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A Clinical Study of Chronic Fatigue Syndrome

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Background. This study examines the hypothesis that more recently ill patients with chronic fatigue syndrome (CFS) might have different characteristics from more chronic patients in tertiary referral centres.
Method. Sixty-four patients who fulfilled strict diagnostic criteria for CFS had detailed medical, viral, immunological and psychiatric assessment. Patients were advised to remain within their energy limits. Patient and doctor monitored progress using a scoring system.
Results. Using the Schedule for Affective Disorders and Schizophrenia, patients were placed into four groups: group A (no psychiatric disorder, 35 patients), group B (psychiatric disorder before onset of CFS, 7 patients), group C (coincident psychiatric disorder and CFS, 11 patients), and group D (psychiatric disorder after onset of CFS, 11 patients). There were no viral or immunological differences between the groups. Patients in groups B, C and D had more severe illness than those in group A ($P<0.05$), but patients in group A had more muscle pain ($P<0.05$) than patients in group C. Counselling resulted in 52 patients becoming better; nine remained the same and three became worse.
Conclusions. A lower incidence of psychiatric disorder may characterise patients who are more recently ill, as may the type of associated emotional disorder and better outcome.

Controversy about findings in patients with chronic fatigue syndrome (CFS) has demanded consistent case definition (Sharpe *et al*, 1991; Ho Yen *et al*, 1991). Other factors may influence the clinical presentation of chronic fatigue states, however. Tertiary referrals to specialist centres often present patients who have been ill for many years, and whose symptoms and behaviour may be characteristic of a late stage of the disorder. Descriptive analysis at this chronic stage may delineate adaptation to fatigue (Ho-Yen, 1993) and have less relevance to more recent onset of the condition. The patients in this study came from a secondary referral centre. As these patients are usually more recently ill, it was hoped that our results may explain some discrepancies in the literature. Measures of psychological, viral and immunological states were taken to determine the relative importance of these different factors in the pathophysiology of CFS.

Method

The study population consisted of 64 consecutive patients who fulfilled the entry criteria (Sharpe *et al*, 1991). The patients were physically examined and blood was taken for biological investigations, including a screen for infective agents, as previously described (Ho Yen *et al*, 1991), for influenza A, influenza B, adenovirus, cytomegalovirus, Epstein–Barr virus, respiratory syncytial virus, enteroviruses, including Coxsackie B viruses, psittacosis, *Mycoplasma pneumoniae*, Q fever, *Toxoplasma gondii* and *Borrelia burgdorferi*. The precipitating infection was determined by considering the patient's history and the results of the laboratory investigations. Total B, T cells, T cell subsets (CD2, CD3, CD4, CD8 and CD4/CD8 ratio) and natural killer cells were measured as before (Ho-Yen, 1993). The severity of the illness was measured as previously (on a scale of 1 to 10, with 1 being in bed all day and 10 the patient well; Ho-Yen, 1993). Statistical significance was assessed by the use of the Mann–Whitney test and χ^2 with Yates' correction.

The patients were advised to remain within their energy limits and recognise both physical and mental stress in their lives (Ho-Yen, 1993). All consented to psychiatric assessment. They were interviewed using the Schedule for Affective Disorders and Schizophrenia, which focuses on current and lifetime symptoms of affective disorder. Diagnostic information was amplified where necessary in follow-up interviews at regular intervals over 18 months (as part of a separate treatment trial) and by report from relatives and friends. The fatigue criterion was excluded for the major depressive syndromes. The self-rating General Health Questionnaire and Hospital Anxiety and Depression scale were used to determine outcome.

Results

The characteristics of the patients are shown in Tables 1 and 2.

Table 1
Clinical, immunological and virological findings in the patient groups

	Sex	Mean (s.d.) age: years	Mean (s.d.) duration of illness: months	Mean (s.d.) severity score	Experiencing muscle pain: %	Working or at school: %	Mean (s.d.) T-cell subsets [% of total lymphocyte count]				Virology
							NK: %	CD4: %	CD8: %	CD4/CD8 ratio	
Psychiatric disorder											
before	3F:4M	34.4 (9.3)	18.3 (12.6)	4.7 (2.3)	57	27	10.9 (4.6)	42.6 (7.0)	29.4 (5.2)	1.5 (0.2)	Coxsackie B (2) Adenovirus (1)
coincident	8F:3M	35.6 (11.8)	20.5 (23.1)	3.6 (1.6)	36	9	12.9 (8.8)	37.7 (9.8)	30.8 (8.5)	1.3 (0.4)	Coxsackie B (4) Herpes simplex (1) Lyme disease (1)
after	7F:4M	41.2 (8.4)	30.5 (25.9)	3.8 (1.4)	73	18	13.4 (8.5)	43.7 (19.2)	27.0 (5.7)	1.7 (0.7)	Coxsackie B (5) Influenza B (1)
No psychiatric disorder	26F:9M	35.7 (11.0)	19.4 (15.9)	4.8 (1.5)	75	25	13.1 (8.8)	43.9 (7.1)	29.1 (5.5)	1.5 (0.5)	Coxsackie B (18) Adenovirus (2) Influenza B (1) Epstein–Barr virus (1)

Table 2
Outcome in various patient groups

	Mean (s.d.) severity score		Mean (s.d.) interval: months	Result		
	start	finish		better	same	worse
Psychiatric disorder						
before ($n=7$)	4.7 (2.3)	7.1 (2.1)	15.9 (8.3)	6	1	-
coincident ($n=11$)	3.6 (1.6)	8.0 (1.0)	24.4 (7.2)	11	-	-
after ($n=11$)	3.8 (1.4)	7.2 (2.3)	12.8 (6.5)	9	2	-
No psychiatric disorder ($n=35$)	4.7 (1.5)	7.0 (2.3)	15.8 (10.1)	26	6	3

Diagnoses of premorbid psychiatric disorder were made in 11 patients, 7 of major depressive disorder (10 episodes), 1 of panic disorder, 1 of generalised anxiety disorder, and 2 of alcohol dependence. In 29 patients psychiatric diagnoses associated with CFS were made; 7 developed before, 11 coincident with, and 11 after the fatigue. In 35 patients, no associated psychiatric diagnoses were made. This group had short-lived depressive and anxious symptoms, which were usually reactive to social anxieties and fears of being unable to perform adequately, either physically or mentally, in situations which would not previously have stressed them. Depressed mood in these patients was not accompanied by self-blame or guilt, and appetite and interest were always maintained. Any insomnia tended to be initial and related to physical discomfort. From the psychiatric assessment, the patients could be placed in four subgroups: no psychiatric disorder (35); psychiatric disorder before onset of CFS (7); coincident psychiatric disorder and CFS (11); and psychiatric disorder after onset of CFS (11).

Group comparisons

The clinical, virological and immunological results are summarised in Table 1. Using t and χ^2 tests, and analysis of variance, there were no significant differences with regard to sex, age, length of illness, muscle pain and whether working or at school. The immunological and virological results were also similar in all groups.

The patient's self-rated and the doctor's scores for severity of CFS were not significantly different, and the results in Table 1 represent the average score. The 29 patients with psychiatric disorder had globally more severe illness (lower scores) than the 35 patients without psychiatric disorder. The mean (s.d.) score for the psychiatric group was 3.9 (1.7) and for the non-psychiatric group 4.8 (1.5) ($P<0.05$). Patients without psychiatric disorder had more muscle pain ($P<0.05$) but less severe illness than the patients with coincident psychiatric disorder ($P<0.05$). There were no other significant differences between the groups. The outcome in the various patient groups is shown in Table 2. Significant improvement occurred in all groups: 52 patients were better, 9 the same, and 3 worse.

Discussion

Three-quarters of hospital patients with CFS will have an associated psychiatric illness (David & Wesseley, 1991). This prevalence of psychiatric disorder is high even by comparison with patients in medical or surgical wards, or with other types of chronic medical disorders (Mayou & Hawton, 1986). Such findings in patients with CFS and the overlap with diagnostic criteria for depressive illness have naturally led to questions of aetiology. The significance of associated emotional disorders remains uncertain, however, despite attempts to sequence fatigue and psychological distress and to invoke cognitive processes of attribution and somatisation (Ray, 1991).

About one in four hospital patients are judged emotionally well at the time of assessment (David & Wesseley, 1991). In the present study of a CFS population, with sex ratio, age structure and illness duration closer to that seen in community practice (Ho-Yen, 1993), the proportion of emotionally well individuals is almost one in two. Our patients were ill for a mean of 20.8 months, compared with means of 42–156 months in the hospital studies (Kruesi *et al*, 1989; Manu *et al*, 1989; Hickie *et al*, 1990). The prevalence of 45% for psychiatric disorder is closer to that found in studies of medical patients (Mayou & Hawton, 1986). Hickie *et al* (1990) found a similar prevalence, of 50%, in hospital CFS patients with mean duration of illness of 56 months, although their population was selected from a much larger group and therefore are not clearly representative.

Investigations of hospital patients also find high premorbid and lifetime prevalence rates of psychiatric

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disorder, especially depression (Kruesi *et al*, 1989; Manu *et al*, 1989). The premorbid prevalence rate for all psychiatric illness for our CFS patients is 17%, and this is comparable with epidemiological studies of community samples (Robins *et al*, 1984) and with the findings of Hickie *et al* (1990). This population, therefore, seems no more prone to overt psychological disorder before the illness than the general population.

The role of viral and immunological factors in CFS remains to be defined (David & Wesseley, 1991; Ho-Yen, 1993). There was evidence of a precipitating viral infection in 58% of our patients, and this finding is consistent with our previous results (Ho-Yen *et al*, 1991). The immunological findings are also similar to our previous study (Ho-Yen, 1993). The similar viral and immunological results in those with and without psychiatric disorders suggest that in these terms at least the two populations are biologically similar, and argues against any simple theory of psychological causation or maintenance of CFS. They suggest that the prevalence and type of psychiatric symptoms associated with CFS will depend on the population characteristics and the duration of fatigue.

There is little published evidence on outcome. Of our patients, 80% improved (Table 2) as a result of counselling, and this suggests a better prognosis for patients seen in the clinic at an earlier stage of their illness.

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