The Battle for a Cure

When the CFS Research Foundation was launched in1993 we knew that we had a fight ahead of us. Twelve years later when we can examine the basis of the disease it is difficult to remember all the problems which faced us then and how we won through so that our present programme of gene research could go ahead.

In 1993 very little was known about the illness, there was little research and even that was fragmentary and not of the highest standard. The biggest problem with all its ramifications was the result of a letter in the BMJ in 1970 from Dr.C P McEvedy and Dr.A W Beard of the Department of Psychological Medicine at the Middlesex Hospital, stating that the illness was due to mass hysteria. It is difficult to understand why doctors and scientists accepted this. These doctors had no personal experience of the disease

This had a devastating effect; the efforts of doctors such as Dr. Melvin Ramsay, who had been caring for CFS/ME patients at the Royal Free Hospital, were scorned. Patients were told by their GPs that the illness was all in the mind and research was virtually at a standstill. There was then an unfortunate, but understandable, backlash from patients, their families and carers. The hostility between doctors and patients became common knowledge and for a while the press had a field day. This reinforced the scientist's determination to avoid becoming involved in researching the illness. No ambitious scientist wished to become involved in such murky waters.

The Foundation had to tackle all these problems. First, it was necessary to distance ourselves from the strife surrounding the disease. We joined no pressure groups and did not publicise our existence. We decided to keep our heads down and concentrate entirely on research.

'Gold Sandard' Research

It was necessary to bring respectability to the cause of CFS/ME so we established a research committee of doctors and scientists pre-eminent in their fields – three were Fellows of the Royal Society. The Committee decided that it would fund research only if it was of the 'gold standard' and this paid dividends. We now have a substantial portfolio of papers published in prestigious journals.

But the next battle came near to defeating us. Twice I had to consider closing the Foundation, not because of lack of funds, but because we were receiving no grant applications in spite of having contacted every university and medical school in the country. Scientists were just not interested.

It was on the second of these two occasions that in 1999, that we held a meeting of a few distinguished virologists to look at the situation and see if there was a way through. This is where the gene research began. Professor Jeff Almond, who was then at the University of Reading, suggested we should carry out a small pilot study to see if it was possible to examine the genes of sufferers using blood samples and compare them with the genes of healthy controls.

GENE Expression

Gene expression was being used in research of many diseases, but always scientists had taken specimens from a lesion. But there are no lesions in CFS/ME so this research was taking us into new territory and we had to face the fact it might not be successful although we were convinced that it would reveal some new facts. Members of the research committee decided to go ahead and when the results came through they showed that there was a difference in the behaviour of the genes in people with CFS/ME and the healthy controls. This research was undertaken by Dr. Rob Powell, first under Professor Almond and then, after he moved, under Professor Stephen Holgate at Southampton University.

With the accumulated evidence from previous studies and from Dr. Powell's work the research committee met to decide how this could be taken forward. It was decided that a multi-centre study should be undertaken to find precisely which genes were affected and so were producing chemicals which cause the distressing symptoms of the disease. A six-year study was planned of which the first three years are completed.

Initially blood was taken from patients in one clinic together with matched controls and then analysed by scientists from three laboratories in medical schools in the UK and one American laboratory. Fifteen genes were found to be over active and one under active in the patient group, but were normal in the control group. This came as a great relief; we were aware that we were the first in the world to use blood to study gene expression in a disease.

At the time Dr. Jonathan Kerr of Imperial College London was carrying out a study funded by the Foundation examining the genes of patients who had been infected by the parvovirus B19 and had gone on to develop CFS. The committee suggested that Dr. Kerr should submit a grant application for funding to carry out a multi-centre project to study gene expression in CFS/ME patients and matched controls. The grant application that Dr. Kerr submitted was assessed by all the members of the research committee and by two external referees after which it was accepted.

Dr. Kerr identified a CFS/ME clinic in Dorset and with the help of a consultant Dr.Selwyn Richards and a research nurse C R McDermott suitable patients were chosen, including the bed bound, and blood samples were taken for analysis. Because this approach was new and, to a certain extent, experimental a group of scientists from the research committee together with Professor Stephen Holgate, a specialist in this area, met with Dr. Kerr from time to time to discuss progress. We were making use of the best brains to ensure that our research was of the highest standard.

Before the two years were complete the results showed that a number of genes were affected, but Dr. Kerr and his group decided to check the results by using a different scientific technique. The original results were confirmed and fifteen genes were found to be over active and one under active in the patient group but were normal in the control group. This called for the research to be extended so a new programme was instigated. It had been found that the affected genes are in so many different systems of the body so it was imperative that a multi-disciplinary team should undertake the next phase of the project in order that all the different facets could be addressed. The team is built up of scientists with a track record of academic achievement in areas which are affected by the disease.

The Future

And now for the future. Analysis of genes and healthy controls is continuing. Nine clinics in England, Scotland and Wales are providing patients who have agreed to donate blood together with a group of healthy controls. The team will also go on to compare the genes of CFS/ME patients with those of people with other diseases to prove that the genes found to be abnormal are peculiar to people with CFS/ME. The other diseases that are acting as controls are endogenous depression, rheumatoid arthritis, osteoarthritis, MS and prolonged fatigue of one to six months. The team will be looking for variation in gene expression in patients from different parts of the country, hence the clinics being chosen to cover the whole of the Great Britain. The team is also working towards a diagnostic test through the discovery of protein biomarkers of CFS/ME compared with normals and with other diseases.

The researchers will also examine the genes of patients with CFS/ME following documented acute infection with a specific infectious illness. The illnesses that have been chosen are parvovirus B19, Q fever and entroviruses. Another part of the study is to examine, in a smaller group, the relationship between variation in expression of particular genes with variation in particular symptoms of CFS/ME patients.

In yet another part of the study the blood of ten patients with well defined and characterised CFS/ME will be sampled at monthly intervals over nine months and their genes will be examined and detailed records will be taken of the clinical symptoms present at each time of sampling.

Working for a diagnostic test

This is a challenging undertaking the scientists will need hundreds of patients, extra resources for contacting and documenting patients clinically, and resources to do hundreds of laboratory tests. We shall also need to recruit skilled and energetic laboratory workers and provide them with the necessary equipment. However, we have an inspirational research programme ahead of us and a team of distinguished scientists to carry out the work. The scientists are now working towards a diagnostic test and plans are in hand for clinical trials of an appropriate drug.

Those who have suffered from this awful illness for a long time will have also suffered from promises of a cure or a breakthrough, which is expected to solve the problem. They have then been bitterly disappointed when the cure did not materialise or the promised breakthrough was only in the mind of the person who claimed it. Sufferers from the illness have deserved better treatment.

The CFS Research Foundation is determined that all its research will receive the same meticulous care as it has had in the past and there will be no unsubstantiated claims. Doctors, scientists and sufferers can rely on our findings as we progress towards a cure. The battle is not yet won, but we know that victory is not far away.