

# **FREE RADICALS IN CHRONIC FATIGUE SYNDROME**

**A method for assay and treatment**

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## **Introduction**

Chronic fatigue syndrome (CFS) is a clinical syndrome characterized by abnormal fatigue, myalgia, muscular weakness, neuro-psychiatric symptoms, slight fever, lymphadenopathy, sore throat, and other symptoms. The symptoms sometimes start after a period of stress or after a viral disease, sometimes without any obvious release mechanism. Typically, the fatigue and other symptoms is aggravated by physical exertion. The cause is unknown and there is no simple diagnostic test and no effective treatment. Among many published findings of abnormalities in CFS have been described morphological changes in muscle mitochondria (1). Such damage to muscles might, theoretically, have been caused by a lack of oxygen, caused by damage to erythrocytes. We, therefore, studied the possible existence of fragile erythrocytes in CFS, using a simple method (2), recently described for the assay of damage to erythrocytes caused by free radicals. We also treated the patients with a potent antioxidant preparation to see, if erythrocyte damage, and clinical symptoms could be ameliorated.

## **Material and Methods**

**Patients.** 31 patients, 8 males and 23 females, age 24 - 67, all fulfilled the criteria for CFS, as described in ref. 3.

**Analyses.** Symptom score, erythrocyte fragility and leucocyte mobility were analysed as described earlier (2). Assays were made before treatment and after one, two, three and four months of treatment. These assays measured degree of subjective ill-being (symptom score), damage to erythrocyte membranes caused by free radicals (erythrocyte fragility) and disturbance of the activity of leucocytes (leucocyte mobility).

**Treatment.** All patients were given Polbax<sup>R</sup>, 7 tablets/day. This is a preparation from pollen and pistils, free from pollen grains and large molecules, thus not being allergenic. It contains very active antioxidants, such as bioflavonoids, tannins and polyphenols (4).

## Results

**Symptoms.** Nineteen of the patients experienced a strong improvement according to their own assessment. Five experienced a slight improvement. Six noticed no clinical change of their ill-being and one patient felt a slight deterioration. The improvement was statistically significant already after one month of treatment and remained so after four months, the decrease in symptoms becoming more marked with time (Table 1). All symptoms tended to decrease with no prevalence for any specific symptom.

**Free radicals.** Erythrocyte fragility was obvious in all patients at the start (Table 1). In twenty-two patients a strong decrease was noted during treatment. In five a slight decrease was found, while in three no change was seen. In one patient a slight increase was noted. Already after one month of treatment fragility had decreased by one third and after four months to less than half. This decrease was statistically significant from one month of treatment and on to four months (Table 1).

**Leucocyte mobility.** Leucocyte mobility was normal in twelve of the patients and decreased in nineteen. During treatment there was no change in eleven of those that were normal at the start, while one showed a decrease. All of the patients that had a decreased activity at the start improved their leucocyte mobility up to normal or near normal. When calculated for the whole group, there was a statistically significant improvement of leucocyte mobility after one - four months of treatment (Table 1).

## Discussion

**Diagnosis.** There is no single test for the diagnosis of CFS (5). Our findings add no new method for the diagnosis, but could rather be a clue to mechanisms involved.

**Etiology of chronic fatigue syndrome.** Although many different causes for CFS have been proposed, such as virus, stress, activation of the immune system or damage to mitochondria, there is no firm knowledge or consensus. The present study gives support to one type of mechanism, damage by free radicals, but does not show, why such damage appears.

Actually, increased formation of free radicals is a general mechanism, known to occur in many situations, such as inflammatory conditions, infections, cancer, physical stress, etc. There are no indications, or at least no documentation, that free radicals could be induced by mental stress.

More importantly, the present findings of damage to erythrocyte membranes by free radicals can explain many of the known symptoms.

**Possible mechanisms.** For some as yet unknown reason, possibly an effect of infections, toxins and other negative factors, cells fail to produce energy, necessary for the maintenance of the normal electrical potential of 70 mV between the interior and exterior of the cells. In this situation the ability to handle free radicals comes in imbalance and a surplus of free radicals will further damage all cells (6). When erythrocytes are thus damaged they become fragile and rigid (4) and their ability to transport and deliver oxygen to cells is impeded. This can explain the earlier findings of muscle mitochondrial damage, muscle fatigue and myalgia, as well as neuro-psychiatric and other symptoms.

**Treatment.** Many different treatments have been tried in CFS, with very varying results. No treatment has become generally accepted and most patients are, in fact, left without effective help. The spontaneous out-come in most patients is a slow improvement, a few experiencing total remission and some remaining severely affected. The present treatment by antioxidants seems logical in view of

the finding of free radical damage with no hint of a possible cause. Further studies using adequate double-blind technique and long-term observations must be performed before antioxidant treatment can be evaluated.

The fact, that there was no tendency to remission and, above all, the logic behind the treatment and the finding of an improvement of erythrocyte fragility and thus a better balance of the handling of free radicals, would indicate that antioxidant treatment may, in fact, be of value in CFS.

Since there is a much larger fraction of the population with fatigue syndrome at a less marked degree (5) and since many patients with similar symptoms, but with more myalgic dominance get other diagnoses, such as fibromyalgia, evaluation of treatment with antioxidants must take a much larger fraction of the population into consideration.

Choice of antioxidant. Most studies using antioxidants have used selenium, vitamins C and E and beta-carotene, singly or in combinations. It is a well-known fact, that there are hundreds of antioxidants, many of them in red, orange, yellow, green and violet vegetables, forming the basis for dietary recommendations in most western countries. (Five servings a day are often recommended in order to improve antioxidant status and thus improve health and decrease cancer risk). So far there are only few antioxidant preparations containing more than a few antioxidants. It can be supposed that the facts mentioned will lead to the increased use of such "broad-spectrum" antioxidants.

## **Summary**

Assay of erythrocyte fragility, a new technique for the determination of cell membrane damage by free radicals, demonstrated the presence of such damage in 31 cases of chronic fatigue syndrome.

Treatment for four months with a preparation from pollen, containing hundreds of antioxidants, a "broad-spectrum" antioxidant, brought about a statistically significant improvement of clinical symptoms to less than half the symptom score after four months. Free radical damage to membranes also decreased to less than half. An important immune defence factor, leucocyte mobility was also measured and an improvement to near normal could be demonstrated in those patients (19 of 31) that had decreased mobility before treatment.

Month	0	1	2	3	4
<b>Symptom score</b>					
Mean	25.4	17.8	17.6	12.6	12.6
S.D.	6.9	7.3	9.2	8.8	7.5
p	-	***	**	**	**
<b>Free radical score</b>					
Mean	21.5	14.3	12.5	13.4	10.3
S.D.	7.3	8.0	8.8	6.9	4.0
p	-	*	**	*	***
<b>Leucocyte activity score</b>					
Mean	3.87	5.37	5.57	5.63	5.40
S.D.	2.13	1.16	0.65	1.06	1.34
p	-	**	***	**	*

\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , probability that the value has changed from time zero = before treatment.

Table 1: Score for symptoms, free radical activity and leucocyte mobility.



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