

The course of severe chronic fatigue syndrome in childhood

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SUMMARY

Little has been reported on prognostic indicators in children with chronic fatigue syndrome (CFS). We used interviews with children and parents, a mean of 45.5 months after illness onset, to follow up 25 cases of CFS referred to tertiary paediatric psychiatric clinics.

At its worst, the illness had been markedly handicapping (prolonged bed-rest and school absence in two-thirds); mean time out of school was one academic year. Two-thirds, however, had recovered and resumed normal activities—mean duration of illness to recovery/assessment 38 months—and none had developed other medical conditions. Recovery was associated with specific physical triggers to the illness, with start of illness in the autumn school term and with higher socioeconomic status.

Severe fatigue states in children can cause serious and longstanding handicap but most children recover.

INTRODUCTION

In the past few years there has been a growing interest in conditions with chronic fatigue as a main symptom. The names that have been used range from myalgic encephalomyelitis (ME) to neurasthenia. Lately 'chronic fatigue syndrome' (CFS) has been preferred, since it has no connotations for aetiology or underlying pathological processes, about which little is known.

In contrast with the published work on adults with chronic fatigue syndrome, little research attention has been given to children. Several clinical reports—often from tertiary paediatric infectious disease clinics—have described the main features and outcome in children and young adolescents^{2–9}. When the standard criteria^{10,11} are applied, children resemble adults in that clinical and laboratory investigations offer no explanation. The rule that the illness should have been present for at least six months before a diagnosis is made is not always followed: one report, for example, includes children with illness duration of only 1 month². However, the impression is that most children or young people with CFS have been ill for a long time.

Follow-up enquiry indicates that many children recover or improve^{12,13}. However, the follow-up time in different studies has varied from 4 to 45 months, the length of illness to recovery is usually unclear and the cursory nature of the

enquiry (usually telephone contacts) does not allow detailed assessment of physical and psychological status. Thus, we know little about prognostic indicators.

The aim of the present study was to ascertain through detailed interviews the 2–4 year outcome of handicapping fatigue syndromes in children who had been assessed and/or treated at tertiary paediatric units and to document illness-related and social factors related to outcome.

METHOD

The sample

The case notes of 50 children and adolescents who had attended two London tertiary paediatric/psychiatric centres over the previous 5 years with complaints of tiredness/fatigue were reviewed. Only youngsters who had fulfilled the 'Oxford criteria' for chronic fatigue syndrome as defined by Sharpe *et al.*¹¹ (Box 1) were included in the study.

Of the 50 cases 18 (36%) were excluded. 3 children were below 12 or above 20 years of age at the time of follow-up (and therefore outside the age-range covered by some of our measures), and the parents of one child who fulfilled the criteria had had a markedly oppositional attitude towards staff on assessment. This left 46 cases. In one other case the fatigue had not been severe enough to cause impairment; in 2 cases physical illness could have contributed to the complaint. 11 children (or 24%) did not fulfil the Oxford criteria for CFS and had an explanatory psychiatric disorder for the fatigue: depressive disorder and other somatoform disorders were each present in 4 cases;

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Box 1 Oxford research criteria for diagnosis of chronic fatigue syndrome

Syndrome characterized by fatigue of definite onset as the main symptom

The fatigue should have been severe and disabling, affecting physical and mental functioning

The symptom of fatigue should have lasted for a minimum of 6 months during which it was present for more than 50% of the time

Other symptoms may be present, particularly myalgia and mood and sleep disturbance

Patients with established medical conditions known to cause chronic fatigue should be excluded from the definition. All patients should have a history and physical examination

Patients with current diagnosis of schizophrenia, manic depressive illness, substance abuse, eating disorder or proven organic brain disease should also be excluded from the diagnosis. Other psychiatric diagnoses, such as depressive illness, anxiety disorders and hyperventilation syndrome are not necessarily reasons for exclusion

schizophrenia, bipolar disorder and school phobia in one case each. This left 32 eligible adolescents fulfilling the Oxford criteria, who were then approached for the study.

Measures**Information about patients**

A semi-structured interview was developed for the study and given to both parents and children individually. It provided information on sociodemographic data and present physical status, details on the history and characteristics of the CFS with special emphasis on the worst episode of the illness, medical contacts and treatments, and early medical, developmental and psychiatric history. The socioeconomic status of the family was defined by the occupation of the main breadwinner¹⁴.

We assessed the severity of fatigue over the month before the research interview (last week's fatigue in the 2 cases where there had been major fluctuations over the previous month) and the predominant levels of fatigue during the worst episode of illness, with a visual analogue 0–10 point scale. The degree of associated social handicap was assessed through direct questioning on school attendance, stress or problems in interactions with family members or in peer relationships, and ability to perform usual age-appropriate household chores.

Impairment in school attendance was scored as: no impairment (child having only occasional days off school); mild (child attending at least 85% of the time); marked (child attending between 50% and 85% of the time); severe (less than 50% attendance), and very severe (child has not attended school at all for at least a month). Impairment in performing usual activities at home was scored as: none (child performs most of the activities he/she used to before the illness or those expected premorbidly); mild (child

performs more than half the usual activities he/she used to do); marked (child performs less than half these activities); severe (child is dependent on a carer for basic tasks and spends most of the day resting).

Impairment, caused by the tiredness, of relationships within the family and with friends was rated as: none (symptom has no effect on interactions); mild (relationships slightly affected); marked (interactions markedly affected); severe (symptoms interfere a great deal with child's ability to interact with others—i.e. the child gets into frequent arguments, is extremely irritable or severely withdrawn at home, contact with previous friends only by telephone and occasional).

We assessed sleep pattern and disruptions and associated physical symptoms at follow-up and through retrospective enquiry about the worst episode of CFS. First we asked parents and children whether the children had had problems with sleep. If yes, they were asked what the disturbance was—whether initial, middle, or terminal insomnia; whether circadian reversal, non-restorative sleep, hypersomnia or a combination of these. The severity of the sleep disturbance was rated as none; slight (happens occasionally); moderate (happens around half the nights); severe (present almost every night).

The presence of associated physical symptoms was enquired about in two ways. Patients and parents were asked to report any associated symptoms over the previous month and also to fill in the Children's Somatisation Inventory (CSI)¹⁵ to record symptoms experienced over the three months before the interview. The CSI contains a list of 35 physical symptoms rated on a 5-point intensity scale.

Information about the parents

We obtained details on the family's medical and psychiatric history. We developed a family health index where 1 point was given to the presence of any current or past illness (psychiatric, physical, psychosomatic or a combination of these). Additional points were given to each if it was described as chronic (lasting for more than one year) and if it had caused marked impairment (1 month off work or school). This score system was applied to problems reported for each member of the nuclear family and of the extended family. The psychiatric status of the parent (mother) at the time of the research interview was assessed by use of the General Health Questionnaire–12, a well-validated self-administered screening test for psychiatric disorder¹⁶.

We used the statistical package SPSS for Windows. Because of the small sample size and the non-normal distribution of many of the variables, the results of non-parametric tests of significance are presented here. However, in most cases parametric tests resulted in similar findings. The Mann–Whitney test and chi square test of

association (or Fisher's exact test when appropriate) were used to compare ill and recovered groups (the latter encompassing the fully recovered and the recovered-with-residual-symptoms group).

RESULTS

Of the 32 adolescents with CFS approached for the study, the families of 25 (75%: 15 girls and 10 boys) agreed to take part. The mothers of 25 (their main carer) and 21 children agreed to be interviewed separately. The mean age at follow-up was 15 years (range 12 to 19). All children were white and all but one were born in the UK, 76% were from social classes 1 and 2 and 80% were from intact families. Half were in private education and 7 (28%) had left school and were at work, college or university. 64% lived in the London areas and the rest in surrounding counties. The 7 who refused to take part were comparable to those taking part in age, gender, and socioeconomic status and also in illness features at the time of the original assessment.

Onset of illness

The mean age of onset was 11.7 years (standard deviation 2.2) and in 76% the condition had started in the autumn school term (September to December). It had been precipitated by physical illness in all but one case (flu-like illnesses in 10; glandular fever in 7; other infectious conditions in 5; injury in 1 and acute allergic reaction to wasp sting in 1).

The illness at its worst

We enquired from children and their families about the main features when CFS was at its worst. Since only 2 patients were experiencing their worst episode at the time of interview this information is largely retrospective.

The mean duration of the worst episode had been 17 months (SD 12.3). Functional handicap when the illness was at its worst had been very severe: 57% had been bedridden and 68% totally unable to attend school, with a mean time out of school of one academic year (3.2 terms, SD 1.4). All had stopped socializing with their friends, and family relationships had become strained in 56%.

Most children had physical symptoms other than fatigue when the condition was at its worst. Most commonly they reported headaches and disrupted night sleep (present in 87%), muscle pains/discomfort (62%) and concentration problems (50%). The sleep disturbance was characterized by initial insomnia and/or disrupted night pattern (hypersomnia was a feature in only 17.4%), and it had affected over half the nights in most cases.

Patients were asked to recall symptoms indicative of having suffered a depressive disorder when the illness was at

its worst. Nearly a third (6/20) could not recall major mood changes and it was not possible to make a judgment on whether they had had a depressive illness. Depressive disorders were found to have been present in 40% (8/20 interviews) but in only 12% had the disorder reached the severity of a major depressive disorder.

Child's developmental and premorbid health status

Developmental problems were reported in 16%. Most of the children (72%) were regarded as healthy before the start of the CFS but 28% had had persistent troubles throughout childhood (e.g. repeated infections, speech problems, constipation). Fatigue had been a major feature premorbidly in 12% of the total sample. Serious illnesses in the first year of life had been present in only one child. 7 adolescents (28%) had complained of 'aches and pains' premorbidly, but in none of these had the symptoms been severe or handicapping. Most parents reported the children to have been psychologically healthy before CFS (16% had had behaviour problems and mood changes; one child had an Asperger syndrome diagnosis). Academic difficulties were reported by 16%.

Outcome

The mean time from the start of the illness to follow-up was 45.5 months (SD 21.5). 17 of 25 children had recovered (i.e. they no longer fulfilled the Oxford criteria), recovery being associated with resumption of social activities and school attendance; half of these (8) still had mild fatigue and mild impairment in social life and school attendance. One-third (8) continued to fulfil the Oxford criteria for CFS at follow-up. The mean duration of illness (start of illness to time of substantial recovery) for the whole group had been 37.5 months (SD 19.9). The mean time from end of the worst episode to assessment was 23.8 months (14.4).

There were considerable differences in severity of the fatigue and associated physical symptoms, as well as in functional handicap, between children who had recovered and those who continued to qualify for the diagnosis of CFS. Thus the median fatigue score on the 0–10 point fatigue scale rated by youngsters was 7.5 in the 8 who were still ill, 3.2 in the 8 who had recovered with residual symptoms, and 1.0 in the 9 fully recovered (their parents' respective ratings were 6.7, 3.0 and 2.2). Children in these three groups rated themselves as 45%, 80% and 90% recovered; and the corresponding figures from parents' accounts were 47%, 82% and 100%.

In terms of associated physical symptoms and functional impairment the median number of symptoms on the Child Somatisation Inventory for the 8 still-ill children was 15.5 (total CSI score median 31.5) and 8.5 (total CSI score 11.0)

in the 14 recovered children who completed this questionnaire. Presence of physical symptoms other than fatigue was reported by all 8 still-ill children and by 47% in the recovered group. Marked or severe impairment in peer relationships was reported by 7/8 still-ill children and 2/17 recovered children; marked/severe problems in family interactions by 3/8 and 1/17, and in home activities by 5/8 and 1/17; and school attendance of less than 50% by 5/8 and 0/17. Of the recovered group 11/17 were attending school full time, 3/17 at least 85% of the time and 3/17 between 50% and 85% of the time.

All children had been fully investigated at the paediatric clinic and had been informed and counselled about the illness. In addition, 56% had had some form of alternative medicine (e.g. acupuncture, reflexology, hormonal derivative or mineral replacement, osteopathy), 52% psychological and 36% paediatric treatment. The number of different health professionals seen throughout the illness ranged from 2 to 22 (mean 6.7, SD 3.9). None of the children had developed a physical illness to explain the ongoing or past fatigue symptoms. At the time of the research interview nearly half had physical disorders—eczema/allergies (excluding asthma) in 6, constipation and asthma in 2, migraine in 1 and Osgood–Schlatter disease in 1.

The factor regarded most commonly as helpful was the attitude of the paediatricians at the tertiary centre (being listened to, receiving information about the illness from a doctor familiar with it, ruling out organic disease and reassurance about outcome). This was valued highly by all parents. Half the parents reported unhelpful responses from doctors or schools—lack of sympathy for the child, demanding more than the child could perform, not believing them, implying that there were emotional issues and not valuing physical symptoms as much as parents did. Current chronic illness was present in nearly half the mothers (11/24) and it was as likely to be psychiatric as physical in nature. In 2 mothers the resultant handicap was described as marked. 9/24 mothers had scores on the GHQ indicative of psychiatric morbidity.

Factors associated with outcomes
(Tables 1 and 2)

We examined the association of several demographic, premorbid and illness factors with outcome by comparing the 17 recovered children with the 8 still ill at follow-up.

There were no associations between outcome and gender, age at the start of the illness, or various aspects of illness during the worst episode (e.g. severity of fatigue, duration, severity of sleep disorder, impairment caused by the condition, concurrent depression). Neither were there differences between the outcome groups in numbers of

Table 1 Illness factors associated with recovery

Illness factors	Still ill (n=8)	Recovered (n=17)
Illness starting outside autumn school term*	4 50%	2 12%
Non-specific trigger		
None/non-infectious	1 12%	2 12%
1 Flu-like illness	6 75%	4 23%
Specific trigger†		
Glandular fever	1 12%	6 36%
Other viral or bacterial infection	0 0%	5 29%
Paediatric treatment	1 12%	9 53%
Physical problems at follow-up	1 12%	5 29%
Early developmental problems	3 37%	1 6%

*P=0.05, Fisher's exact test
†For specific versus non-specific P=0.02

Table 2 Family factors associated with recovery

	Still ill (n=8)	Recovered (n=17)
Social class		
I & II	2 25%	17 100%
III & V	6 75%	0 0%*
Broken home	3 38%	2 12%
Maternal health:		
Severely impairing chronic ill-health	3 38%	1 6%†
Psychiatric GHQ-12 score median (quartiles)	6.0(0.5–9.5)	1.0 (0.0–3.0)‡

*P=0.000, Fisher's exact test
†P=0.08, Mann-Whitney
‡P=0.08, Mann-Whitney

professionals seen or experience of psychological or alternative treatments.

Outcome was not linked to earlier history of physical disorders, aches and pains, emotional problems or difficulties with academic work. Features which were found to be linked to a poor outcome at a significant statistical level were: illness starting outside the autumn term (P=0.05, Fisher's exact test), and flu-type illness or no precipitants versus more definite diagnoses as precipitants (P=0.02). At levels short of statistical significance better outcome was associated with fewer developmental problems (P=0.08) and with more medical treatment: of 9 in the recovered group, 6 had had antibiotics, 2 immunoglobulins and 1 a combination of the two; only 1 still-ill child had had antibiotics.

There was a significant association between poor outcome and low socioeconomic status. There were trends for more psychiatric maternal symptoms on the GHQ and

more mothers with chronic health problems in the poor outcome group. We did not find an association between outcome and broken homes. Nor was family health on our family health index associated with outcome status.

DISCUSSION

Unlike previous outcome work on childhood chronic fatigue syndrome, our study used detailed face-to-face follow-up interviews with parents and children. Our results show a favourable outcome in the sample of severely affected children seen and offered treatment in tertiary paediatric infectious diseases/psychiatric clinics: two-thirds resumed normal lives. Follow-up studies in adults seen in specialist clinics have likewise reported the best outcomes^{1,12,17-21}. However, the disorder in the children in our sample had been of long duration (mean 3 years from illness onset), it was associated with other unpleasant physical symptoms and it had severely impeded the child's social adjustment. Health service use had been high. Even after recovery several children were left with residual symptoms and handicap. School absence (mean time off school one year) had been much higher than for most other severe chronic physical disorders of childhood^{22,23}. Together with the lengthy social withdrawal, this means that functional handicap is a key feature of CFS in childhood.

There was a story of infectious precipitants in most of the children; mean age of onset of illness was 11 years, usually during the autumn school term. In many children, therefore, onset would have coincided with secondary school transfer, a well-recognized stress requiring both physical and psychological adaptation. A combination of physical and psychological stresses may have contributed to the development of CFS through reduction in sense of wellbeing. Interestingly, our results indicate that the presence of discrete stress triggers (illness start in the autumn months and more definite medical conditions as precipitants) was associated with a better outcome.

None of the children had developed another physical illness to explain the fatigue syndrome. As in previous samples²⁴ allergic conditions other than asthma were reported commonly (in one-quarter) but were not linked to outcome. The serious reduction in physical activity itself seems likely to have been a perpetuating factor for physical and mental malaise^{10,25}.

Most of the children came from intact families and high socioeconomic groups, and we found little evidence to suggest social stress other than secondary school entry. However, low socioeconomic status did predict poor recovery. Increased psychiatric morbidity and handicapping chronic health problems in mothers were also more common in the poorer outcome group. Whether maternal

psychiatric and physical morbidity are vulnerability factors for the child's condition or whether the former is a response to the stress of the child's illness²⁶, both are likely to undermine mothers' ability to provide sufficiently robust support to promote recovery in the child. However, neither these parental findings nor the presence of early developmental troubles in the child (another possible vulnerability factor) reached statistical significance. The most helpful intervention mentioned by parents was the paediatric assessment at the tertiary centre, which took seriously the family's concerns about medical illness.

Our study is an improvement on earlier reports of childhood CFS outcome because of the larger size of the sample and the thorough nature of the follow-up assessment but it is still based on small sample sizes. Moreover, our results cannot be assumed to apply to samples of less severely affected children not attending tertiary clinics. Further work is required to elucidate the significance of family factors and to identify effective ways of reducing handicap and promoting future physical and mental wellbeing in these children.

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