Chronic fatigue syndrome

SUMMARY OF A REPORT OF A JOINT COMMITTEE OF THE ROYAL COLLEGES OF PHYSICIANS, PSYCHIATRISTS AND GENERAL PRACTITIONERS

ABSTRACT—Chronic Fatigue Syndrome (CFS) is not a single diagnostic entity. It is a symptom complex which can be reached by many different routes. The conceptual model of CFS needs to be changed from one determined by a single cause/agent to one in which dysfunction is the end stage of a multifactorial process. Although it is important to recognise the role of factors that precipitate the condition, greater understanding is required of factors that predispose individuals to develop the illness, and those that perpetuate disability.

The relationship between CFS, viral infections and psychological disorders is still not completely understood. There is no evidence that infections have a primary causal role in the vast majority of cases, although they appear to precipitate the disorder in some. Previous personality factors and psychological distress appear to be more important than common viral infections. They may also play an important role in perpetuating disability.

The evidence for structural or functional abnormalities of brain or muscle, or for a disturbance of autonomic or immune function as a primary aetiological factors in CFS is weak. Many of the findings may be phenomena related to the confounding effect of psychological distress, sleep deprivation or prolonged inactivity.

The issues surrounding CFS in children are similar to those identified in adults but there is less research based evidence. The principles of assessment are identical, with the addition of a consideration of family and school factors. Most children should do well with simple management strategies involving behavioral activation, goal setting and return to school. A small number may need more specialist care.

Management of children with severe CFS requires genuine multidisciplinary working and a commitment to physical and psychological rehabilitation.

Most patients should be managed within primary care, not in the general hospital. At present treatment should include appropriate education about the nature of the condition, encourage activity and reduce exercise intolerance, and address relevant psychological and sleep disorders. Recent trials of graded exercise and/or cognitive behavioral treatment indicate that these are helpful in management. The success of these trials emphasizes the importance of doctors encouraging and supporting their patients while they gradually extend their activities. This runs counter to the advice still given to many patients, that activity is harmful and needs to be restricted.

In April 1995 the Chief Medical Officer (CMO) requested that the Conference of Royal Colleges produce a report on the subject of CFS with specific reference to the issues of management and service provision. The initial reason for the request was to enable him to respond to a report produced under the auspices of the charity Westcare, which exists to provide support for sufferers from ME (myalgic encephalomyelitis) in the west country. That report was produced by a committee under the chairmanship of Dr David Tyrrell, and was published in September 1994 [1].

In order to respond to the CMO's request the President of the Royal College of Physicians and the Royal College of Psychiatrists, and latterly the Royal College of General Practitioners nominated an expert committee. This met on several occasions between July and December 1995 under the chairmanship of Professor Francis Creed. The members of the committee were drawn from medicine, psychiatry, paediatrics and general practice. Each had relevant clinical experience of this subject, and nearly all were actively involved in original research in the area. The non-clinical member was Mr John James, Chief Executive of the Kensington, Chelsea and Westminster Commissioning Agency, who contributed a summary with the permission of the editor specifically in mind. Members of the committee were asked to produce a series of short working papers covering infectious diseases, immunology, adult psychiatry, neuroimaging, epidemiology, neurophysiology, child psychiatry etc. Specific instructions were given that the committee would be guided by the principles of evidence-based medicine. This is particularly relevant in the field of CFS, where opinions are often held with considerable intensity in variance with the quality of the evidence. Any recommendations were to be accompanied by published evidence, supplemented where necessary by clinical experience.

This paper summarises the final report, which has been approved by the councils of the three Colleges.
References to the original literature are found in the full report [2].

Background to CFS

Chronic fatigue and CFS are not new. The illnesses now considered under these labels have been recognized for many years. An historical perspective induces a certain humility—we have been here before. Many of the problems that confront both patients suffering from fatigue syndromes and the doctors attempting to understand and heal them have been addressed in the past, sometimes more successfully than at present. Why, therefore, was this report requested at the time it was? One reason is the recent rise in prominence of patients with the label myalgic encephalomyelitis (ME), itself linked to several well publicized claims from both sides of the Atlantic of a viral aetiology for otherwise unexplained fatigue. Although these claims now appear premature they attracted considerable interest from patients, doctors and the media.

Raising the profile of the chronically fatigued patient was helpful, but the accompanying controversy was not. The debate on CFS/ME is often accompanied by simplistic and inaccurate polemics, especially the contrast between ‘real’ and ‘unreal’ disease, the latter frequently being seen as synonymous with psychological disorder. The term ME is itself contentious; it is currently attached to too wide a range of conditions to be meaningful.

Definitions—what’s in a name?

The most accurate term for the syndrome under consideration is the chronic fatigue syndrome (CFS). This can be operationally defined, a prerequisite for clinical research. It is a short and accurate label, free from proven aetiological claims. Like other operationally defined conditions, it can be graded according to severity.

The committee rejected the use of the term ME. Encephalomyelitis describes a distinct pathological process, absent from this condition. Use of the term erroneously endorses the existence of a specific pathology for which there is no evidence. It has been suggested that there is a wide group of disorders, which fall under the term CFS, which is a primarily psychosocial and a core called ME, which is more severe, has a characteristic pattern of fatigue, and is primarily of organic origin. We found no evidence to support this. That group within CFS with more symptoms, profounder fatigue, greater disability, and longer illness duration is the subset with the strongest association with psychological disorder. Such an association does not indicate that psychological disorder is the cause of greater disability. However, suggestions that the greater the severity of symptoms or disability, the greater the chance of finding an ‘organic’ aetiology, are misguided.

Epidemiology

The historical literature contains many examples of unusual illnesses, often in confined populations. The term epidemic is used to describe these phenomena. The evidence for epidemic transmission is usually based on case reports and case series. The study of epidemic transmission is based on case reports and case series. The study of epidemic transmission is based on case reports and case series. The study of epidemic transmission is based on case reports and case series. The study of epidemic transmission is based on case reports and case series. The study of epidemic transmission is based on case reports and case series. The study of epidemic transmission is based on case reports and case series. The study of epidemic transmission is based on case reports and case series. The study of epidemic transmission is based on case reports and case series.
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Muscle dysfunction

The report identifies ten studies dealing with muscle function and CFS. There is no consistent evidence of a primary disorder of muscle in most, and no evidence of any changes in muscle structure that could not be explained by the consequence of illness. This is consistent with the frequent observation that fatigue in CFS affects both physical and mental functioning, and is worsened by physical and mental effort.

Immunology

The Committee were aware of a considerable number of studies of possible immune dysfunction in CFS. There are technical differences between studies, perhaps explaining the inconsistent nature of the reported findings. The possibility that any changes might be secondary to confounders such as neuroendocrine variables, sleep disorder or psychological distress has been insufficiently addressed. The presence of immunological dysfunction has not been associated with clinical status or clinical outcome. This is an area for more multidisciplinary research.

Psychiatry and neuropsychology

We agree that chronic fatigue syndromes often do not fit neatly into the conventional view that disease is either ‘physical’ or ‘psychological’ [1]. In this respect, CFS does not present a new or unique problem in medical practice. It illustrates the difficulty that modern medicine sometimes has in responding to disorders that have both physical and psychological components, and the limitations of an over-narrow biomedical model.

There are over 20 published studies concerning the possible role of psychiatric disorder in CFS. Between one half and two-thirds of individuals seen in either primary or specialist care with a diagnosis of some form of chronic fatigue syndrome also fulfill criteria for psychiatric disorder, chiefly depression, anxiety or somatisation disorder, in all studies, at least one third do not.

There are a number of explanations for these findings. The first is that psychiatric disorder is simply a reaction to physical illness. However, five studies that compare CFS with chronic neuromuscular or rheumatological disorders show that this is untenable.

The possibility of selection bias was also considered, but studies in primary care have shown similar associations. The report favoured three, overlapping explanations. The first is that CFS and psychiatric disorder share a common origin in both neurological and psychosocial dysfunction. The second is that the overlap is partly aetiological, since the operational definitions for CFS and the common psychiatric disorders themselves overlap. The third is of misdiagnosis. The key word is heterogeneity—we noted a recent study
that suggested that in some patients symptoms were associated with psychiatric disorder, some with abnormal exercise responses and some with neither.

We also considered the welcome recent upsurge of neurobiological research into CFS, including studies of neuropsychology, neuroimaging and neuroendocrinology. At present no particular pattern can be discerned in the results. Formal disorders of intellect and memory cannot be confirmed in CFS, despite the severity of the subjective complaints, but a disorder of sustained attention seems probable. Functional neuroimaging shows abnormalities, but whether these are associated with psychological morbidity, or indeed are a consequence rather than a cause of cognitive difficulties, remains to be determined. There is no pathognomonic neuroimaging finding in CFS, nor is neuroimaging a diagnostic tool. Finally, we noted recent work on the neuroendocrinology of CFS indicating a disturbance of the hypothalamic-pituitary axis (HPA). Such work has considerable attraction, since the function of the HPA axis has relevance to the clinical characteristics of CFS. However, the nature of these abnormalities remains to be confirmed; recent research has suggested that some are secondary to other behavioural changes in CFS, such as sleep disorder.

Key points

- CFS cannot be considered either physical or psychological—both need to be considered simultaneously to understand the syndrome.
- The depression which is found in one half of patients cannot simply be regarded as secondary to the disability and dysfunction associated with CFS.
- The number of psychiatric symptoms increases with number of somatic health problems—the most severe forms fulfills criteria for somatisation disorder, in which disability is profound.
- Structural and functional neuroimaging and neuroendocrine investigations have not led to consistent abnormalities being demonstrated in CFS. More clearly established normal ranges are necessary to interpret the observed abnormalities. These changes may be characteristic in some subgroups, but may also be due to such confounding factors as sleep disturbance and prolonged inactivity.
- Reports of cognitive abnormalities are similarly inconsistent.
- Current findings in relation to muscle dysfunction and immune abnormalities are open to several interpretations. There is no compelling evidence for a substantial primary role of neuromuscular dysfunction.
- Further research should be encouraged into neurobiological aspects of CFS, using adequate case definitions, sample sizes and assessment of confounders.

Presentation, assessment, investigation and management of CFS

At the core of CFS is the concept of easy to profound fatigue, which is made worse by physical or mental exertion. Symptoms labelled 'typical' are not unique and can be encountered not only in CFS, but in a variety of conditions, physical or psychological. The diagnostic abnormal physical signs in CFS patients can be any tenderness of the neck, but cervical lymph nodes are unusual. Some patients develop tender lymph glands. Clinically significant lymphadenopathy should not be accepted as a cause of CFS—cause for concern.

Patients need to be assessed using a biopsychosocial approach. Some doctors and patients report biological and psychological symptoms are inadequately recognised, and a thorough medical examination is necessary to ensure that a social assessment, generic mental health care also lack the relevant skills, or be unacceptable.

The report strongly endorses the role of the clinician in the management of CFS. It acknowledges the importance of early treatment in primary care, with development of a collaborative therapeutic relationship and the need to prevent chronicity. There are still problems and limitations. We are aware of claims that some do not exhibit the patient's symptoms with such as to pull yourself together, although such reports are known to decline.

In assessing patients with exhaustive fatigue important to strike a balance between under Investigation. There is too often a tendency to ignore physical illnesses to be overinvestigating possible psychosocial disorders to be investigated. The need for investigations will vary largely by the results of a good clinical history and physical and psychiatric examination, all are mandatory. Unless these are pointed in the examination, other laboratory tests were largely unhelpful in anyone with fatigue less than six months. Studies of selected patients have revealed changes in neurotransmitters, but these must be interpreted in the context of the patient's clinical symptoms. Their significance is unclear, and reliance on them is unwise. The following simple tests are a guide to under-and over-investigation.

- Full blood count
- Acute phase protein changes (ESR, CRP)
- Liver function tests
- Creatine and electrolytes
- TSH and free thyroxine
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- Creatine kinase
- Urine test for protein and sugar

The aims of assessment for patients presenting with symptoms suggestive of CFS may be summarised as follows (Table 1):

1. To clarify the nature of the complaint and consider alternative diagnoses
2. To assess the current disability
3. To elicit the beliefs and fears of patient and family about symptoms, diagnosis, and treatment
4. To elicit the beliefs of patient and family about the role, benefits and consequences of rest and activity
5. To identify psychological distress
6. To formulate the problem in terms of predisposing, precipitating and perpetuating factors
7. To provide a basis for negotiating a management plan

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Key points

- Profound fatigue, made worse by minimal physical or mental exertion, lies at the core of CFS but there are no other cardinal features, abnormal physical signs or laboratory tests which can confirm the diagnosis.
- Biopsychosocial investigation is essential—this is best provided in primary care. Secondary care units should provide facilities for such assessments when required.
- Unless there are atypical features, limited investigation for alternative diagnoses is appropriate and should be accompanied by assessment of patient’s disability, psychological state and illness beliefs.
- Untreated, the prognosis for those seen in specialist care is of concern. The prognosis in primary care remains uncertain, and requires further research.

Management

Good clinical management relies on the biopsychosocial approach. The doctor should give relevant information, seek to solve problems, look at coping strategies and use a multidisciplinary approach. Depression or anxiety, when identified, should be treated.

The committee was aware of the frequent misgivings and misconceptions that continue to surround the subject of activity, exercise and rest in CFS. The report strongly affirms that cautious, controlled increases in activity remain the cornerstone of the management of CFS. Overcoming the consequences of reduced or variable levels of activity by a programme of controlled increase in activity, often over a time-scale measured in weeks or months, is a crucial part of good clinical care. Rest is contraindicated in CFS; if it has a role, it is only at one component of a strategy for a short period, measured in days or weeks. Activity can be restored in a number of ways. Simple exercise programmes are used in several centres, supported by two randomised controlled trials. There is no evidence that cautious exercise leads to permanent damage or disability in CFS. However, the intensity of exercise should be chosen in the light of the subject’s current capabilities based on knowledge of the degree of physical unfitness and deconditioning. The setting of realistic goals that can be increased in a stepwise manner is important. Over-ambitious or aggressive exercise programmes, or following advice to ‘exercise away the fatigue’ are likely to fail. This can be understood by reference to exercise physiology and the neuromuscular response to uncustomised activity, and does not imply any pathological process specific for CFS. Many CFS sufferers adopt a pattern in which brief bursts of activity, inevitably followed by a worsening of the symptoms of pain and exhaustion, in turn give way to periods of prolonged rest and avoidance of activity.

Effective psychological and physical management may involve replacing varying activity levels with a consistent programme of rest and activity, avoiding extremes of both. Patients should be advised that such a programme of gradually increasing activity (in which each increment may be spread over several weeks) may
cause a transient (activity associated) rather than a persistent, increase in muscle fatigue and pain.

Cognitive behaviour therapy (CBT) is another collaborative approach to rehabilitation that incorporates elements of attributional change (looking for alternative explanations for symptoms), activity management and graded target setting. A recent systematic review of three randomised controlled trials concluded it is a promising and cost-effective approach recommended for the outpatient management of CFS.

The prevention of disability, particularly in primary care, requires encouragement to be active. Prolonged rest is associated with secondary disability. We are therefore concerned about such advice as the need to reorganise life in order to live within your limits, which carries a risk of perpetuating disability. Certain illness beliefs may have an adverse effect on outcome—such as the fear that any activity causes an increase in fatigue is damaging; that 'doing too much' causes permanent muscle damage; and that CFS is irreversible or untreatable. Such inaccurate beliefs might fuel avoidance of activity and, then be reinforced by the pain and fatigue which inevitably follow such attempts to increase activity levels. This in turn might lead to increasing restrictions on activity, frustration, loss of control and demoralisation.

There is also anecdotal opinion suggesting that rehabilitation needs to take account of the 'stages' of illness which usually implies that during 'active' phases of illness patients need to restrict their activity. We know of no evidence to support this. Two classic randomised controlled trials suggest that early exercise in the aftermath of a proven viral illness is not only safe, but beneficial.

Many sufferers make significant lifestyle changes as a result of illness. These may include altering their response to stressful events, adjusting their goals and leisure activities, altering their coping strategies, and reassessing their priorities and values. These need to be acknowledged, but in the context of encouraging recovery and preventing relapse, rather than reinforcing further withdrawal.

Drug therapy

The list of treatments for which therapeutic claims are made in the context of CFS is a source of concern. There is no conclusive evidence supporting any drug regime for CFS. We found no role for immunoglobulins, antistaminics or immunotherapies or viral agents. Experimental treatments such as immunotherapy should be given only as part of controlled clinical trials. The committee saw no role for vitamin or dietary supplementation, and was unconvinced of the efficacy of magnesium or evening primrose oil.

Antidepressants are used by a variety of clinicians. It is not clear what proportion are used in the care of patients with CFS. At present most of the favourable evidence comes from controlled studies. Two placebo-controlled trials of fluoxetine are inconclusive—one study evidence of efficacy, the other finding no evidence. At present we continue to endorse the antidepressants in those CFS patients with depression whilst accepting that the evidence is incomplete in other indications.

**Key points**

- Acupuncture of the patient's symptoms and use of therapeutic alliance are the starting points in the management of CFS.
- Gradual return to exercise is sometimes successful. The process should be monitored.
- Cognitive-behavioural therapy has been shown to be effective in recent controlled trials.
- Some patients need help to adjust their present lifestyle to one of consensual and more modern activity.
- More randomised controlled trials of treatment in primary care are required.

**Children**

CFS does occur in children and adolescents, but no firm information on its prevalence. We are aware of no evidence that severe forms are more common in children than in adults. The symptoms encountered in children are similar to those in adults. The period of illness and the outcome may be quite different, with a more rapid improvement, and some children may experience a second illness. Children may also have a variety of psychological problems, such as anxiety, depression, and the symptoms of CFS may be influenced by these.
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Assessment

It is important to appreciate the validity of the child's complaints. Children are as, if not more, sensitive to any suggestion their ill health might be 'spurious' or 'all in the mind'. As we undermine the reality of the child's symptoms reduces the risk of a defensive reaction by either the child or family. This, though, although exploration of education, family and psychosocial issues is always indicated, this must always be done with tact and sensitivity, especially as many families continue to see the problems as 'merely organic'.

Investigation

As in adults, it is essential that a full and precise physical examination is performed in every case, but the number of physical investigations should be kept to a minimum unless there are specific pointers in the history or examination. Laboratory investigations are usually unhelpful, with the exception of tests for infectious mononucleosis. Recent EBV infection can only be diagnosed by the presence of VCA IgM antibody.

Management

Measles epidemiologists exist to inform appropriate management in children. Case series from specialist centres report the success of behavioural activation packages, often linked with a family therapy approach. Children at home should be reserved only for the most severely affected and should be for as short a time as possible and always in close liaison with the school. In severely affected children, work with the family and liaison between health and education services is invariably required.

Outcomes

A recent paper reported the outcome of a case series of 80 children with severe chronic fatigue, most of whom recalled a triggering upper respiratory infection. A programme beginning with careful assessment and engagement, followed by symptomatic relief, reduction of secondary gain by regular school attendance and the gradual resumption of activity despite ongoing fatigue, resulted in a good outcome in 80% of cases. Such findings are uncontrolled and based on selected cases, but contradict unsupported statements such as 'the average length of illness in teenagers lasts about four and a half years'.

Service provision

Most children will be adequately managed by a combination of primary care, school nurse and school authorities, with the support of local paediatric, psychiatric or psychology services where appropriate. Referral to a specialist team may be indicated if there is evidence of specific psychiatric disorder, severe or prolonged disability, or family factors interfering with progress. In the absence of such factors, basic management involves reassurance, explanation, exploration and alleviation of school factors (learning difficulties, exam stressors, bullying), basic goal setting and monitoring with planned increases in activity and planned return to school. These can usually be provided by the GP or primary care team, who will need to monitor the child and family closely. Good clinical practice for severely affected children will usually involve access to a combined unit with facilities for assessment, treatment and rehabilitation. Such units will require close cooperation between paediatricians and psychologists. The necessary skills may involve psychology, occupational therapy, nursing, physiotherapy, dietetics and education.

Key points

- The presentation and management of CFS in children is similar to that of adults. The same criteria for CFS may be shorter than for adults. Early rehabilitation is particularly important.
- Multidisciplinary care is appropriate especially for more severe problems.
- There is an even greater lack of systematical acquired data in children than in adults with CFS and more research is required, particularly on treatment.

Facilities and service provision

Overall, the report emphasises that the management of CFS is first and foremost the responsibility of the primary care team. The majority of cases can be managed satisfactorily in primary care provided that:

- the GP has sufficient understanding, empathy and skills to manage the condition
- other members of the primary care team (physiotherapist, social worker and/or psychologist) can be involved when necessary.

Nevertheless a small number of patients may develop severe, prolonged or complex disabilities that require specialist care. This is an area of utmost need which we see as broader than the narrow perspective of CFS, including chronic functional symptoms and syndromes such as irritable bowel, fibromyalgia, non-cardiac chest pain and chronic pain. All these overlapping syndromes are associated with morbidity and high resource consumption. Their management is
unsatisfactory for both doctor and patient. There is a need for a reconfiguration of general hospital services to address these problems more effectively and efficiently [3]. Service provision for CFS should combine a physical and psychological multidisciplinary care approach. All models for delivering such care involve some form of multidisciplinary working and some form of rehabilitative management strategies. Table 2 gives the essential skills necessary for the task.

Implications for purchasers

In an appendix the report includes some implications for commissioners. The conclusions point out to purchasers that it is likely that CFS is attracting significant resources in both pre- and post-secondary care, some of which has been benefit to the patient. Purchasers should be aware of developments in good clinical practice to improve this situation, whilst acknowledging that uncertainties surrounding the condition.

Commissioners of services can take informed to identify which specialist units in their area are treating patients with established needs reviews to these units their knowledge and understanding of the issues raised in the Joint Committee report, and to draw the findings in the report to the attention of GPs. More effective management of patients, particularly at the primary care level, should avoid waste of resources.

References

1. Report from the National Task Force on Chronic fatigue (CFS) and other fatigue syndromes (PFS, malaise) (NICE), Bristol, 1984.

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Copies of the full report can be obtained by sending a cheque for £12.00 (overseas £15.00) to: The Publications Dept, Royal College of Physicians, 11 St. Andrews Place, London NW1 4LE.