

**Introduction**

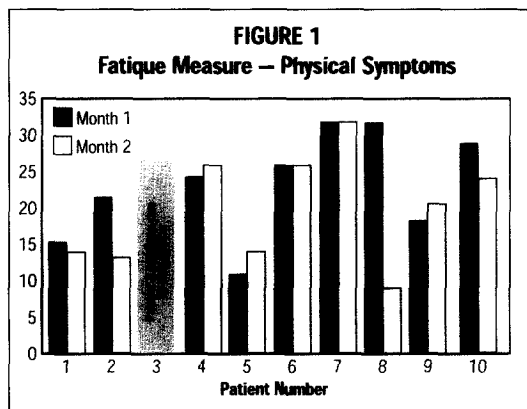
Biobran (MGN-3, an Arabinoxylan compound), is a glyco-protein derived from rice bran and is produced by the partial hydrolysis of the water-soluble hemicellulose fraction of rice bran by carbohydrases derived from *lentius edodes mycelia*. This preparation has been shown to enhance human natural killer cell activity (Ghoneum, 1998). Chronic fatigue syndrome is characterized by deficiency of natural killer cell activity (Caligiuri M., Murray C., Buchwald, et al., 1987). We therefore decided to try the use of Biobran on 10 patients with chronic fatigue syndrome for a 2-month period, assessing their progress by the use of a visual analogue scale, a Likert scale of fatigue (Guyatt G.H., Townsend M., Berman L.B., Keller J.L., 1987) and fatigue scale (Chalder T., Berelowitz G., Pawlikowska T., et al., 1993).

Chronic fatigue syndrome (CFS) is a debilitating disease of increasing social and economic importance. Although women are statistically more susceptible than men, the disease has been diagnosed in children, adults and wide range of ethnic groups (Jordan et al., 1998). Current observation suggests a prevalence of between 10 and 100 cases per 100,000 in the USA. (Levine, 1997). CFS is characterized by persistent relapsing fatigue of greater than six month's duration that is not alleviated by rest and is exacerbated by moderate exercise (Fukuda et al., 1994, Krupp et al., 1991).

Against this background of fatigue, a range of other manifestations are common, but they vary greatly amongst sufferers. These include muscle and joint pain, sore throat and swollen lymph nodes. A further range of symptoms relates to brain dysfunction such as poor concentration, light

sensitivity, sleep disturbance and migraine attacks. Case definition requires the presence of four symptoms in addition to chronic fatigue, and the exclusion of other medical conditions which may present a similar picture (Komaroff et al., 1996).

convincing evidence points to an involvement of an enterovirus in some cases (Archard et al., 1998, Behan et al., 1991, Bowies et al., 1993, Cunningham et al., 1990, Galbraith et al., 1997, Nairn et al., 1995, Swanink et al., 1994).



The diversity of the clinical picture of chronic fatigue suggests a multi-factorial disease with perhaps a common underlying mechanism. Many models of the illness have been studied, but causation remains obscure. The evidence for the involvement of a pathogenic agent, such as a virus or a toxin or a variety of toxins, in at least a proportion of CFS sufferers seems likely. Most noticeably, on several occasions where the disease has produced localized epidemics suggestive of a transmissible agent (Jenkins, 1991). The majority of sporadic cases, are characterized by acute onsets and often described as post-viral syndromes (Behan, 1997, Chalder et al., 1995).

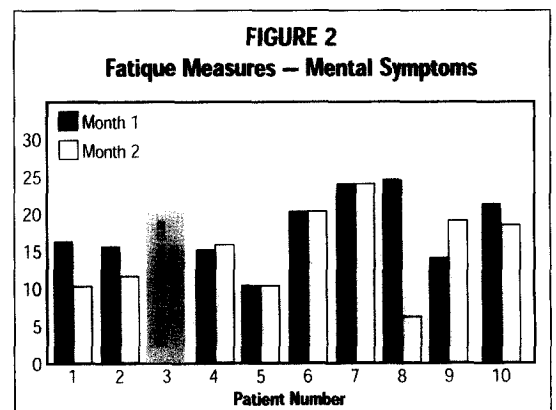
Attempts to identify a specific pathogen have been inconclusive although several agents remain under suspicion, including the Epstein Barr virus and cytomegalovirus (Di Luca et al., 1995, Koo 1989, Martin 1997, Patnaik et al., 1995). The most

Perhaps the most contentious model for CFS is that it is a neurological and psychiatric illness. The extensive neurological symptoms, supported by objective measurements certainly demonstrate that brain function is impaired (Dopino and Kane 1996, Tiersky et al., 1997). At the molecular level, measurements of neurotransmitters indicate that brain disturbances are

related to, but distinct from, depressive conditions (De Luca et al., 1997, Gorbach and Barlett, 1996). Cognitive behavioral therapy has been offered to patients with varying degrees of success, but these studies shed little light on the initial cause of the illness (Deale et al., 1997).

**Material and Methods**

Ten patients were recruited from the author's clinical practice. These were ten consecutive chronic fatigue



patients who came to see the author following the delivery of sufficient Biobran (supplied by Daiwa

Pharmaceuticals, Tokyo, Japan), to carry out this study. The patients were given an Informed Consent for to sign and asked whether they wished to take part in the study. They were then issued enough Biobran (supplied in sachets of powder, taken three time a day, each sachet mixed with a glass of water and taken by mouth half an hour after each meal), to last two months. They were asked to fill out a fatigue scale (Chalder et al., 1993), and a visual

got worse, and three patients (5,6 &7), showed no change.

Of this group of chronic fatigue syndrome patients, Patients 1,2, 8 and 10 had clear viral etiologies. Patient 3, also had a clear viral etiology but withdrew from the study. Patients 4 and 9 had unclear initial causation. They both experienced significant stress in their business and personal lives during the time of the study so there is a possibility of these external factors being responsible for the deterioration seen over the two-month period in these patients.

Patients 5,6 and 7, had clear toxic causations to their chronic fatigue syndrome. Patient 5 had had long-term exposure to poisonous laboratory chemicals, which brought on the slow onset of chronic fatigue syndrome. Patients 6 and 7

had long continued exposure to organophosphate pesticides used in cultivation of mushrooms commercially. Following this, chronic fatigue syndrome developed in both of them.

### Comments

The only patients to show significant improvement had clear viral etiologies. It is in this group of patients that decreased natural killer cell activity has been noted, (Caligiuri M., et al., 1987).

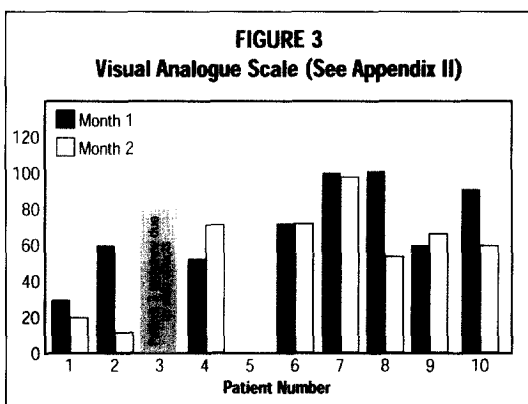
Chronic fatigue syndrome has been commonly noted after toxic exposure, particularly to organophosphates. In these patients no abnormalities in natural killer cell activity has been observed. Two of the patients with unclear etiologies, are difficult to comment on.

Two side effects were observed in Patient 3 and Patient 10. The side effects in Patient 3 have been noted and resulted in this patient withdrawing from the study. In Patient 10, marked cervical lymphadenopathy developed after two weeks of taking Biobran, and continued throughout the whole time the patient was on Biobran. This was taken as indicating immune system activation. Nonetheless this was Patient 10, who obtained an improvement.

### Conclusion

In those patients with a clear viral etiology of chronic fatigue syndrome, Biobran produced significant improvement. This improvement persisted for approximately six weeks following stopping Biobran, (an effect noted by Ghoneum, 1998).

This study shows that Biobran is effective in patients with chronic fatigue

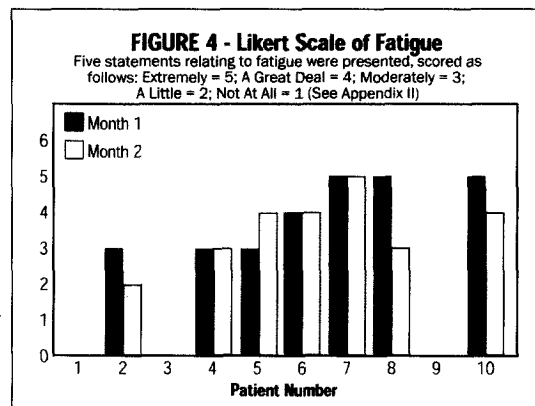


analogue scale, and a Likert scale of fatigue (Guyatt et al., 1987). They were required to fill out the same questionnaire, visual analogue scale, and Likert scale of fatigue again at the end of two months.

### Results

The fatigue questionnaire was scored with the first box scored as one, the second as two, the third as three and the fourth as four. The scores are presented in Figure 1.

From these results, four patients clearly improved (Patients 1,2,8 & 10). One patient withdrew (Patient 3), because following three weeks' course of Biobran she developed mouth ulcers and facial spots appeared; it was unclear as to whether these symptoms were related to the Biobran; she decided at that point to withdraw from the study). Two patients, (4&9),



syndrome who have a clear viral etiology. It does not appear to benefit patients with alternative causations of chronic fatigue syndrome. It would be wise to measure natural killer cell activity of patients with chronic fatigue syndrome before commencing Biobran treatment, and to reserve treatment only for those patient with depressed natural killer call activity. This paper would support such an approach.



