon monoxide (blood carboxyhaemoglobin)

- **Urinalysis:** organic acids (glc/ms), amino acids (by 2D lc), toxicology screen
- **Imaging:** Chest X-Ray
- **Formal educational & psychometric assessment**
- **Formal psychiatric assessment:** in order to establish a psychiatric differential diagnosis

Assessment of other immunological parameters such as lymphocyte markers may form part of research protocols but are very unlikely to contribute to routine clinical management.

Other Investigations

These may be used in rare situations for a disease that is not clinically indicated but where the possibility of that disease has become an anxious concern for the child/ young person or family and explanation has failed to reassure. In this situation it is only helpful to do tests with a high specificity so that everyone will be reassured by a negative result. These include HIV serology and MRI scan of the brain (to exclude tumour, multiple sclerosis).

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.

3.1.4 Assessment of Psychological Well-being

Assessment of psychological well-being is an important part of the diagnostic process in children and young people with CFS/ME, as it is necessary to exclude major psychiatric disorders, which feature symptoms similar to CFS/ME (page 26). It is also important to identify psychological co-morbidity accompanying CFS/ME which can impact the course of the illness or the effectiveness of any treatments, and may be treatable in its own right. Both or either of these explanations might apply in individual cases. The presence of psychological co-morbidities in a patient does not necessarily indicate a psychological aetiology for the condition. Clinicians should reassure patients and their families about this, explaining that it is important to establish if any psychological co-morbidities exist just as medical co-morbidities would be identified and treated and emphasising that psychological co-morbidities often accompany other chronic illnesses in children and young people.

Symptoms of depression and anxiety can be associated with a diagnosis of CFS/ME in children and young people (44;45;47), ((46;85;86) level 2+) as are categorical diagnoses of depression or anxiety or both ((24;48;85) level 2+). Depression might be an understandable secondary consequence to the debilitation experienced by children and young people with CFS/ME ((50) level 2++). However depressive symptoms in patients with CFS/ME have a different pattern to those in patients with major depressive disorder (45;47), ((24; 49) level 2+), ((50) level 2++). Although symptoms of and categorical diagnoses of depression and anxiety can be associated with a diagnosis of CFS/ME in children and young people it is not yet clear whether they are cause, consequence or due to symptoms shared by the differential diagnoses.

Other psychological conditions and psychological co-morbidities reported to be associated with CFS/ME include school phobia or poor attendance (44;45), ((48;49;86) level 2+), somatisation (45;47), ((49;86) level 2+), social withdrawal (45;47), ((48) level 2+), ((52) level 2++), and personality features such as conscientiousness, vulnerability, sensitivity, eccentricity, anxiousness, dependence, rigidity, a sense of worthlessness and emotional lability ((24;49;85) level 2+). It is important that paediatricians managing a child or young person with CFS/ME should have sufficient awareness of the possible psychological co-morbidities to be able to identify their existence and refer as appropriate.

Careful attention to psychological wellbeing is an important part of the assessment and management of CFS/ME in children and young people.

The results of two small case control studies have suggested that both children and young people with CFS/ME and their parents may have higher expectations of activity levels and be less tolerant of fatigue symptoms compared to controls (88), ((46) level 2+). Parents of children and young people with CFS/ME may have less belief in psychological contributing factors than matched controls (44;87), ((86) level 2+) and more belief in constitutional or environmental factors ((86) level 2+). Children and young people with CFS/ME may be more likely to use an emotional language that emphasises physical symptoms, than an emotional language that emphasises internal states or feelings (44). Professionals should be aware that parents and patients may use language differently and allow for this during discussions about diagnosis, causation and management.

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.

Some families may wish to make use of family therapy, if available locally. Individual support for the child or young person may be available from a variety of sources including physiotherapist, occupational therapist, school counsellor or local CAMHS paediatric liaison service.

3.2 Communicating a Diagnosis

There have been no studies investigating the impact of a positive diagnosis of CFS/ME on patients or families. However by the time the patient has been referred to a paediatrician they are likely to have been unwell and worried for some time. It is therefore important to explain to the patient and family that CFS/ME is a *possible* diagnosis as soon as possible, while emphasising that before making this diagnosis other possibilities need to be excluded.

It should be explained that there are no definitive tests to diagnose CFS/ME and that the diagnosis is made as a result of negative findings. A full explanation of what investigations are being completed to exclude other conditions will help the child/young person and family to have confidence in any final diagnosis.

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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.

Once a diagnosis has been made (page 28), this should be communicated to the patient as soon as possible. Giving patients and their families an explanation for their symptoms will reassure them that a diagnosis of other severe illnesses such as malignancies has been excluded, and will allow them to receive advice and information so that appropriate management of the illness can begin.

When a diagnosis of CFS/ME is made, the reasons for the diagnosis should be carefully explained to the patient and their family and documented in the clinical notes. Recording the criteria on which the diagnosis has been based is not only good clinical practice but will also help to further the understanding of the condition in children and young people.

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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.

Given the lack of definite markers for CFS/ME and the absence of diagnostic criteria in children and young people, there will always be room for clinical uncertainty around a diagnosis of CFS/ME in children and young people. Referral to an experienced colleague should be considered where such uncertainty exists or where patients or their families request it.

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.

Once a diagnosis of CFS/ME has been made, the illness attributions and health attitudes of both patient and parents should be sensitively explored and carefully listened to (40;66;67;87). Patients with CFS/ME and their families can have strong beliefs about the illness, often shaped by their own experience, as well as by their encounters with the medical community, as indeed can health professionals. Early acknowledgement of the patients' and families' viewpoint is essential in establishing rapport and facilitates shared decision making between the paediatrician and the family as to the appropriate management strategy. However, although a willingness to listen is crucial, it is important for the paediatrician not to endorse possibly unfounded theories of aetiology (38). It is important for the paediatrician both to admit honestly the lack of current knowledge but also not to endorse potentially harmful illness beliefs held by the family. For example, families should be reassured that a gentle degree of activity which is close to current baseline levels need not be harmful (see page 44 for determining baseline levels).

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 whilst not endorsing possibly unfounded theories of aetiology.

3.2.1 Discussing Prognosis

When patients receive a diagnosis of CFS/ME one of the first questions is likely to be 'how long will I be ill for?'. When answering this question it is important to be both optimistic and realistic (2;59;60;62;64;88-90).

The research evidence in relation to the prognosis of CFS/ME is limited but is discussed in the epidemiology section (page 23). When discussing prognosis, the clinician should explain that CFS/ME is an extremely unpredictable condition and that patients vary with respect to severity and duration of illness although there is some evidence that young people are more likely to make a full recovery than older adults. Some young

people recover after a period of months, whereas others have been known to take years, but the clinician should explain that this does not mean the young person is going to feel this ill for all that time and that it is hoped that over time a slow gradual improvement will be seen. The patient leaflet enclosed with this guideline may help with these discussions.

3.3 Management of CFS/ME

When a positive diagnosis of CFS/ME is given, the paediatrician should work with the child/young person and family to develop a comprehensive management plan. The health professionals involved in the management will largely depend on the local situation. Some areas will set up multidisciplinary teams which allow health professionals to be involved quickly and easily as and when they are required, whereas other areas may rely on one clinician (e.g. general practitioner or paediatrician) who will refer the patient on to others where necessary. The aim, in either situation, is to enable patients with the help of their family and the guidance of health professionals to manage their own rehabilitation with the goal of a return to health and full participation as soon as possible. A lead health professional should be identified to support the family in the implementation of the management plan (management plan coordinator). The specialty of this individual will depend on the local circumstances which will include availability, skills and experience of the team members.

The clinician should explain to the patient and family the difference between precipitating factors and maintaining factors, and reassure the child/young person and their family that they will not come to harm if the cause, which is unknown, is not treated.

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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 management plan coordinator.

As a minimum for all children and young people 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**

In some patients (according to the level of functional impairment, local circumstances and patient/family preferences) the management plan could additionally include:

- Multidisciplinary assessment for referral for a behavioural intervention (section 3.5.1)
- Referral to other health professionals (section 3.6)
- Liaison with education if more than 15 days of school missed (section 3.8.2)

These components are covered in subsequent sections of the guideline.

3.3.1 Establishing a Relationship with the Family

Developing a rapport with the family and establishing a cooperative and empathetic relationship using a sensitive and flexible approach is essential to the success of the management plan. Treatment should be collaborative, involving parents and family, who are in a powerful position with respect to the treatment of their child/young person and can effectively withdraw the child or young person from treatment. Making it clear to the patient and family that the clinician believes the symptoms and in the reality of the illness will help in establishing a therapeutic relationship. In a therapeutic relationship, the child/young person and or parent will feel they have someone to turn to if a problem arises. This means that the paediatrician is more likely to find out when a problem arises, rather than months later (59;60;62;63;65;88).

Early engagement of the family, as well as maintaining a therapeutic alliance throughout the illness is crucial for successful implementation of the management plan.

Avoiding a Breakdown in Communication

With a condition as complex as CFS/ME there is clearly potential for a breakdown of communication between doctors, children and young people with CFS/ME and their families. In these situations patients and their parents can feel that they are not being listened to or believed, or are being asked to do more than is manageable. Careful use of language might help to prevent these situations occurring; for example 'How about school?' might sound like a question to the paediatrician, but may be interpreted as an instruction by the patient. Other approaches might be to ask the patient what activity they think is manageable, rather than telling the patient what is manageable.

However, as with any condition, there may be situations in which a therapeutic relationship cannot be established or becomes irretrievably damaged for a number of reasons. If this does occur then the paediatrician has a responsibility to refer the family to a paediatric colleague who has the skills and expertise to support the family in a comprehensive management plan (section 3.7.3).

It is not acceptable that the individual beliefs of a paediatrician about the nature of CFS/ME contribute to a breakdown in communication.

3.3.2 Managing Activity

Establishing a baseline

When a diagnosis of CFS/ME has been made, a baseline of activity that the child/young person can manage even on a bad day should be established. Establishing a baseline can take several weeks, although an interim management plan can be implemented within this timeframe.

An activity diary can help with establishing the baseline and will enable the child/young person, family and clinical team to be aware of the severity of the condition and to plan realistically ((46) level 2+). Diaries can be useful in the assessment phase to evaluate sleep wake cycles, nutritional intake, activity, school attendance, social contact and emotions. This can also be useful as a baseline to monitor outcome.

There was no consensus over what should be recorded in an activity diary and how often. It was felt that any recommendation in this area would be too proscriptive; advocating daily use may impose an unnecessary burden on patients and families. There was also concern that using the diary to record symptoms could result in a negative focus on symptoms rather than on activities that can be managed, although an alternative view is that a record of symptoms such as pain could help patients link cause with effect. Therefore families, patients and the multidisciplinary team should agree the level of detail recorded in the diary to ensure that completing it does not become a burden. Ideally, the patient should take responsibility for making entries into the activity diary with the family contributing where necessary.

D **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.**

Functional Ability Scales

Functional ability scales can also help in the establishment of a baseline and reviewing progress. Validated scales used in children and young people with CFS/ME include the Chalder Fatigue Scale, an 11-item verbal rating measure of fatigue intensity (39;91) and the Karnofsky scale of physical ability developed for studies on cancer but subsequently adapted for many chronic illnesses including CFS (35), although there is some concern that this is too insensitive for use in CFS/ME. Other scales include the AYME Young Persons Ability Scale (92) which has been developed from the perspective of children and young people with CFS/ME. Fatigue scales used in studies on adults

with CFS/ME are reviewed in Reeves (53). However it is important that these scales are used alongside an activity diary, which allows a child or young person to compare activities and see improvements which might not be obvious if only a scale was used. For example a child/young person who is managing 3 lessons a day rather than 2 might still be at the same place on the activity scale, but has made progress which should be the focus. Paediatricians should be aware that the use of scales and activity diaries may be dispiriting for patients who are deteriorating.

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. **D**

Gradual Increases

Patients with CFS/ME and their families need advice about balancing the amount of activity carried out each day. The advice should include the need to intersperse rest with activity, managing the same amount consistently each day. Activities can be physical (e.g. walking), mental (e.g. reading, schoolwork) and social (e.g. telephoning or meeting friends). What activities are attempted will depend on how the individual child/young person is affected and what they can manage. The patient should start with a level of activity they can manage, even on days they are feeling particularly bad and be advised not to do more on days they are feeling slightly better.

Once the child/young person is achieving this amount of activity consistently then the amount of activity can be gradually increased and rest decreased. Over-rapid increase in activity is not advisable and the child/young person and parents need to be involved in determining what increases of activity can be managed. It is essential that these increases are achievable from the patient's perspective. The plotting of improvement in an activity diary will give the responsibility and control to the child or young person, assisting motivation ((93), (40;55;94)).

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. **D**

3.3.3 Advice and Symptomatic Treatment

Once a diagnosis of CFS/ME has been made, the paediatrician should provide advice and support to the patient and family as well as discussion of the management plan.

The advice should cover the following topics:

- Dietary advice including the importance of eating regularly and the physiological consequences of not doing so
- How to regulate sleep patterns
- How to manage troublesome symptoms including pain; although there is a pattern of common symptoms (page 25), each child/young person will be affected differently

The patient leaflet included with this guideline may be helpful in discussions covering the above points.

Diet

In some children and young people with CFS/ME, fatigue, lack of appetite and nausea can result in a poor diet. The management team needs to acknowledge how hard it is for the child/young person, while encouraging them to eat and explaining why it is important. Although there is no evidence for the role of diet in a child/young person's recovery, general principles would suggest that a well balanced diet is the ideal, although this may not be achievable in all cases. There may often be weight fluctuations, even when the child/young person is eating a normal diet. Even with weight gain the child/young person still needs to be encouraged to eat normally rather than use a restrictive diet, unless there is well-founded evidence of specific food allergy or intolerance. The management team should advise patients and families against "faddish" diets and consider referring patients with severe nausea or other eating problems to a paediatric dietician with an understanding of the condition and the management plan. The evidence for the effectiveness of dietary interventions for CFS/ME is considered in section 3.5.2.

D **The management team caring for children and young people 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.**

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.**

In a minority of patients optimum nutrition may not be maintained by dietary manipulation and supplements and for these patients the help of an appropriately trained dietician is essential. In some severe cases the young person is so disabled that nutrition and/or hydration is actually or potentially seriously impaired. In these cases tube feeding should be started, preferably on a children's ward and continued, if necessary, at home under the supervision of a community paediatric nurse. In these situations, it is important to consider whether the diagnostic criteria are met for anorexia nervosa as a co-morbidity, as this is likely to require involvement of an expert in this field.

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.

Sleep Regulation

There is clinical and research evidence of sleep disturbance in children and young people with CFS/ME with phase delay and interruptions being the commonest problems (42). The types of sleep disturbances experienced by children and young people have already been described (page 26).

A review of sleep disturbances in CFS (42) acknowledges the distress to patients caused by these problems. Sleep problems deserve attention and need to be acknowledged by the paediatrician. Effective treatment will depend on accurate diagnosis of the sleep disorder underlying the sleep problem in each individual case, so a good history of the sleep pattern is essential.

A good history of the sleep pattern and sleep hygiene must be taken in patients with sleep problems before any interventions are started.

Sleep problems can initially be addressed by cognitive and behavioural means such as keeping sleep patterns consistent if possible, not exercising or watching TV before bedtime and simple measures like warm baths and a hot milky drink before bedtime.

The first line treatment for sleep problems in children and young people with CFS/ME should be behavioural and cognitive interventions to promote a revision of the sleep regime.

Persistent problems do merit a multidisciplinary approach if possible and can be treated with medication if behavioural methods are unsuccessful and the sleep problem severe

or distressing. The evidence for the effectiveness of pharmacological treatments for sleep regulation is lacking in children and young people. Practitioner reviews suggest that antihistamines or low dose antidepressants may be of help in the management of sleep problems in children and young people with CFS/ME (88;95). Although there is no research or safety evidence there is anecdotal evidence of the use of Melatonin in this area and published evidence for its effectiveness in treating sleep disorders in children and young people with other conditions (96;97) (see *Medicines for Children* (98) for doses). There is also anecdotal evidence that some children with CFS/ME may be sensitive to drugs and it is important that any pharmacological measures are started at low doses. Benzodiazepines are generally not recommended because of the dangers of tolerance and dependence.

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 and young people as they can be more sensitive to effects and side-effects of drugs.

Pain Management

Some children and young people with CFS/ME suffer from severe joint and muscle pain although the origin of this pain is unclear. Appropriate assessment and management of pain is important. In most cases simple analgesics such as paracetamol and ibuprofen are appropriate. Practitioner reviews have suggested a range of non-pharmacological measures although there is no evidence of their effectiveness (95;99). Transcutaneous Electrical Nerve Stimulation (TENS) treatment has been found to be effective in managing pain from a number of causes.

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.

If simple analgesics and other non-pharmacological measures do not work, then alternative approaches will be required. These can include involving a psychologist to help the patient learn cognitive behavioural techniques to manage the perception and symptoms of pain, the use of medication, and referral to a specialist pain clinic. The approach chosen will depend on the severity of the pain, patient preference, and the local availability of specialist services, but severe pain will need treatment even whilst waiting for referrals to psychology or pain clinics.

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. D

If pain is a persistent and prominent symptom then medication may be necessary. The evidence base for effective pharmacological treatment of pain in children and young people with CFS/ME is lacking. Short-term non-steroidal anti-inflammatory drugs (NSAIDs) and low dose tricyclics have been tried (95;99). A review of management of CFS/ME in children and young people, recommended a 10-25mg nightly dose of Amitriptyline, based on effectiveness studies in adults (88) for the treatment of muscle and joint pain.

Although there is no research evidence in children and young people for the effectiveness of low dose Amitriptyline or Nortriptyline for managing pain in children and young people with CFS/ME, the reviewers have experience of the effective use of low dose tricyclics as an analgesic in young people with chronic pain (see *Medicines for Children* (98) for dosages). The sedative effects can be an added benefit in the child or young person with sleep problems. Given the possibility of adverse effects and the toxic effect in overdose, this medication should only be prescribed after initial approaches have been shown to be ineffective and in consultation with a colleague experienced in their use and harmful side-effects in children and young people.

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 10mg can be gradually increased up to 1mg/kg (maximum 50mg), depending on effect and patient tolerance. D

There was no consensus over the referral of children and young people with severe pain to a pain management service. Concerns included limited availability of such services resulting in pain not being treated or a lack of experience of treating children and young people with CFS/ME within the service. Some felt that paediatricians should try low-dose amitriptyline before referral although concerns were also expressed about paediatricians prescribing anti-depressants. Given this lack of consensus, the approaches to managing severe pain will depend on clinical and family preference.

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. NC

Treatment for Depression and Mood Disorders

As mood and emotional disorders can be co-morbidities in children and young people with CFS/ME (page 26) they will need treatment and are an indication for referral to a psychiatric team. The first line treatments for such disorders are often behavioural including counselling and other cognitive and psychological therapies, although there may be circumstances in which the paediatrician will need to consider prescribing antidepressants for symptomatic treatment in the management of the condition. This should always be done in consultation with a colleague experienced in their use and possible harmful side-effects in children and young people. At the time of writing, the NICE guidance on the identification and management of depression in children and young people, which includes the use of antidepressants, was in its first draft.

Evidence for the use of antidepressants in children and young people who suffer from CFS/ME is scarce. At present there are no RCTs on children and young people in this area, and the evidence is based on the observations of practicing clinicians and extrapolated from adult studies (5;7;8). Some paediatricians support the use of antidepressants for children and young people with CFS/ME, especially if there is evidence of a severe mood disorder, although the acceptability to families and patients with this course of treatment may be low (99).

The reviews of RCTs of antidepressants in adults with CFS/ME concluded that there was insufficient evidence about the effects of antidepressants in people with CFS/ME (5;7;8). These reviews found only two RCTs of antidepressants that could be used in children and young people (fluoxetine) (100)*, (101)*. One showed no effect but the second suggested that six months of SSRIs may be useful for co-morbid anxiety or depression in some cases (100)*. If antidepressants are to be started, then the medication of first choice should be fluoxetine.

D **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.**

D **If antidepressant treatment is considered appropriate, evidence from adult studies suggests 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 6 months.**

3.3.4 Regular Paediatric Review

There have been no primary studies to inform the optimum frequency for review of children and young people with CFS/ME. Recommendations range from "frequent brief office visits" to evaluate changes, adjust treatment and provide family support (102) to a comprehensive, multidisciplinary review every 3-4 months (38). In general terms the interval between appointments will be dictated by the severity of the illness, the availability of test results, the patient's ability and desire to travel to see the paediatric team, the level of support available locally within the primary care team and the modality of treatment. However, the paediatrician remains responsible for the patient and must ensure that the review is sufficiently frequent to support patients and their families to begin an active rehabilitation programme, which they are in control of and at a pace that they dictate. There may be circumstances in which the paediatrician will need to consider a home visit to ensure ongoing paediatric input and to ensure that the therapeutic relationship is continued (section 3.7.2).

A good model might be to see the patient fairly frequently while initiating baseline, and getting to grips with management, and less frequently once the family is managing well. Giving patients a phone number to call so they can get seen quickly in the case of relapse/new symptoms will facilitate the establishment of a therapeutic partnership.

When reviewing patients with CFS/ME the paediatrician should:

- Enquire how the patient and family are coping with the condition
- Discuss the activity diary
- Identify any new or more severe symptoms (medical or psychological) which require symptomatic treatment or referral
- Establish if there are any sleep or dietary problems
- Review management plan in consultation with the family

Managing relapses

As a condition CFS/ME is characterised by relapses and it is important to ensure that the child/young person and their family understand that at times there may seem to be little progress. Care must be taken not to attach blame to the child/young person for not getting better. If a scale or scoring system has been used to establish functional ability, using this too frequently when the child/young person is deteriorating or not improving might be demotivating.

While trying to explore the cause of a relapse, it is important to be understanding if the child/young person has overdone things. Sometimes a cause is not obvious and it

is at this moment that patient/parent might decide that the management plan is not working, and give up on it.

If there has been a relapse it is vital that the paediatrician (or multidisciplinary team) works with family to assess what baseline is now appropriate and whether other support services are now required because of the change in situation. The doctor must reassure the family that their child can return to their previous level of functioning in time. It is better to see these relapses as a setback on the road to recovery, rather than an irreversible step downhill.

D **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.**

Indications for reassessment

Once a management plan has been initiated, progress should be regularly reviewed (see page 51) although paediatricians should acknowledge that in some cases progress can take months to be noticeable and even then it might seem very little. For example, a patient walking for 10 minutes three times a day, whereas 3 months earlier they were managing only 5 minutes three times a day is progress, albeit small, and should be recognised as such. However a complete lack of significant progress over a period of time is an indication for reassessment of the management plan. If after 6 months no significant progress has been made, the multidisciplinary team should help the patient and family with a thorough reassessment of the plan. The reassessment is not for the purpose of apportioning blame or making the patient or family feel guilty, but is instead an acknowledgement that the current management plan may not be appropriate for that patient and a different strategy may be required. Children and young people who are deteriorating and who are becoming severely incapacitated will need earlier reassessment.

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.**

3.3.5 Further Information for Families

Many patients and their families want to find out as much as they can about the condition. A recent Department of Health report (103) on the information needs of

chronically ill or physically disabled children and adolescents concluded that there were both medical and psycho-social information needs which should be addressed by a range of information sources. These sources included health professionals, parents, other young people with the condition and, increasingly, the internet. However the report also concluded that the role of health professionals as a source of information and a sign-post to other resources was often jeopardised by poor communication between doctors and young people.

Furthermore the quality and accuracy of health information in the public domain, particularly on the internet, can be variable and may conflict with the advice from the health professional team. A survey of internet information on CFS/ME in children and young people found conflicting advice about rest and recommendations about medication despite the lack of research evidence and concluded that few websites provided useful management advice (104). Patients should be alerted about this and encouraged to discuss any information they have come across with their health professional team. The Judge web-site (http://www.judgehealth.org.uk) provides helpful guidance for consumers about making informed decisions about health websites. The content of individual websites in relation to CFS/ME in children and young people have not been reviewed but nationally recognised charities supporting CFS/ME in children and young people are more likely to provide mainstream advice than individuals or small support groups.

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.

Patient Support Groups

CFS/ME can be an extremely isolating illness especially for children and young people who are not able to attend school. Patient support groups may help to overcome isolation and to provide contact with similar aged patients. It should however be acknowledged that not all patients/families will want to contact support groups.

Some patient support groups provide information about managing the condition and promote particular theories of aetiology. Patients who do contact support groups should be encouraged to discuss the support groups information on how to manage their CFS/ME with their paediatricians and multidisciplinary team to ensure that the patient, family and multidisciplinary team can work together to agree the management plan. The guideline development group have not critically appraised the literature

produced by the national CFS/ME support groups which are listed in Appendix 5.

D

Patients wishing to contact patient support groups should be encouraged to discuss the information provided by the group with their paediatrician or multidisciplinary team.

Counselling or Family Therapy

Young people with CFS/ME can find themselves in pain, isolated from their friends, unable to take part in normal daily and social activities, and often very dependant on their families for assistance in meeting their most basic needs. Seeing the effect their illness has on the rest of their family can be an added source of distress for the young person. The uncertainty of how long the condition will last for adds to the emotional strain placed on the young person as well as the rest of the family. Counselling or family therapy might help them cope with the emotional stress they are under as a consequence of being ill.

3.4 Inpatient care

There have been no studies comparing the outcome for children and young people with CFS/ME treated as inpatients with that for similarly affected children and young people on an outpatient programme. There have been some case series descriptions of inpatient programmes for children and young people with CFS/ME reporting improvements post discharge (55;58;105-107) but variable outcome measures and follow-up periods make it difficult to draw conclusions.

In general, if a local multidisciplinary team is available to support a rehabilitation programme on an out patient or day case basis then inpatient care for rehabilitation is not indicated for children and young people with CFS/ME.

D

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.

Although outpatient care is the optimal for the majority of children and young people with CFS/ME, there may be some circumstances when a short admission to an appropriate unit with a multidisciplinary team may be beneficial if the reason for the admission cannot be undertaken on an outpatient basis. These circumstances might be to:

- Facilitate a rapid medical investigation to enable a definitive diagnosis of CFS/ME to be made

- For assessment and to explain the management plan to the family in a setting where all members of the local multidisciplinary team are on-site.

The admission of children and young people with severe CFS/ME is considered separately in section 3.7.2.

The type of unit children and young people with CFS/ME are admitted to will vary with local circumstances. The precise type of unit matters less than the presence of a local multidisciplinary team experienced in the management of CFS/ME in children and young people and the availability of a ward or room environment appropriate for the patient's age and medical condition. An assessment of the young person's needs prior to admission will help to ensure that the environment is suited to the individual. Where there are appropriate dedicated inpatient treatment facilities these should be offered to families.

The majority of children and young people 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.

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.

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.

3.5 Interventions for CFS/ME

The evidence for the interventions for CFS/ME was drawn from recent systematic reviews as described on page 18 in the Guideline Methodology section. In interpreting this evidence it should be recognised that there can be a wide range of severity in patients with CFS/ME and that evidence of effectiveness in the patient groups studied does not necessarily mean that the intervention will be effective in patients more or less severely affected. None of the studies reported in the reviews were carried out on completely bed-bound patients.

3.5.1 Behavioural Interventions

A number of behavioural interventions have been evaluated in the treatment of CFS/ ME, notably cognitive behavioural therapy (CBT), graded exercise therapy (GET), pacing and rest. These interventions are discussed in alphabetical order so that the order is not interpreted as a list of interventions to be tried sequentially. The research evidence for each intervention is presented so that clinicians, patients and their families can decide together the most appropriate strategy. When deciding on a management plan for individual patients, barriers to treatment, particularly rehabilitative psychiatric or psychological modalities, may need to be identified (60;62;67;68).

Although CBT, GET and pacing each have their advocates, and to a degree have been evaluated individually, there is a considerable overlap in what they are and what they are trying to achieve. When evaluating research studies it is important to be aware of precisely what the intervention entails and not be guided only by what it is called because of the lack of standardised definitions for these terms. In each case the aim of the professional is to work with the patient to empower them to take decisions about the appropriate management of their illness.

Cognitive Behavioural Therapy

Cognitive behaviour therapy uses an individualised approach to rehabilitation. It incorporates two major components: the cognitive element which focuses on the identification and modification of thoughts, beliefs and assumptions which may shape the patient's understanding of their disease, and the behavioural element which aims to gradually and consistently introduce a change in behaviour, such as an increase in activity. Treatment needs to be tailored to the needs of the patient and can include techniques such as use of diaries to monitor thoughts and condition, and establishing new routines (such as sleep and lifestyle changes). A CBT model can include treatment of accompanying anxiety and depression and CBT can be tailored to include the involvement of the family.

The systematic reviews of CBT in adults with CFS/ME identified 4 relevant RCTs (108)*,(109)*, (110)*, (111)* and concluded CBT was an effective treatment in adults (5-8). There are no published results of RCTs of CBT in children and young people. We are however aware of two recently completed trials in children and young people but with no published data as yet: these are a trial of CBT versus general advice (112) and CBT versus waiting list treatment (113). One cohort study (114) describes family-focused CBT treatment in adolescents 11-18 years fulfilling the Oxford criteria for CFS, referred to a specialist centre and unwell for a mean of 2.4 years. Although this was a small study without a control group, the study concluded CBT was effective in

reducing fatigue and improving functionality. The self reported 'global improvement' and 'satisfaction with treatment' ratings were 100% at 6 month follow-up.

There are no studies that have compared the individual with the family-focused approach to CBT and there is no available evidence in children younger than 11. More research is also needed on how to treat the more severely affected children and young people who are unable to travel to outpatient centres for rehabilitation therapy.

Extrapolated evidence from adult studies suggests that CBT is likely to be a beneficial management strategy for some children and young people with CFS/ME.

B

The results of recently completed RCT's of CBT in children and young people with CFS/ME should be available within the near future to further inform the choice of CBT as a management strategy. However it is also important to consider how often and where the treatment will be delivered, as many patients with CFS/ME are not able to travel long distances to receive treatment on a weekly or bi-weekly basis. In some cases, members of the paediatric multidisciplinary team such as occupational therapists have sufficient expertise to offer CBT (see section 3.6.2).

Graded Exercise Therapy

GET is a structured and supervised programme of exercise agreed between doctor, therapist (usually a physiotherapist) and the patient. It is based on the patient's current level of ability. Intensity and duration of exercises begin at a very low level and are increased very slowly depending on progress. The aim of graded exercise therapy is to increase fitness and stamina and to reduce physical deconditioning.

Two reviews (5;7;8) evaluated RCTs on GET in adults; of three RCTs, two showed overall beneficial effects (115)*, (116)*, and one showed partial benefit with no additional benefit when the GET was combined with fluoxetine (100)*. The reviews concluded that a GET programme can improve fatigue and functioning in adults with CFS/ME ((5;8) Level 1+). More recently there has been a systematic review of exercise therapy for CFS (117 level 1+) which identified 5 RCTs in adults; and concluded that some patients may benefit from exercise therapy and that there was no evidence that exercise therapy may worsen outcomes on average.

In children and young people, two studies, one comparing GET as part of a rehabilitation programme with general support (118 level 2+) and the second a pilot study of graded activity and CBT versus pacing (93 level 1-) reported significant improvement

in illness severity. However the second study (93) was a very small pilot study with some methodological flaws which may mean the results are not applicable to other populations.

B **Children and young people with CFS/ME should be considered for graded exercise or activity programmes supervised by an experienced therapist.**

Pacing

Pacing is popular with some groups as a means by which a person with CFS/ME balances their daily activity, working from an established baseline of functional ability.

Pacing can mean different things to different people. In the CMO's document it is described as an energy management strategy in which patients are encouraged to achieve an appropriate balance between rest and activity (1). For the purpose of this guideline the definition is that used in a recent study reporting pilot data (93). This describes pacing to include:

a) pacing the amount of activity to the changing needs and responses of the body by exercising to the point of tolerance and avoiding over exertion
b) managing energy within an overall limit (glass ceiling)
c) Resting when necessary but avoiding total rest
d) Avoiding physically and/or emotionally stressful situations until ready
e) Tailoring return to school to the needs of the young person taking careful heed of symptoms, the young person and family.

There have been no trials of pacing as an intervention in adults although at the time of writing adult patients are being recruited to a four arm Medical Research Council (MRC) funded trial with adaptive pacing as one of the interventions. The pilot RCT on 13 children which found graded activity combined with active rehabilitation (family focussed CBT) to be more effective than pacing ((93) level 1-) is too small to draw any conclusions from. Until a larger study has been carried out comparing pacing with other interventions there is no evidence for the efficacy or otherwise of pacing as an effective management strategy for children and young people with CFS/ME.

Rest

There have been no studies of the effectiveness of bed rest as a prescribed treatment for CFS/ME in children and young people. The clinical evidence review (7) also found no RCTs of prolonged rest as an intervention in any age patients. This review concluded that on a basis of indirect observational evidence in healthy volunteers and people recovering from a viral illness, that prolonged rest may perpetuate or worsen fatigue and symptoms. It seems reasonable to assume this would also apply to children and

young people with CFS/ME.

Some children and young people are so incapacitated by their illness that bedrest or complete inactivity is a consequence of functional impairment and not a management strategy. The following recommendation does not apply to this group of children and young people.

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. **D**

3.5.2 Pharmacological Interventions

Immunoglobulin

Although there is limited evidence that there is initial benefit of using immunoglobulin, there is very little hard data to support the long-term beneficial effects of immunoglobulin treatment in adult or childhood CFS/ME. The only RCT in children and young people ((119) Level 1-) showed initial subjective improvement but on follow-up (25) there was no difference between the treated and control groups. The reviews identified a number of RCTs mostly on adults using immunoglobulin with variable results (two some positive effect, two overall beneficial effect and one no effect ((119), (120) *, (121) *, (122) *, (123) *. Many authors note the problems with side-effects and the risks associated with using blood products (5;8;25), ((124) level2 +) ((119) level 1-). The systematic reviews therefore conclude that immunotherapy is unlikely to be beneficial. Given the lack of convincing evidence of effectiveness and taking into account the very real risks associated with administering blood products and documented side-effects, it is not recommended that immunoglobulin be administered.

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. **C**

Magnesium Injections

There have been no RCTs on the effect of magnesium injections on children and young people with CFS/ME and the systematic reviews (5;7;8) identified only one RCT in adults (125)* where symptoms were improved at six weeks but there was no statement in relation to any adverse reactions and the reviewers were unable to draw reliable conclusions from this small study. Many authors warn of the side-

effects and the dangers of toxicity. The injections are not well tolerated in the adult population (8), which causes particular concern in the paediatric population (95;126).

D

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.

The systematic review (5) found a number of other pharmacological interventions which had been evaluated in RCTs in adults. Oral nictinamide adenine dinucleotide (NADH)(127*) had some positive effect in a small group of adults although there is no evidence of effectiveness in children. The review also listed a number of other agents including galanthamine hydromide which had all been associated with serious adverse events in adults.

Dietary Interventions

Some RCTs have been conducted with essential fatty acids and high dose Vitamin B12 supplements. The results of these trials show that there may be benefits, although there are no clear data for children and young people, and the results from the adult trials have been conflicting and unconvincing (5;8;54;128).

Steroids

Hydrocortisone has been found to have some beneficial effect in the adult population with CFS/ME ((5;8) Level 1+), although there have been no studies in children and young people with CFS/ME.

Antiviral Agents

The York systematic review found 4 RCTs using antiviral agents in adults with CFS/ME ((5;8) level 1+). RCTs using alpha interferon and interferon had a positive effect, aciclovir had a negative effect and ganciclovir had no overall effect.

Liver Extract

The reviews found one small RCT on liver extract in adults which showed no overall effect (129)*.

Staphylococcus Toxoid

The updated search identified one RCT in adults published since the systematic reviews which was an RCT of staphylococcus toxoid vaccine on adult patients with fibromyalgia and CFS/ME (130). This RCT reported that injections over 6 months lead to some

improvements although maintenance treatment was needed to prevent relapse.

For all these interventions, the lack of conclusive evidence in adults and the fact that any limited benefits are outweighed by painful administration and/or the risk of adverse effects together with the lack of evidence in children and young people, leads us to not recommend these interventions.

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.

D

3.5.3 Complementary Therapies

There is no evidence for the effectiveness of complementary or alternative therapies for treating children and young people with CFS/ME. The York systematic review found two adult RCTs on homeopathy, one with an overall beneficial effect although the American systematic review (9) felt this trial was inconclusive, and the second with some beneficial effect. One small RCT of massage therapy which found an overall beneficial effect although these were all poor quality trials. Osteopathy has also been tested in a non-randomised trial in adult patients with some possible benefit (9). Since the last search, an RCT of homeopathic treatment in adults with CFS/ME has been published (131)*. This has not been reviewed for the guidline.

Although these treatments are not necessarily transferable or acceptable to children and young people, if patients and families express an interest in trying complementary therapies they should be encouraged to find out the details of the proposed therapy and therapist. This should include the extent of the therapist's previous experience with CFS/ME, the risks and proposed benefits, the costs and whether or not it would conflict with, or interfere with current treatment.

They should also be advised to avoid trying too many things at the same time or persisting with something that is either not helping or apparently causing adverse effects. It can be valuable for patients to feel able to discuss such treatment with the multidisciplinary team. Given the lack of evidence for children and young people, patient/parent choice should dictate the choice of treatment if complementary therapy is desired.

If patients and families express an interest in trying complementary therapies, they should not be discouraged, providing this does not interfere with current treatment.

D

3.6 Referrals to other Health Professionals

Given the complex nature of CFS/ME and the number of systems across which symptoms can arise, the paediatrician may need to consider making a referral to another health professional for further investigation, symptom control or for the implementation of a multidisciplinary management plan. Such specialists may include members of the CAMHS team, pain specialists, neurologists, psychiatrists, psychologists, infectious disease experts, physiotherapists, occupational therapists and general practice.

Whenever a referral is made, an explanation should be given to the young person and parents about the individual's role in supporting them and how the paediatrician will be liaising with them. If a referral is made outside of the multidisciplinary team it is important that the health professional has a good understanding of the management plan.

In January 2004 the Department of Health announced the establishment of 13 new centres in England for people with CFS/ME (listed in Appendix 6). These centres will be led by local CFS/ME specialists and aim to improve the care of patients by providing access to specialist assessment, diagnosis and treatment, developing education and training resources for health professionals and supporting clinical research. There will also be 28 new local support teams throughout the country created in phase 1 of the project, increasing to 50 local multidisciplinary units after phase 2. These units aim to provide specialist rehabilitation services, develop networks of local services for the more severely affected and support GP's and local self-help groups. It is anticipated that these centres will be a valuable resource for paediatricians and patients.

3.6.1 Psychiatry/Psychology

Paediatricians should be alert to possible psychological issues at any stage of a young person's illness and an assessment of psychological and emotional well being is important at initial assessment and during ongoing care.

The indications for referral to the psychiatric team will depend on the severity of psychosocial factors and local circumstances. In many cases the paediatric multi-disciplinary team would have sufficient psychosocial expertise, and may include a child and adolescent mental health professional, that can provide adequate assessment and treatment. If this expertise is not available the decision to refer should be informed by a detailed history and careful mental state examination if clinically important psychological symptoms are present. School assessment reports should be sought especially for bullying and/or undisclosed educational and learning difficulties (62). Family history of psychiatric disorder, particularly anxiety or depression should also be explored (62;66).

The availability of treatments such as those that are family focussed is also an important consideration in deciding whether to refer to psychiatric or psychological services. Patients referred to psychiatry/psychology should be reassured that chronic illness can easily affect ones psychological well being and being referred is not something to be ashamed of.

A referral to psychology/psychiatry is not necessary in every case. However when assessment of psychological well being 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.

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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

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Particular care needs to be taken when making a referral to the psychiatry/psychology service as this can sometimes evoke a defensive reaction in patients and families, which can be damaging to the therapeutic alliance. A full explanation of the purpose of the referral should be given, whether it is for help with coping with the illness, or treatment of symptoms such as depression and anxiety. It should be made clear that such a referral does not mean their illness is not believed, or that the doctor thinks it is 'all in their mind'. If possible practitioners in child and adolescent mental health should be presented as an essential part of the paediatric team. Some families may nevertheless refuse referral and their decision has to be respected unless the young person is clearly at risk from severe depression or other clinically important psychological illness.

When making such a referral it may help to explain that behavioural interventions have been shown to be effective in management of other chronic conditions such as diabetes (132).

When making a referral to the psychiatry/psychology services the reasons for the referral should be clearly explained.

✓

As with other conditions, the possibility of fabricated illness must be borne in mind (67) and may be relevant in a small minority of cases (133). Family discord, and the possibility of abuse, should be sensitively explored (134). The families' views of sexuality, increasing separation and the developing adult role of the adolescent may also be relevant themes (57;135).

3.6.2 Physiotherapy/Occupational Therapy

The main reason for referral to physiotherapy is for symptom control and for mobilising children and young people with gross and fine motor problems, muscle atrophy, joint and muscle pain and contractures. Contractures are most likely to occur in the severe cases as patients are at risk if they have been immobile and in severe pain for more than a few weeks or months.

There is evidence that physiotherapy interventions reduce the deleterious effects of lack of activity, abnormal postures, movements and gait and also reduce pain especially head and neck pain (55;65). Physiotherapy should be advocated for the relief of symptoms by such modalities as passive and active movements, heat/ice, mobilisation techniques, gait re-education and hydrotherapy. Carers can be taught how to perform gentle passive movements under the supervision of a physiotherapist.

Occupational therapists (OTs) are trained in the area of life-style management, activity analysis, and daily living programmes, which may include a behavioural component. An experienced OT or physiotherapist will therefore be able to explain and supervise a graded activity/exercise programme (65) and referral to an experienced therapist should therefore be considered if the patients and family agree and local expertise is available. There is no evidence that rehabilitation by physiotherapist or OT is better or worse that rehabilitation by other health professionals (2;94). An occupational therapist or physiotherapist suitably trained with experience of CFS/ME may be the person best placed to supervise rehabilitation programmes with or without a behavioural component.

Physiotherapists and occupational therapists may also be part of the multidisciplinary team integral in the management of CFS/ME.

D **When 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.**

If mobility is severely affected then the use of a wheelchair can offer an opportunity to get out of the house and maintain social contacts. An occupational therapist or physiotherapist can make a referral to the NHS wheelchair service for the long-term loan of a suitable wheelchair. Short-term loans can be arranged through the Red Cross (http://www.redcross.org.uk) or local disabled living centres, although care needs

to be taken to ensure the wheelchair is appropriate to the needs of the child or young person. Occupational therapists or physiotherapists will also be able to assess the needs of the child or young person and suggest other appropriate assistive technologies.

3.6.3 General Practice

General Practice is the most likely source of referrals of patients with possible CFS/ ME. The ability of a GP to make a diagnosis of CFS/ME in children and young people will depend on the individual's knowledge and experience. Although GP's with paediatric training are well able to undertake the steps required to make a diagnosis (page 32), referral to a paediatrician can reassure patients and their families that the condition is being taken seriously and allows for a confirmation (or otherwise) of the diagnosis. In the case of unexplained and severe fatigue in children and young people, the GP has a duty to ensure that a diagnosis is made. This may be possible in primary care, but is more likely to require a referral to a paediatrician particularly for those cases with significant impairment.

In "mild " or early cases (i.e. those children and young people who exhibit sufficient symptoms in the absence of another cause to merit the diagnosis, but without significant functional impairment resulting in substantial time off school), an informed and experienced GP will be able to diagnose and manage the patient without referral to a paediatrician. However any child or young person significantly impaired by the CFS/ ME or those with "mild" CFS whose condition deteriorates should be referred to a paediatrician.

There is no research evidence on the effectiveness of different models of provision of ongoing care for children and young people with CFS/ME after a diagnosis has been made. However recent research suggests that GP's often are the main care provider for children and young people with CFS/ME; in a study of young people with CFS/ME recruited through primary care, although 82% had been referred to a paediatrician, the GP was the primary carer in 62% of cases and the paediatrician in 24% (34). The report of the Joint Royal Colleges Working Party (2) recommended that most cases of CFS/ME in children and young people would be adequately managed by a combination of primary care, school nurse and school authorities, although there is no primary research evidence as to the "adequacy" or otherwise of this arrangement.

The Working Party (2) report does not make any clear recommendations about

criteria for referral to paediatrician from general practice. In practical terms, once the diagnosis of CFS/ME has been made and management initiated, whether the GP or a paediatrician acts as lead clinical co-ordinator is likely to depend on individual local abilities, preferences, resources, and illness severity. Furthermore, since the management of CFS/ME in children and young people is likely to require regular monitoring, and an on-going relationship with education and a therapist or some sort, the local availability of experienced staff to support the management plan will also influence how involved GPs become in individual cases. Where paediatricians are responsible for the on-going care they should keep the GP informed with the patient's progress, on the understanding that at some point the GP will take back the care. The GP remains responsible for other aspects of care (minor illness, social and family problems, intercurrent serious illnesses).

If a paediatrician is responsible for the on-going clinical care of a child or young person with CFS/ME, the young person's GP must be kept informed about the patient's progress on a regular basis.

3.7 Management of Severe and Very Severe Cases

3.7.1 Definition of Severe/Very Severe CFS/ME

There are no consistently used definitions of severe CFS/ME in children and young people. The only paper to explicitly do so defines severe cases as those conforming to the Fukuda diagnostic criteria (51), with a diagnosis confirmed by a health professional, illness duration of more than two years and who are unable to leave home without assistance (43).

It seems sensible that severity is primarily defined in terms of the effect on the patient, which will be a combination of degree and duration of functional impairment. For this reason for purpose of this guideline, the following definitions are used for severe and very severe CFS/ME:

Severe: Any child or young person who is so affected as to be effectively housebound for a prolonged period of time (3 months or more) must be considered to be severely ill.

Very Severe: Any child or young person who is so affected as to be bedridden for a prolonged period of time (3 months or more) must be considered to be very severely ill.

3.7.2 Management

There is no RCT or high quality evidence to guide the management of the severe or very severe cases. The research evidence that does exist suffers from a lack of comparable or explicit definitions of "severe", no clear diagnostic criteria and/or very small numbers (35) (48) level 2+).

In general terms the management of severe and very severe requires the same approach as that of the less severely affected, although the severe cases are very likely to need more intensive support and therefore more paediatrician time. However paediatricians should be aware that the RCT's of interventions for CFS/ME in adults and children (section 3.5) have generally been carried out on ambulant patients. Therefore there is potentially a danger in extrapolating the findings to all patients as there is no evidence for their effectiveness in patients at the extreme ends of the spectrum of severity.

In general the recommendations made in other sections about rehabilitation, symptomatic treatment, use of antidepressants, referral to psychology/ psychiatry services, and liaising with general practice and with schools also apply to severely affected patients although caution should be exercised as highlighted above. However, there are also some considerations, which are unique to the severe case. This section concentrates solely on these issues.

The management of the severe case needs particular care and expertise because of the distress and high level of disability caused. It is particularly important that the paediatrician, patient and family agree who should be the key health professional responsible for providing secondary (or tertiary) care services and co-ordinating management by other clinical specialists or therapists. This is likely to be either the local hospital paediatrician or community paediatrician but, in some circumstances, might be a tertiary specialist. Where psychiatric co-morbidity is significant, the child and adolescent mental health team may assume this role with family approval.

As well as having an in-depth knowledge of care services, the key health professional should be a calm and reassuring source of support. Simple emotional support and understanding is essential as is helping the family to cope with uncertainty and conflicting opinions. It is helpful to avoid panicking in the face of apparently intractable symptoms as this may lead to over-investigation and may undermine the confidence of the young person and family. It can be helpful to put the family in touch with a support organisation and/or families of similar severe cases where judged they could be helpful.

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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.

Only if appropriate, the child/young person should be introduced to any other therapists whose track records suggest they might be helpful and constructive in alleviating symptoms or otherwise assisting recovery or preventing deterioration. Families and doctors sometimes find it difficult to agree on whether psychiatric help is indicated. This may depend on the experience, interpersonal skills and therapeutic approach of an individual child and adolescent psychiatrist, as opposed to those of the paediatrician.

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Referral to the Child & Adolescent Mental Health Services should be based on the clinical situation, local availability of expertise and family agreement.

Inpatient admission

There have been no primary studies of the effectiveness of inpatient admissions for severely affected children and young people. Although the 1996 Royal College of Physicians report recommended that children debilitated for a prolonged periods should be admitted to a specialist unit (2), no evidence was given in support of this. One paper reports the experiences of managing children in such a unit although the severity of the patients was not explicit (58). Another review suggests referral to an inpatient unit may be appropriate when symptoms cause physical restriction or the patient has been housebound for some time (136).

Given the lack of research evidence for the effectiveness of inpatient care, children and young people with severe CFS/ME should rarely be admitted to hospital for management of their CFS/ME. If the child/young person is too ill to attend outpatient clinics for assessment it is desirable that the paediatrician or key health professional co-ordinating the care is prepared to undertake domiciliary visits to ensure that the child/young person and their families are not left unsupported at home. Guidance for paediatricians on the contract requirements for domiciliary visits can be found by contacting the British Medical Association (BMA).

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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 co-ordinating services should offer regular home visits to ensure that the young person's condition is being appropriately assessed and managed.

Although inpatient care for children and young people with severe CFS/ME is rarely indicated there was a consensus that there may be occasions where admission to an inpatient unit may be helpful. However, there were concerns that specifying the indications for admission in the recommendation could be interpreted as a list of tasks that commonly need to be undertaken on severely ill children and young people in hospital.

The list below therefore provides *examples* of circumstances when admission may be beneficial. These include:

- To provide an opportunity for the multidisciplinary assessment of patients who are unable to attend an outpatient clinic
- To support families in managing a distressing situation
- To facilitate rehabilitation treatment which cannot be carried out at home
- For the treatment of secondary problems such as nutritional support, severe psychological problems or for the management of medical conditions unrelated to the CFS/ME

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 out patient basis.

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.

As with less severe cases (section 3.4) where an admission is planned, this should preferably be to a unit with a multidisciplinary team experienced in the management of children and young people with CFS/ME. However the guideline development group is aware of major difficulties in finding a bed in such units and of a shortage of multidisciplinary teams experienced in severe CFS/ME, a situation which could result in a severely ill child/young person being left to deteriorate at home with the family feeling unsupported. Therefore, where a bed in a multidisciplinary unit is not available and the families and the team feel an admission is indicated, the paediatrician should admit the child/young person to a local unit. If the paediatrician has no experience of looking after children and young people with severe CFS/ME as inpatients they should consult a suitably experienced colleague. It is not acceptable to leave bedridden children and young people with severe CFS/ME at home without support because of

a lack of a suitable facility to admit them to.

Children and young people with severe CFS/ME may also require hospital admission for reasons unrelated to the CFS/ME so it is important that there is some local provision. The NSF Hospital Standards (137) sets out standards in relation to hospital provision for all children and young people with rare, complex or chronic conditions in England which PCT's will need to address and which will include children and young people with severe CFS/ME. The Department of Health is publishing a series of exemplar patient journeys alongside the NSF for Children, Young People, and Maternity Services, using a variety of conditions to illustrate the main themes in the NSF. An exemplar on CFS/ME will be published in December 2004. Clinicians in Wales, Scotland and Northern Ireland should refer to their local versions of the NSF when they have been developed.

An assessment of the individual needs of the child or young person before admission should help to ensure that the hospital environment is appropriate and may mean an admission is more acceptable.

D **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.**

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.**

3.7.3 Doctor-Patient/ Family Relationship breakdown

A breakdown in the therapeutic relationship can occur if the doctor and family have irreconcilable views on how the illness should be managed although good communication could prevent the likelihood of this happening. The paediatrician should behave no differently from when this happens in other illnesses and should reflect on why the breakdown occurred in the first place (Section 3.3.1). The possibility for reconciliation should always be sought, as it is not in a young person's best interests to be in the middle of a parent/doctor feud, and it may be helpful to involve a mediator in the discussions to remedy the situation. If relationships cannot be restored after a

meeting then the paediatrician should facilitate referral to a colleague, either directly or through the young person's general practitioner. Ideally any such second opinion should be from a clinician with a sufficiently different approach or temperament for the chances of engagement to be reasonable. The patient's and family's view should be listened to and taken into account. Breakdown of the relationship on its own is not a reason for referral to social services.

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 in to account with regards of which colleague to refer to.

Referral to social services

Relevant legislation:

In England & Wales, the obligation to refer a child to social services is enshrined in sections 17 and 47 of the Children Act 1989.

Section 17: requires social service departments to safeguard and promote the welfare of children in need, defined as being unlikely to achieve or maintain a reasonable standard of health or development or whose health and development is likely to be significantly impaired without provision of services or who is disabled.

Section 47: If the initial assessment triggered by a referral under Section 17 concludes that the child is at risk of possible harm or has suffered harm then this will lead to a strategic discussion to plan a section 47 enquiry. If the risk of harm is confirmed during the section 47 enquiry then a child protection conference will be convened.

In Scotland the relevant sections of the Children (Scotland) Act are 22, 53 and 93. Section 53 does not demand identification of significant harm, rather that any person who thinks that compulsory measures of supervision may be necessary may give information to the Reporter to the Children's Panel. Section 93 defines a child in need as one unlikely to achieve or maintain a reasonable standard of health unless services are provided; or whose health and development is likely to be significantly or further impaired unless services are provided; or is disabled or affected adversely by the disability of another family member.

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.

Referrals under the Act

The paediatrician has to make a judgement as to whether the child/young person fits any of the criteria for referral under the relevant sections of the Children Act. Any referral must be made with the family's full knowledge and consent. Information may be disclosed without consent only where the doctor can reasonably conclude that failing to do so would place the child/young person at greater risk or hinder enquiries already being made and the content of what is disclosed must be proportionate to the degree of concern.

If the paediatrician has reasonable cause to suspect (that is, can demonstrate a 'well-reasoned' argument) that a child or young person is suffering or likely to suffer significant harm, then a referral should be made. This situation is most likely to arise when the paediatrician suspects an alternative diagnosis, such as fabricated or induced illness (FII). As the differential diagnosis of FII can be very difficult, great care must be taken and the paediatrician should review the Department of Health guidelines (138) and the RCPCH guidelines on FII (133). It is also sensible to seek the advice of a colleague with expertise in the subject as well as the Trust's designated doctor and to document reasoning and actions thoroughly.

Refusal to follow a treatment programme is unlikely to be regarded by a Court as sufficient reason on its own to make an order under the Children Act, especially where it may hear conflicting expert evidence as to the efficacy or otherwise of the proposed treatment. This is endorsed by the report of the CMO (1) which stated: 'Neither the fact of a child or young person having unexplained symptoms nor the exercising of selective choice about treatment or education for such a patient by the parents/carers and/or young person constitutes evidence of abuse… It is important to listen to the child, as well as to family members to respect their experiences and give due weight to their views, especially the child's. The young person should be given the opportunity to speak with the clinician, with or without their parents/carers.'

A referral is likely to be destructive if based on flimsy or ill-reasoned evidence. We believe that far more children and young people with severe CFS/ME fall into the category of 'a child in need' than one in danger. For example, a child may need assistance with wheelchair provision, transport costs, nursing or other care etc. This distinction

needs to be made clear at every point in the care pathway.

The Children Act exists to help children and young people and in some situations a referral can be part of good multiagency co-operation and provide the paediatrician with support in understanding a difficult situation. In difficult cases the paediatrician can discuss the situation with named doctors for child protection with social services without giving any names.

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.

Where social services have been alerted to the patient as a 'child in need' (see above) they will be responsible for providing practical aids, such as hoists or chair lifts and facilitating access to appropriate state benefits, such as Disabled Living Allowance. Some paediatricians, familiar with what is available, may prefer themselves to lobby on the child's behalf.

3.7.4 Education for Young People with Severe/Very Severe CFS/ME

The paediatrician's responsibilities in relation to liasing with education authorities are outlined in the next section. In severe cases the paediatrician has the additional responsibility of letting the school know that because of the severity of the child's or young person's illness, it is unlikely they will be able to attend school for some time.

It is particularly important to relieve stressful encounters from the severely ill child/ young person and their family. Supporting their requests for alternative educational provision and in relation to the timing of reintroduction of learning will assist this.

3.8 Education and CFS/ME

3.8.1 Educational Impact of CFS/ME

There is a substantial body of research showing that CFS/ME can cause a significant disruption to education (20;21;23;39;44;139;140), ((49) level 2+). However comparison between studies is hindered by different reporting methods whilst the use of selected populations and the fact that many of the studies have been on patients referred to tertiary clinics raise questions about the generalisability of the data.

The length of school absence depends on illness severity, ranging from part-time attendance to absences of several years with home tuition as the only educational exposure (20;27;28;34;39;139), ((49) level 2+). Children and young people with CFS/ME miss more school than those with juvenile rheumatoid arthritis (44), ((49) level 2+), cystic fibrosis (39) and migraine ((86) level 2+). A decline in academic performance and a significant reduction in extracurricular activities have been reported (27), ((22) level 2+), as has an adverse effect on GCSE results although the lack of matched control data makes interpretation difficult (23).

There have been no primary research studies specifically looking at interventions to minimise the educational disruption, although return to school has been used as an outcome measure as a proxy for overall improvement (118). It has been suggested that early intervention may minimise the length of school absence and prevent subsequent difficulty in reintegrating into school (141) although the only primary research is a case series reporting an association between receiving medical treatment and increased school attendance, which cannot be interpreted as causal (23).

Cognitive difficulties, mental fatigue, poor sleep the previous night, poor concentration, social withdrawal and the physical demands of travelling to school are likely causes of school absences, whilst in some cases family, social factors, and anxiety may play a part (45;136;60). The relative importance of these is uncertain.

3.8.2 The Paediatrician's Role

Statutory Guidance

Section 19 of the Education Act 1996 requires Local Education Authorities (LEA) to make suitable educational provision for all children and young people who cannot attend school by reason of illness. In 2001 the Government issued statutory guidance setting out minimum national standards for the education of children and young people who are unable to attend school because of medical needs (142). This guidance clarifies the roles of LEAs and schools in ensuring that children and young people unable to attend school because of illness have access to as much education as their condition allows. The guidance states that LEAs have a responsibility to ensure that pupils are not at home without access to education for more than 15 working days. In addition to this there is a category of 'special educational needs' with a code of practice that schools are expected to adhere to. If the paediatrician considers that the child or young person has special educational needs by virtue of their illness, they should make this clear (using this terminology) so that schools can put the appropriate procedures in place and bring the chid to the notice of their special educational needs coordinator (SENCO).

The DfES guidance covers access to education, policies and responsibilities, early identification of needs, continuity of educational provision, collaborative working between agencies, families and pupils, and reintegration into school and sets out standards in these areas. Paediatricians are encouraged to familiarise themselves with this guidance.

Note: The guidance for Wales, Scotland and Northern Ireland may be different and should be followed where appropriate.

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.

Liaison with schools

The literature reviewed in relation to educational provision for children and young people with CFS/ME pre-dated the publication of the DfES guidance(2;59;60;62;90;140;141;143) with the exception of one paper (140). However the reviews were unanimous in highlighting the importance of a close working relationship between the clinical team caring for the patient with CFS/ME and the school. This facilitates raising staff awareness, establishing the child's/young person's pre-morbid abilities and integrating educational needs into a comprehensive management plan as and when appropriate

Liaison with the school begins as soon as a diagnosis of CFS/ME is made. At this time the paediatrician should identify a designated contact within the school with whom they can establish an ongoing dialogue and should offer to attend a conference at the school. The point of contact may be a staff member or school nurse although other professionals who can be involved are the educational psychologist and the education welfare officer. Subjects for discussion with the school might include subjects to be taken, participation in sport, part-time attendance, rest, and access to the building. It is important that the parents and patients are involved and kept up to date with all the discussions to ensure that they are not disempowered. The views of the young person should be taken into account and the paediatrician should ensure that relevant staff have an understanding of the nature of CFS/ME and management strategy. In one study, all respondents (doctors, parents and education staff) felt the diagnosis should be revealed to school staff (21) although this must only be done with appropriate patient consent.

D **Paediatricians or management plan coordinator 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.**

3.8.3 Educational Continuity

The evidence review highlighted the devastating impact that CFS/ME can have on the education of the more severely affected child/young person. These children and young people are likely to require the provision of home tuition and/or distance learning although at times some may be too ill for any education. There has been no primary research evaluating the impact (educational or clinical) of part-time schooling or home tuition. Opinions differ on the value and need for home tuition (20;21). Many families are keen for children and young people to have access to home tuition and for this to be supported by the paediatrician, whereas others have highlighted its social and educational shortcomings and suggested that it is used as infrequently as possible, and for the shortest possible time (2;59;62;136;140;141).

There is no evidence to identify the indications for part-time schooling or home tuition and it is clear that each family would need an individual educational plan (88;90;136, 144). Where patients are not able to attend school, home tuition clearly provides some educational continuity but it should form part of a broader management plan (62). Some hospital schools can also provide a home tuition service. Both the CMO's report and the DfES guidance suggest that a paediatrician is likely to be the individual responsible for an early referral to the Education Welfare Service for children and young people who require special educational provision. It is then the LEA's responsibility to provide education appropriate to the child's/young person's medical needs but the paediatrician will clearly have a role in ensuring that the level of educational support provided is appropriate and the child's or young person's needs are continually monitored. Recent developments in providing continuing education for children and young people with CFS/ME include the establishment of a "virtual" classroom (145).

✓ **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.**

✓ **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 Service and to ensure an appropriate individualised**

educational plan is implemented and monitored.

Reintegration to school

The DfES guidance (142) considers the problem of reintegration of education for children who have had long-term health problems and refers to children with CFS/ME. It states that a resumption of education in whatever form should be planned in a way which ensures that children and young people do not feel under pressure to study. The CMO report emphasises that the resumption of education for children with CFS/ME should be managed in keeping with the general principles of activity management (1).

When a return to full-time schooling is planned for patients with CFS/ME, the speed of reintegration into school must be tailored to the needs of the individual child and should be part of the management plan. In many situations a meeting involving school professionals should be planned to discuss necessary support and future reintegration. As a general rule reintegration should be slow and cautious.

There is no primary research to illuminate the appropriate time to return full-time schooling. There may be anxiety around return to school from both academic and social viewpoint (39). Secondary problems arising as a result of school absence include educational and social exclusions/isolation, fears around coping with questions about the illness, as well as coping with a standard school curriculum (62;141). Most medical authorities suggest a return to part-time schooling as soon as possible (2;59;62) with some suggesting transfer into school of a routine workload begun at home (140;141). A change in school is sometimes made at the child or family's instigation, sometimes with good results.

Anxiety around returning to school should be identified and addressed.

3.9 Transition to Adult Services

The fact that the peak prevalence of CFS/ME in childhood is in late adolescence and that the illness is chronic and can last for a period of years in severe cases, means that in many cases, the paediatrician will need to make arrangements to hand over care to another health professional. This process, often referred to as transition, can be difficult for patients especially where it involves the ending of a positive relationship between the paediatric team and their patients built up over a substantial period of time.

The evidence review failed to find any relevant research literature in this area specific to

CFS/ME on which to base any recommendations. A recent RCPCH publication (147) however highlighted some general good practice points, one of which was that every children's general and speciality clinic should have a specific transition policy. The guideline development group endorses this as good practice. However the policy needs to be flexible enough to allow for the individual needs of adolescents with CFS/ME. A multidisciplinary meeting might facilitate the smooth transition of care, particularly for the complex cases.

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.

In order to inform the guideline, members of AYME were invited to tell us about their experiences on leaving the care of a paediatrician. The role of the general practitioner as "broker" of specialist care appears to be largely unfulfilled, judging by the responses (albeit in a small sample). The experience of some families suggested that their general practitioners were unsure of how to manage CFS/ME, and expected patients and families to suggest courses of action. Soliciting individual patient experiences inevitably highlights the bad rather than the good and it is likely that there are many examples of good practice in relation to transition to adult care.

Part of the problem probably lies with the fragmentation of specialisms in adult medicine compared with child health. On leaving the care of a paediatrician, an adolescent with CFS/ME, their family, and their GP might face a choice between consultants in infectious diseases, endocrinology, rheumatology, rehabilitation, neurology or psychiatry. Other factors also include the lack of recognition of the special health needs of adolescents in the UK compared with other countries particularly in relation to chronic illness (147).

Given that all the evidence for effective treatment appears to favour a multidisciplinary and rehabilitative approach, and given that this is the model adopted by the recent Government initiative for CFS/ME Centres, it will soon be much clearer to both general practitioners and paediatricians where to refer young adults for further care. Until these centres have been established however, the responsibility of identifying an appropriate health professional to take on the care of the older adolescent lies with the paediatrician. When such an individual has been identified, a joint handover appointment will ensure that any management plan in place can be supported.

D

Paediatricians, in consultation with GP's 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 arrangements are in place before discharging their young adults.

With the recent Department of Health CFS/ME service investment it is hoped that services for all people with CFS/ME including children and young people will improve and that the importance of the transition from paediatric to adult service has informed the decision making process.

4. Research Priorities

Given that only 6 of the 45 recommendations in the guideline are based on good or at least reasonable quality evidence, there are clearly huge gaps in knowledge in many areas in relation to CFS/ME in children and young people which need to be filled by well planned and well conducted studies. The guideline reviewers were asked to identify priorities for research to inform the future development of evidence based guideline.

One major area where knowledge is lacking is in relation to the aetiology and biological basis for CFS/ME and research in this area is essential to help inform the development of effective treatments and interventions. However as these topics were outside the scope of this guideline, the extent and quality of evidence in this area has not been reviewed and the research priorities have had to be confined to those areas covered in the guideline.

The new Department of Health Clinical Network Coordinating Centres plan to collect a standardised data set on all patients and this offers great potential for conducting future research studies.

Epidemiology, natural history and diagnosis

- The development of standardised diagnostic criteria for CFS/ME in children and young people including a comparison with those used in adults including the relevance of diagnostic criteria to cases with fatigue of varying duration of 2,3,4 and 6 months and variably defined definitions of CFS/ME
- Research into the level of disability which determines CFS/ME. Such studies could use the WHO International Classification of functioning, disability and health (ICF) (148) which advocates a universal classification of disability and health and may enable researchers and clinicians to use a standard language and classifications thus reducing the inconsistencies in the definitions of functioning, disability and health
- Investigations to describe transitions between fatigue, chronic fatigue and CFS/ME
- Physical findings in children and young people with severe and very severe CFS/ME
- Research to identify subgroups in children and young people meeting agreed diagnostic criteria such those with predominant pain and cognitive problems
- The incidence of CFS/ME and longitudinal studies to understand the natural history and illness duration
- Epidemiological studies using standardised diagnostic criteria to establish any variation in prevalence by sex, social class and ethnicity
- Studies evaluating the usefulness of PET (Positron Emission Tomography) scanning of pain syndromes and as a diagnostic marker in CFS/ME

- Studies of autonomic function, hypotension, POTS, cardiac function, cognitive and sleep functions, muscle and nerve functions and blood tests to facilitate diagnosis
- Studies of features (e.g. age of onset) which predict outcome
- Similarities between CFS/ME and other fatiguing conditions such as chemotherapy and radiotherapy, or depression in terms of abnormalities of neurotransmitters, cognitive functioning and the dysfunction in self-regulation of selective attention/ psychometric measures
- Investigation of possible clusters using a research methodology appropriate for cluster analysis

Management

- Evaluations of the effectiveness of patterns of care including evaluating the effectiveness of occupational therapy, physiotherapy and usual paediatric care
- Evaluations of the effectiveness of inpatient vs. outpatient programmes at all levels of severity
- Quantitative and qualitative studies to describe patients' and families' experiences of this syndrome, the strategies that have been beneficial to them complemented by clinical observations including psychological, sociological and cultural observations
- Studies assessing the belief systems of paediatricians regarding aetiology and treatment and their impact on outcome
- An understanding of whether patterns of family communication, somatisation, illness beliefs and behaviour have a role to play in the perpetuation of the illness

Behavioural Interventions

- Development of agreed definitions of CBT, GET, and pacing
- Comparison of the benefits of graded exercise/activity alone compared with graded exercise/activity combined with regular practical and targeted CBT
- Investigations into the effect of frequency of CBT sessions on outcome; e.g. a trial comparing intensive group CBT administered over 3 weeks compared with one to one sessions monthly for 6 months in both inpatient and outpatient settings with similar severity of condition
- Comparison of individual vs family focussed therapies
- Trials comparing the effectiveness of physical activity regimen; e.g. a trial of adolescents being advised by a personal fitness trainer at a commercial gym as part of a programme of graded activity compared with receiving physiotherapy in hospital

Pharmacological Interventions

- Evaluation of pharmacological treatments for symptoms of CFS/ME in particular a study of the role of amitriptyline on sleep disorders and pain with definitive outcome

measures
- RCT of immunoglobulin in the first six months of illness in severe cases and those with acute onset
- A trial of melatonin for sleep disturbance
- A trial for gabapentin for pain management

Other interventions
- Trials evaluating the effectiveness of alternative and complementary health care particular on sleep, fatigue, pain

Management of severe/very severe cases
- Development of objective, valid and reliable measures of severity which can be used by all stakeholders
- Evaluation of methods for the effective management of severe cases, e.g. hospital compared to home care, hydrotherapy compared to passive stretches, overnight feeds compared to supplements during the day

Educational considerations
- Studies evaluating the impact of the physical and mental outcome of CFS/ME on education.
- An investigation of anxiety around school attendance or return to school across stages of the illness
- Studies evaluating how educational provisions or programmes affect outcome (e.g. home teaching vs. part-time school or flexible vs. rigid programmes) and effect of timing and type of interventions on degree of educational disruption
- Development of standardised measures to report school attendance and scholastic achievement

Referral to other services and transition to adult care
- Studies on effective transition from paediatric to adult care
- Studies of patterns of care in relation to referral to and liaison with GPs

5. Executive Summary and Guideline Recommendations

The guideline has been developed by a multidisciplinary team following the methodology recommended by the RCPCH's Quality of Practice Committee (QPC) and is intended for paediatricians referred a child/young person up to 18 years of age for assessment of debilitating fatigue.

The guideline methodology involved a systematic search of the research literature, critical appraisal of the evidence and formulation of recommendations based on the evidence. The recommendations are graded according to the SIGN grading hierarchy and the grade is indicated by a letter in a circle alongside the recommendations. Those recommendations graded as A-C are based on good research evidence. The evidence underpinning these recommendations was also independently appraised by the RCPCH QPC and the views of this committee were incorporated into the wording of the recommendations and/or the grade. Where the evidence was lacking or of poor quality a formal Delphi consensus methodology was used. Consensus was considered to have been achieved if 75% or more of a panel of experts agreed with the wording of the recommendation. A "D" alongside a recommendation indicates that this is a consensus recommendation. The guideline also contains a number of good practice points. A full explanation of the guideline methodology is provided in the main guideline text. **The guideline recommendations are summarised here but they should also be read in the context of the text in the relevant sections.**

As well as the evidence based guideline this document has a background section on the epidemiology, clinical features and diagnostic criteria for CFS/ME in children and young people where the evidence base was reviewed but no clinical practice recommendations formulated. The guideline also identifies priorities for future research into CFS/ME in children and young people.

Epidemiology

- The UK prevalence of CFS/ME in children and young people is 50-100/100,000 with the highest prevalence in adolescents. However, higher prevalence estimates have been obtained from population surveys where cases are either self or parent reported
- There are no published figures on the incidence of CFS/ME in children and young people
- Although the evidence for a gender difference in CFS/ME is inconclusive, where studies have reported a difference, girls outnumber boys 3:1
- Mean illness duration reported from studies was 37-49 months; however these studies

may not provide a true indication of prognosis as they report percentage recovered at specific follow-up periods and may be influenced by responder bias and participants may not be representative of the severity spectrum
- The limited evidence available suggests that young people with CFS/ME are more likely to make a full recovery than older adults
- A reasonably large body of evidence suggests that, as with older patients, a small percentage of young people (5-10%) remain considerably incapacitated for years

Clinical features of CFS/ME in children and young people

There are a number of common features and symptoms reported in the literature about children and young people with CFS/ME. These are:

- Illness can be of either gradual or sudden onset
- Some patients report a preceding acute illness, often of an infectious nature, although there are rarely corroborating laboratory investigations or a comparative control group
- Debilitating fatigue (both physical and mental), typically exacerbated by exercise or activity, is the most commonly reported symptom
- Other frequently reported symptoms are severe malaise, headaches, sleep disturbances, concentration difficulties, memory impairment, depressed mood, myalgia/ muscle pain, nausea, sore throat, tender lymph nodes, abdominal pain and arthralgia/ joint pain
- Less commonly reported symptoms include feeling too hot or cold, dizziness, cough, eye pain/increased light sensitivity, vision or hearing disturbances (photophobia or hyperacusis), weight gain or loss, muscle weakness, lack of energy for usual activities and diarrhoea
- Some children and young people with CFS/ME have symptoms and/or a diagnosis of depression and anxiety or other psychological conditions and psychological co-morbidities although the presence of psychological co-morbidities does not necessarily indicate a psychological aetiology for the condition.

Diagnostic criteria for CFS/ME

There are no accepted diagnostic criteria for CFS/ME in children and young people. Adult research criteria mostly require specific illness/fatigue duration and the CMO's report on CFS/ME recommended that a diagnosis should have been confirmed by 6 months. This was felt not to be appropriate in children and young people with debilitating symptoms and where diagnostic delays can cause anxiety and delay appropriate management. The guideline development group concluded that:

- A diagnosis of CFS/ME in children and young people should be based primarily on the impact of the condition on the patient and not require a specific illness duration
- When first referred a patient with debilitating fatigue for assessment, an appropriate initial opinion is one of "generalised fatigue"
- The process of assessing the patient for differential causes of the fatigue should differentiate between generalised fatigue and CFS/ME, which will continue to cause functional impairment after alternative differential diagnosis have been excluded
- In CFS/ME the fatigue is likely to be associated with other 'classical' symptoms such as difficulty in concentrating and disturbed sleep patterns and is typically exacerbated by activity (both physical and mental)

Evidence based Guideline

Making the diagnosis

CFS/ME in children and young people is diagnosed after taking a careful clinical and family history, a thorough physical examination and excluding differential diagnoses by undertaking a minimum number of tests and investigations. The following recommendations are made in this area:

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. D

An initial family history should include an enquiry into chronic illness, and in particular CFS/ME or similar conditions in any family member. 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 sensitively explored. However, unless there are immediate concerns regarding the psychological well being of the patient, a detailed exploration of family dynamics or the taking of a full psychiatric/psychological history is not necessary at this point. D

Physical Examination

A thorough physical examination of children and young people with symptoms of CFS/ME should be undertaken at the first consultation to exclude other underlying illnesses and reassure patients and families that the illness is being taken seriously.

D

Particular components of the physical examination include:

- **General physical examination including height, weight and head circumference**
- **A neurological examination (including ophthalmic fundal examination, gait and signs of muscle wasting)**
- **Lymph node/liver/spleen/tonsillar enlargement. Any abnormal clinical signs such as marked cervical lymphadenopathy need full investigation**
- **Palpation over frontal, ethnoid and maxillary sinuses (to identify chronic sinusitis)**
- **Lying and standing BP and HR (for evidence of Postural Orthostatic Tachycardia Syndrome (POTS) or postural hypotension).**

Tests and Investigations

The test and investigations fall into three categories; routine investigations which should be carried out on all patients, second-line investigations and those investigations which should only be carried out rarely.

D

Routine tests on all patients should include a blood test and a urine test for the following investigations:

- **FBC & film to exclude anaemia, iron deficiency and leukaemia**
- **ESR (or viscosity) (unlikely to be elevated in CFS/ME) and CRP (c-reactive protein) (a high level could suggest autoimmune disease (e.g. Systemic Lupus Erythematosus) or chronic infection (e.g. Tuberculosis))**
- **Blood glucose for diabetes mellitus**
- **Blood biochemistry (Na, K, creatinine) to look for renal impairment or endocrine abnormality (e.g. Addison's)**
- **CK 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 leukocytes and nitrites to exclude urinary tract infection**

C

Viral titres or other viral tests to impute or exclude current viral infection are not recommended apart from EBV IgM, IgG and EBNA.

Psychological well-being

There is a reasonable body of evidence that psychological morbidity can occur in some children and young people with CFS/ME. Assessment of psychological well being is therefore an important part of the diagnostic process (as with any potentially chronic condition) both to exclude major psychiatric disorders and to identify psychological co-morbidity which can impact on the course of the illness or the effectiveness of any treatments.

Careful attention to psychological well being is an important part of the assessment and management of CFS/ME in children and young people. 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. C

Communicating the diagnosis

It is important to explain to the patient and family that CFS/ME is a *possible* diagnosis as soon as possible. When a diagnosis is made, the reasons for the diagnosis of CFS/ME should be carefully explained to the patient and their family and documented in the clinical notes. Acknowledging the family's view point will help to establish a therapeutic relationship.

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 whilst not endorsing possibly unfounded theories of aetiology. D

Management of CFS/ME

The review of the evidence did not identify a single approach to management of CFS/ME in children and young people that could be recommended for all patients. There have been a number of research studies evaluating specific interventions but these have mostly been carried out in adults. The general principle of management should therefore be to work with the patient and family and with other health professionals where appropriate to agree a management approach, establish a baseline the patient can manage and increase activity slowly in steps the patient finds manageable. The management team will depend on the individual situation but establishing a multidisciplinary team with appropriate expertise at the outset will ensure that the necessary skills are in place to support the patient and family. Developing a rapport with the family and establishing an empathetic

relationship is essential to the success of the management plan. Management decisions should be on the basis of informed consent.

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 and identify the member of the team who will co-ordinate the plan.

D **As a minimum for all children and young people 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**

D **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**.

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.**

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.**

Regular Paediatric Review

Once a diagnosis of CFS/ME has been made then the paediatrician will need to arrange a regular review to support the patient and family (especially if there are relapses which can be part of the disease pattern of CFS/ME) and monitor progress with the rehabilitation plan and to provide advice and symptomatic treatment.

D **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.**

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 or young person. A significant deterioration in functional ability is an indication for earlier reassessment. D

Advice and Symptomatic Treatment

Once a diagnosis of CFS/ME has been made the paediatrician should provide advice and support to the patient and family on the importance of eating regularly, how to regulate sleep patterns and how to manage troublesome symptoms.

Dietary Advice

In some children and young people with CFS/ME, fatigue, lack of appetite and nausea can result in a poor diet.

The management team caring for children and young people 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. 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. 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. D

Sleep Problems

Sleep problems accompanying CFS/ME deserve attention and need to be acknowledged by the paediatrician although a good history of the sleep pattern and sleep hygiene must be obtained before any interventions are started.

The first line treatment for sleep problems in children and young people with CFS/ME should be behavioural and cognitive interventions to promote a revision of the sleep regime. D

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 and young people as they can be more sensitive to effects and side-effects of drugs.**

Pain management

Severe joint and muscle pain can also be symptoms of CFS/ME and will need treatment, initially with simple analgesics and/or non-pharmacological measures. If however pain is a persistent and prominent symptom then medication may be necessary, although the evidence base for effective pharmacological treatment of pain in children and young people with CFS/ME is lacking. Short-term non-steroidal anti-inflammatory drugs and low dose tricyclics have been tried.

D **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.**

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 10mg can be gradually increased up to 1mg/kg (maximum 50mg), depending on effect and patient tolerance**.

Treatment of depression

As mood and emotional disorders can be co-morbidities in some children and young people with CFS/ME they will need treatment and are an indication for referral to a psychiatric team.

D **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.**

D **If antidepressant treatment is considered appropriate, evidence from adult studies suggests 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 6 months.**

Further information for families

Many patients and their families want to find out as much as they can about the condition. Patient support groups can provide age-specific support and the internet can be searched for information although as the accuracy is variable, patients should be encouraged to discuss any information they find with their health professional team. Nationally recognised charities supporting CFS/ME in children and young people are more likely to provide mainstream advice than individuals or small support groups.

Patients wishing to contact patient support groups should be encouraged to discuss the information provided by the group with their paediatrician or multidisciplinary team. D

Inpatient care

If a local multidisciplinary team is available to support a rehabilitation programme on an out-patient or day-case basis then inpatient care for rehabilitation is not necessary for the majority of children and young people with CFS/ME. There may however be some circumstances when admission is beneficial.

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. D

The majority of children and young people 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. D

Severe and Very Severe CFS/ME

The guideline separately defines severe CFS/ME (any child or young person who is so affected as to be effectively housebound for a prolonged period of time (3 months or more)) and very severe CFS/ME (those incapacitated by the severity of their symptoms to the extent of being bedridden for at least 3 months). The management of the more severe case needs particular care and expertise because of the distress and high level of disability caused.

D **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**.

D **Referral to the Child & Adolescent Mental Health Services should be based on the clinical situation, local availability of expertise and family agreement.**

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 co-ordinating services should offer regular home visits to ensure that the child/young person's condition is being appropriately assessed and managed.**

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 out patient basis.**

D **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.**

D **When admission for a child/young person with severe CFS/ME is indicated, a pre-hospital assessment of the individual needs of the child/young person must be undertaken**.

In severe cases where the doctor/patient/family relationship breaks down and cannot be reconciled, a second opinion should be actively recommended and sought by the paediatrician, taking parental/patient choices into consideration.

Interventions for CFS/ME

There have been very few high quality trials of interventions for CFS/ME in children and young people. Although there have been two recent trials of behavioural interventions in children/adolescents, the results are not yet available, so the evidence for effective

interventions was drawn from systematic reviews of mostly adult studies and extrapolated to children and young people.

As well as the general lack of evidence in children and young people, the following should also be noted when considering these recommendations; the RCTs to date have been carried out on ambulant patients and the precise components of the behavioural programmes labelled as cognitive behavioural therapy (CBT) or graded exercise therapy (GET) may differ between studies. Therefore there is potentially a danger in extrapolating the findings to all patients, as there is no evidence for their effectiveness in patients at the extreme ends of the spectrum of severity. Neither have there been any comparative studies in children and young people to evaluate the most appropriate setting and skill mix of staff for delivering the intervention or which children and young people might benefit most. Although CBT, GET, and pacing each have their advocates, in each case the aim of the professional is to work with the patient and their family to empower them to take decisions about the appropriate management of their illness.

There is no evidence for the efficacy or otherwise of pacing as an effective management strategy for children and young people with CFS/ME.

Extrapolated evidence from adult studies suggests that CBT is likely to be a beneficial management strategy for some children and young people with CFS/ME. **B**

Children and young people with CFS/ME should be considered for graded exercise or activity programmes supervised by an experienced therapist. **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. **D**

Pharmacological Interventions

The evidence for the pharmacological interventions was also largely extrapolated from adult studies reported in recent systematic reviews.

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. **C**

D **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.**

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.**

D **If patients and families express an interest in trying complementary therapies, they should not be discouraged, providing this does not interfere with current treatment.**

Referrals to other health professionals

Given the complex nature of CFS/ME and the number of systems across which symptoms can arise, the paediatrician may need to consider making a referral to another health professional for further investigations.

D **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.**

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.**

D **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.**

Education

Liaison with the school is important for children and young people with CFS/ME and needs to begin as soon as a diagnosis of CFS/ME is made. The Department for Education and Skills has produced statutory guidance in relation to children and young people unable to

attend school because of a medical condition. The guidance for Wales, Scotland and Northern Ireland may be different and should be followed where appropriate.

Paediatricians or management plan coordinator 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.

D

Handover of care

As the peak prevalence of CFS/ME in childhood is in late adolescence the paediatrician may need to make arrangements to hand over care to another health professional. The experiences of a small number of members of the Association of Young People with ME (AYME) suggest that this transition of care is sometimes handled badly.

Paediatricians, in consultation with GP's 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 arrangements are in place before discharging their young adults.

D

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Glossary Of Abbreviations

ALP	Alkaline phosphatase
ANA	Antinuclear antibodies
ASOT	Antistreptolysin-O test
AST	Aspartate transaminase
AYME	Association of Young People with ME
CAMHS	Child and Adolescent Mental Health Services
CAYP	Children and Young People
CBT	Cognitive Behavioural Therapy
CDC	Communicable Disease Centre
CFS	Chronic Fatigue Syndrome
CI	Confidence Intervals
CK	Creatine kinase
CMO	Chief Medical Officer
CSF	Cerebrospinal fluid
DCT	Direct Coombes Test
EBV	Epstein Barr Virus
EDS	Ehlers Danlos Syndrome
EMG	Electromyography
ESR	Erythrocyte sedimentation rate
FBC	Full Blood Count
FM	Fibromyalgia
GET	Graded Exercise Therapy
GSD	Glycogen Storage Disease
LEA	Local Education Authority
ME	Myalgic Encephalopathy
MRC	Medical Research Council
MHRA	Medicines and Healthcare Products Regulatory Authority
MRI	Magnetic Resonance Imaging
MSLT	Multiple sleep latency test
NSAIDs	Non-steroidal anti inflammatory drugs
NSF	National Service Framework
RCP	Royal College of Physicians
RCT	Randomised Controlled Trial
SIGN	Scottish Intercollegiate Guideline Network
SLE	Systematic Lupus Erythematosus
SSRI	Selective Serotonin Reuptake Inhibitor

TB	Tuberculosis
TENS	Transcutaneous Electrical Nerve Simulation
TSH	Thyroid stimulating hormone
VEP	Visual evoked potentials
VMA	Vananyl mandelic acid

APPENDIX 1 - Clinical Questions

Epidemiology of CFS/ME in Children and Young People (CAYP)

1. What is the prevalence and incidence of CFS/ME in young people up to 18 years of age (with confidence intervals)?
2. What are the variations in prevalence and incidence by age, gender, social/economic class, race/ethnicity?
3. What are the variations in prevalence and incidence by place (local, national, international variations)?
4. What are the variations by time (possible changes over time, eg seasonality)?
5. What is the prevalence of mild/moderate/severe CFS/ME?
6. What is the prognosis/duration of illness in CAYP (including any factors affecting prognosis) with CFS/ME and course of the illness over time, including mortality?

Clinical features of CFS/ME in children and young people

1. What are the clinical symptoms of CFS/ME in CAYP, the most common and the most severe, including psychiatric or psychological symptoms such as depression?
2. What is the nature of the fatigue in children with CFS/ME?
3. What is the nature of the onset of CFS/ME in CAYP and does the nature of onset have any clinical significance?
4. What are the findings (early and later) of a physical examination of a child/young person with CFS/ME?
5. What are the features of atypical CFS?

Diagnostic criteria for CFS/ME in CAYP

1. Definition/diagnostic criteria for CFS in CAYP for the purpose of this guideline.
2. What should be included in an initial physical examination of children with symptoms consistent with CF/ME?
3. What steps should be taken by the paediatrician before making a diagnosis?
4. Are there any groups of patients for whom a diagnosis of CFS/ME not appropriate?
5. What is the evidence for harm or benefit associated with a positive diagnosis of CFS/ME?

Differential diagnoses and co-morbidities, tests and investigations

1. What are the more common diseases/conditions with similar symptomatology which should be excluded before making a diagnosis of CFS/ME?
2. What is the overlap/relationship between CFS/ME and other syndromes (fibromyalgia, IBS)?
3. What medical co-morbidities, confounding or complicating conditions can occur in CAYP with CFS/ME?

4. What are the essential laboratory tests/investigations a paediatrician should order on a patient with possible CFS/ME?
5. Are there any tests/investigations which might be considered which are not routinely recommended?
6. Are there any particular circumstances where additional tests might be considered and if so, which?
7. What are the indications for repeating previously normal tests/investigations?
8. Is there any value in carrying out a test for viral infection?

Psychiatric/psychological aspects; differential diagnoses for psychiatric and psychological conditions

1. Are there any other psychiatric/ psychological conditions which have a similar symptomatology in CAYP which should be excluded before making a diagnosis of CFS/ME?
2. What is the purpose and value of a psychiatric/psychological assessment in patients presenting with possible CFS/ME?
3. What are the indications for referral for psychiatric/psychological assessment after a diagnosis has been made?
4. What is the evidence that psychological factors have an impact on outcome?
6. Is cognitive behavioural therapy an effective intervention in CAYP with CFS/ME?
7. Is there any evidence for sub-groups of patients with preferential response to behavioural interventions?

Role of paediatrician in the management of patients with a possible diagnosis of CFS/ME

1. What medical information should be sought when taking history from a patient referred with symptoms consistent with a diagnosis of CFS/ME?
2. What family history should be taken at an initial consultation?
3. Exploring patients' views on aetiology at initial consultation.
4 When should the paediatrician see the patient after the initial consultation?
5. What is the recommended frequency of paediatric review?
6. What are the indications for referral to a paediatric sub-speciality service?

Monitoring progress/allied health profs

1. Are activity diaries of value in the management of CAYP with CFS/ME?
2. Should the paediatrician carry out a formal assessment of fatigue/functional ability using a validated scale?
3. If so which scales/scores can be recommended?
4 When should the assessment be carried out and how often should it be repeated?
5. What are the indications for referral to physiotherapy and occupational therapy services?

6. Is graded exercise therapy an effective intervention in CAYP with CFS/ME?
7. Is rest an effective intervention in CAYP with CFS/ME?
8. Is pacing an effective intervention in CAYP with CFS/ME?
9. Are physiotherapeutic interventions effective in children?
10. Is occupational therapy an effective intervention in children?

Liaison with general practice

1. Should the paediatrician always be lead clinical co-ordinator in the management of CAYP with CFS/ME?
2. Are some patients more appropriately managed by GPs?
3. What is the role of the GP in the management of CAYP with CFS/ME?

Pharmacological interventions/symptomatic treatment

1. What is the evidence that anti-depressants are beneficial in the treatment of CFS/ME in CAYP?
2. What is the evidence that immunoglobulin is beneficial in the treatment of CFS/ME in CAYP?
3. What is the evidence that magnesium is beneficial the treatment of CFS/ME in CAYP?
4. Is there any evidence that sleep regulators are beneficial? What advice should be given about sleep regulation? (including SSRIs)
5. Is there evidence that the use of analgesia is beneficial? What advice should be given?
6. What advice should be given about pain management?
7. Is there any evidence that nutritional supplements are beneficial?
8. Is there any evidence about other pharmacological or symptomatic treatments not mentioned here?
9. Is there any evidence that complementary/alternative therapies are of benefit?

Inpatient care for CAYP with CFS/ME

1. Is inpatient treatment of benefit in management of CFS/ME CAYP?
2. Which patients might benefit from in-patient care?
3. When is inpatient care indicated?
4. Where should patients requiring inpatient care be managed?

Management of severe cases

1. What is the paediatrician's role in management of bed-ridden or severely disabled patients?
2. What is the paediatrician's role in relation to referral to social services for severely disabled CAYP?

3. Tube-feeding.
4. Management of contractures.
5. What are the indications for referral to the child protection team?
6. What is the paediatrician's role if the relationship with the family/patient breaks down?

Engagement with Family

1. How should the paediatrician engage with the family?
2. What is the importance of acknowledging illness and illness beliefs?
3. Discussion regarding possible diagnosis and steps to arrive at firm diagnosis.
4. When and how should a possible/definite diagnosis of CFS/ME be communicated to patient and family?
5. How should the purpose and value of psychiatric assessment be communicated to patient/family?
6. Initiating holistic management plan with agreement of patient and family.
7. What advice about specific information sources?

Education and Liaison with schools

1. What is the impact of CFS/ME on a young person's education?
2. What is the paediatrician's role in liasing with the patient's school?
3. What is the paediatricians role in liasing with the LEA?
4. What are the indications for recommending part-time schooling/home tuition?
5. What are the indications for advising a return to full-time schooling?

Leaving the care of a paediatrician

1. When should a paediatrician caring for a young person with CFS/ME consider transferring care to the adult services?
2. To which adult services should the care of the young person with CFS/ME be transferred?
3. When is it appropriate for a paediatrician to finally discharge a child or young person from their care?

APPENDIX 2– Search Strategy

The search strategies for the guideline was run on t he following databases using the OVID platform:

MEDLINE	1966-2004
EMBASE	1980-2004
PsycLIT	1887-2004
CENTRAL	2002/4
Social Science Citation Index	1981-2004
Science Citation Index	1981-2004
ASSIA	1987-2004
Index to Scientific & Technical Proceedings	1982-2004
PASCAL	1973-2004
MANTIS	1880-2004
CINAHL	1980-2004
ERIC	1966-Oct 2004
NTIS	1964-Oct 2004
Inside Conferences	1993-Oct 2004
Life Sciences	1982-Oct 2004
CAB Health	1983-Oct 2004
BIOSIS	1969-Oct 2004
TGG Health & Wellness	1976-Oct 2004

The main search strategy used the following terms:

1. fatigue-syndrome-chronic.mp. or Fatigue Syndrome, Chronic/
2. chronic fatigue syndrome.ti,ab.
3. myalgic encephalomyelitis.ti,ab.
4. akureyri disease.mp.
5. chronic epstein barr virus.mp.
6. cfids.mp.
7. (chronic fatigue and immune dysfunction syndrome).mp. [mp = ti, sh, ab, it, tn, ot, dm, mf, rw, hw, ty, id]
8. chronic mononucleosis.mp.
9. chronic mononucleosis syndrome.mp.

10. chronic mononucleosis like syndrome.mp.
11. chronic mononucleosis-like syndrome.mp.
12. effort syndrome.mp. or Neurocirculatory Asthenia/
13. iceland$ disease.mp.
14. low natural killer cell syndrome.mp.
15. neuromyasthenia.mp.
16. post viral fatigue syndrome.mp.
17. postviral fatigue syndrome.mp.
18. post-viral fatigue syndrome.mp.
19. post viral syndrome.mp.
20. postviral syndrome.mp.
21. post-viral syndrome.mp.
22. post infectious fatigue.mp.
23. postinfectious fatigue.mp.
24. post-infectious fatigue.mp.
25. chronic postviral fatigue syndrome.mp.
26. chronic post viral fatigue syndrome.mp.
27. chronic post-viral fatigue syndrome.mp.
28. raggedy ann$ syndrome$.mp. [mp=ti, sh, ab, it, tn, ot, dm, mf, rw, hw, ty, id]
29. raggedy anne.mp. [mp=ti, sh, ab, it, tn, ot, dm, mf, rw, hw, ty, id]
30. royal free disease$.mp.
31. royal free epidemic.mp.
32. royal free hospital disease.mp.
33. tapanui flu.mp.
34. yuppie flu.mp.
35. yuppy flu.mp. [mp=ti, sh, ab, it, tn, ot, dm, mf, rw, hw, ty, id]
36. chronic infectious mononucleosis like syndrome.mp.
37. chronic infectious mononucleosis-like syndrome.mp.
38. FIBROMYALGIA/
39. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 30 or 31 or 33 or 34 or 36 or 37 or 38
40. child$.mp. [mp=ti, ab, rw, sh, it, tn, ot, dm, mf, hw, ty, id]
41. infant$.mp. [mp=ti, ab, rw, sh, it, tn, ot, dm, mf, hw, ty, id]
42. adolescent.mp. [mp=ti, ab, rw, sh, it, tn, ot, dm, mf, hw, ty, id]
43. adolescent/
44. adoles$.mp. [mp=ti, ab, rw, sh, it, tn, ot, dm, mf, hw, ty, id]
45. teenage$.mp. [mp=ti, ab, rw, sh, it, tn, ot, dm, mf, hw, ty, id]

46. teenage.mp. [mp=ti, ab, rw, sh, it, tn, ot, dm, mf, hw, ty, id]
47. young people.mp. [mp=ti, ab, rw, sh, it, tn, ot, dm, mf, hw, ty, id]
48. youth$.mp. [mp=ti, ab, rw, sh, it, tn, ot, dm, mf, hw, ty, id]
49. 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48

Supplementary searches were also carried out for the individual questions; details available on request.

APPENDIX 3–List of Delphi Participants

Name		Job Title
Beverley	David	Consultant Paediatrician
Boon	Andrew	Consultant Paediatrician
Campion	Peter	Professor of Primary Care Medicine
Chalder	Trudie	Professor of Cognitive Behavioural Psychotherapy
Clinch	Jacqui	Consultant Paediatric Rheumatologist & Adolescent Chronic Pain
Colby	Jane	Former Head Teacher, CFS/ME specialist author and educator
Colver	Allan	Consultant Community Paediatrician & Reader in Community Child Health
Conway	Steve	Consultant Paediatrician
Cooke	Richard	Professor of Neonatal Medicine
Cox	Diane	Senior Lecturer in Occupational Therapy
Davies	Sheila	Parent of Child with CFS/ME
Dunsire	Alison	Parent of Child with CFS/ME
Evans	Sarah	Senior Educational Psychologist
Garralda	Elena	Professor of Child and Adolescent Psychiatry
Glaser	Danya	Consultant Child & Adolescent Psychiatrist
Goddard	John	Consultant in Paediatric Anaesthesia & Pain Management
Leitch	Alisdair	Young person with CFS/ME
McFarlane	Peter	Consultant Paediatrician
McKechnie	Sue	Head of Children's Physiotherapy
Moss	Jill	Support Group Representative
Naeem	Ahmad	Consultant Paediatrician
Ninan	Titus	Consultant Paediatrician
Pearce	John	Consultant Paediatrician
Perrett	Christine	Young person with CFS/ME
Pinching	Anthony	Professor of Clinical Immunology
Platt	Mary Jane	Senior Lecturer Public Health Medicine
Richards	Jo	Consultant in Child and Adolescent Psychiatry
Rideout	Susan	Clinical Specialist Physiotherapist – Paediatric Neurosciences
Speight	Nigel	Consultant Paediatrician
Spender	Quentin	Child and adolescent Psychiatrist
Stanton	Alan	Consultant Community Paediatrician
Tamhne	Rashmin	Consultant Behavioural Paediatrician
Taylor	Sharon	Specialist registrar & Hon lecturer - Child & Adolescent Psychiatry
Taylor	Tim	Consultant Paediatrician

Tripp	John	Senior Lecturer/Consultant Paediatrician
Tyrrell	Jenny	Consultant Paediatrician
Tyrwhitt	Charlotte	Parent of Child with CFS/ME
Vickers	David	Consultant Paediatrician (Community child health)
White	Peter	Honorary Consultant Liaison Psychiatrist and CF Clinic Lead
Whitehouse	William	Consultant Paediatric Neurologist
Wright	Barry	Consultant Child and Adolescent Psychiatrist

All members completed the first round,
37 members completed the second round, 27 members completed the third round.

APPENDIX 4 – CFS/ME Diagnostic Criteria Table

These tables offer summaries of the specified diagnostic criteria. For fuller details on each set of criteria, readers are advised to consult the original papers (see p. 117).

Oxford Criteria (Sharpe et al 1991) Research Criteria, Adult	• Fatigue as the principal symptom • A definite onset and not life long • Severe and disabling fatigue affecting physical and mental functioning. • The fatigue should have been present for a minimum of 6 months, during which it was present for more than 50% of the time. • Other symptoms may be present, such as myalgia, mood and sleep disturbance. **Exclude** A. Patients with established medical conditions known to produce chronic fatigue B. Patients with a current diagnosis of schizophrenia, substance abuse, manic depressive illness, eating disorders and organic brain syndrome.
US Centre for Disease Control (CDC) 1988 (Holmes et al 1988) Research Criteria, Adult	**Major:** - **New onset of persistent or relapsing disabling fatigue for 6 months with at least 50% activity reduction and that does not improve with bed rest.** - **Exclusion of other diagnostic possibilities after thorough history, physical examination and appropriate lab tests.** **Minor:** **6 or more of the following symptom criteria.** • Mild fever • Sore throat • Painful lymph nodes • Unexplained muscle weakness • Myalgia • Prolonged fatigue (>24 hr) after exercise • Headaches • Migratory arthralgias • Neuropsychologic symptoms • Sleep disturbance • Onset of symptom complex from a few hours to a few days. And 2 or more of the following physical criteria: • Low grade fever • Nonexudative pharyngitis • Palpable or tender lymph nodes.
Australian Lloyd et al (1990) Working case definition (used for research) Adults and Children	• Chronic persisting or relapsing fatigue of a generalised nature, exacerbated by minor exercise, causing significant disruption of usual daily activities, and present for greater than six months. • **Neuropsychiatric dysfunction** including impairment of concentration evidenced by difficulty in completing mental tasks which were easily accomplished before the onset of the syndrome; and new onset of short term memory impairment. • **No alternative diagnosis** reached by history, physical examination or investigations over a six month period.

US Centre for Disease Control (CDC) 1994 (Fukuda et al 1994) Research Case definition- Adults	**1. Clinically evaluated, 'unexplained', persistent or relapsing fatigue for 6 or more months that is of new or definite onset.** • Not the result of ongoing exertion • Not substantially alleviated by rest • Resulting in substantial reduction in previous activity level. **AND -** **2. Concurrent occurrence of 4 or more of the following symptoms during at least 6 consecutive months and not predating the fatigue.** • Impairment in memory or concentration • Sore throat • Tender lymph nodes • Muscle pain • Multijoint pain without arthritis • New headaches • Unrefreshing sleep • Post exertional malaise (>24 hours) **Exclusions:** • Active or unresolved medical conditions that may explain fatigue. • Current or past diagnosis of major depressive disorder with psychotic or melancholic features; bipolar affective disorder; schizophrenia; delusional disorder; dementia; anorexia nervosa; bulimia nervosa. • Substance abuse within 2 years before onset or any time afterward. • Severe obesity. **Inclusions:** The following conditions do not exclude a patient from the diagnosis of unexplained chronic fatigue. • Conditions defined by symptoms that cannot be confirmed by laboratory tests (e.g., fibromyalgia, anxiety disorder, multiple chemical sensitivity disorder etc) • Conditions documented to be under adequate treatment • Conditions definitively treated before development of chronic symptomatic sequelae (e.g. Lyme disease). • Isolated findings insufficient to suggest an exclusionary diagnosis.

Canadian Definitions (Carruthers 2003) Clinical Diagnostic Criteria	For a diagnosis of CFS/ME, a patient must meet the stated criteria 1-4 and 7, and must have two or more of the manifestations listed under 5 and at least one symptom out of two of the categories listed under 6. **1. Fatigue.** **2. Post Exertional Malaise and/or Fatigue**. **3. Sleep disorder.** **4. Pain**. **5. Neurological/cognitive manifestations**: Confusion, impairment of concentration and short term memory consolidation, difficulty with information processing, categorising and word retrieval, intermittent dyslexia, perceptual/sensory disturbances, disorientation, and ataxia. **6. At least one symptom out of two of the following categories** • Autonomic manifestations: Orthostatic intolerance, POTS, delayed postural hypotensions, vertigo, light headedness, extreme pallor, intestinal or bladder disturbances with or without IBS or bladder dysfunction, palpitations, vasomotor instability, and respiratory irregularities. • Neuroendocrine manifestations: Loss of thermostatic stability, heat/cold intolerance, anorexia or abnormal appetite, marked weight change, hypoglycaemia loss of adaptability and tolerance for stress, worsening of symptoms with stress and slow recovery, and emotional lability • Immune manifestations: tender lymph nodes, sore throat, flu-like symptoms, general malaise, development of new allergies or changes in status of old ones, and hypersensitivity to medications and/or chemicals. **7. The illness persists for at least 6 months in adults or at least 3 months in children**

References

Oxford criteria: Sharpe MC et al; A report - chronic fatigue syndrome: guidelines for research. Journal of the Royal Society of Medicine. 1991; 118-121.

US Centre for Disease Control (CDC) 1988: Holmes,G.P.; Kaplan,J.E.; Gantz,N.M.; Komaroff,A.L.; Schonberger,L.B.; Strauss,S.E.; Jones,J.F.; Dubois,R.E.; Cunningham-Rundles,C.; Pahwa,S.; Tosato,G.; Zegans,L.S.; Purtilo,D.T.; Browh,N.; Schooles,R.T.; Brus,I. Chronic fatigue syndrome: A working case definition. Annals of Internal Medicine; 1998. 108; 387-389.

Australian criteria: Lloyd, A.R.; Hickie,I.; Boughton,C.R.; Spencer,O.; Wakefield, D. Prevalence of chronic fatigue syndrome in an Australian population. Medical Journal of Australia ; 1990 Vol 153; 522-528.

US Centre for Disease Control (CDC) 1994: Fukuda,K.; Strauss,S.; Hickie,I.; Sharpe,M.; Dobbins,J.; Komaroff, A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. Annals of Internal Medicine 1994. 121; 943-949.

Canadian Definition: Carruthers et al; Canadian ME-CFS Clinical working case definition, Diagnostic and Treatment Protocols. Journal of Chronic Fatigue Syndrome. 2003. 11 (1)

APPENDIX 5–National CFS/ME Organisations

Organisations listed in alphabetical order:

Action for ME
Web address: http://www.afme.org.uk
Telephone: 01749 670799
Contact: Chris Clarke
Address: Information, membership and services:
PO Box 1302
Wells, Somerset, BA5 1YE

AYME – Association of Young People with ME
Web address: http://www.ayme.org.uk
Telephone: Helpline: 08451 23 23 89 Admin 01908 379 737
Local rate telephone helpline open from Monday - Friday, 10am - 2pm
Membership Contact Services (Professional Pack available).
Address: Association of Young People with ME
(reg charity 1082059)
P.O Box 605
Milton Keynes, MK2 2XD

The ME Association
Web address:http://www.meassociation.org.uk
Telephone: Members: 0870 444 1835
Non Members: 0871 222 7824
Address: The ME Association,
4 Top Angel,
Buckingham Industrial Park,
Buckingham, MK18 1TH

TYMES Trust - The Young ME Sufferers Trust
Web address: http://www.tymestrust.org
Telephone: 01245 401080
(Advice Line hours : 11am-1pm & 5pm-7pm Weekdays – or leave a message)
Address: Tymes Trust
PO Box 4347
Stock' Ingatestone, CM4 9TE

WAMES

Welsh Association of CFS & ME Support
Web addres: http://www.wames.org.uk
Email address: enquiries@wames.org.uk

25% ME Group

Web address: http://www.25megroup.org/
Email address: enquiry@25megroup.org
Address: 25% M.E. Group
4 Douglas Court, Beach Road
Barassie, Troon
Ayrshire, A10 6SQ

APPENDIX 6 – Department of Health CFS/ME Network Coordinators

These details are correct as of April 2005. If you find that the details have changed, please contact Karen Hart at the RCPCH, email karen.hart@rcpch.ac.uk .

Name	Service Area	Email Address	Telephone No.
Louise Wilson	Newcastle	louisewilson365@hotmail.com	0191 2919401
Hiroko Akagi	Leeds	Hiroko.Akagi@leedsmh.nhs.uk	0113 3056731
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Pauline Powell	Liverpool	frednye@blueyonder.co.uk	0151 7063836
Mark Adams	Sheffield	mark.adams2@nhs.net	0114 2718708
Lynne Birchall	Nottingham	Lynne.Birchall@derbyhospitals.nhs.uk	01332 785913
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Angela Tomkins	Surrey	Angela.Tomkins@epsom-sthelier.nhs.uk	0208 296 4274/ 4152 (PA)
Hazel O'Dowd	Bristol	Hazel.O'Dowd@nbt.nhs.uk	0117 975 3890
Michelle Selby	Dorset	michelle.selby@sedorset-pct.nhs.uk	01929 557564
Carol Wilson	Cornwall	Carol.Wilson@centralpct.cornwall.nhs.uk	01326 434764/ 01872 252935

APPENDIX 7– Organisations Consulted on Draft Copy

A draft copy of the guideline was submitted to the following organisations for comments:

- Action for ME – Comments received
- Association of Educational Psychologists
- AYME – Comments received
- Bath/Bristol CFS/ME Young Persons Service – Comments received
- British Association of Counselling and Psychotherapy – Comments received
- British Dietetic Association
- British Paediatric Neurology Association – Comments received
- British Psychological Society
- CFS/ME Collaborative Centre – Comments received
- Chartered Society of Physiotherapy – Comments received
- College of Occupational Therapists – Comments received
- Edinburgh ME Self Help Group – Comments received
- MERGE – Comments received
- Royal College of General Practitioners – Comments received
- Royal College of Physicians – Edinburgh – Comments received
- Royal College of Physicians – London
- Royal College of Psychiatrists – Comments received from a member
- The 25% Group – Comments received
- The ME Association – Comments received
- The National ME Centre
- The Pain Society
- TYMES Trust – Comments received
- Welsh Association of ME & CFS Support – Comments received

Royal College of Paediatrics and Child Health

50 Hallam Street, London W1W 6DE

Telephone: 020 7307 5600 Fax: 020 7307 5601

Registered Charity 1057744