8. We need to find reliable bio-markers for ME (details)

A bio-marker is an objective measurement that shows an illness is present. Some bio-markers are general purpose measures. For example, a measurement of ESR or CRP in a standard blood test simply shows that there is some underlying inflammation. Some illnesses are spotted through a combination of symptoms and nonspecific tests. Rheumatoid Arthritis, for example, has typically been diagnosed by using several blood tests common to multiple autoimmune diseases, along with with symptoms and possibly joint images. Recently a more specific test for RA has been developed: the CCP antibody test. (Still, it misses many people with RA and some people with CCP antibodies may have other diseases such as lupus, Graves Disease, Sjogren's Syndrome, or even a viral infection such as hepatitis C.)

The best bio-markers either reflect severity or are diagnostic of a specific illness.

While certain bio-markers and other assessments have been suggested for use in ME/CFS patients, agreement on which tests are diagnostic, or even useful in a majority of patients, has been complicated by a devastating lack of funding and by persistent use of a variety of definitions of ME/CFS, some of which are far too broad, and clearly include a variety of illnesses. This inconsistency prevents any useful comparison of results.

The Oxford criteria are so broad that very large sample sizes would be needed to determine subgroups, much larger than have been used up to now. The Fukuda definition of CFS has been used for most of the research into bio-markers, but this still includes a heterogeneous (varied) group of patients. More recently, the tighter Canadian Consensus Criteria has become more prominent. Hopefully, the closely-defined International Consensus Criteria for ME will become the primary diagnostic criteria for such research, and this will make it easier to find bio-markers by reducing the proportion of patients with other illnesses in each group under study. (See 1-further details for explanations of these criteria.)

Until the definitions and bio-marker issues are resolved, there is always doubt that any research can properly represent these patients. Differential diagnoses into subgroups should be a high priority for research, particularly as they would help pinpoint patients who do not have ME/CFS (possibly 40% of the group – see section 4-more), and send them in more useful directions.

We recommend the use of the International Consensus Criteria to identify which patients have ME in a research setting, and to ensure that a representative proportion of more severely affected patients are included. This is the most up-to-date criteria supported by many key researchers who are interested in differential diagnosis; and the inclusion of more severely affected patients is more likely to produce significant markers.

Potentially useful bio-markers and pathophysiological findings cover most of the major systems in the body, and include abnormal proteins, gene expression, oxidative and nitrosative markers, and other aspects of physiology, but there is a need for old bio-markers to be re-evaluated under any new, stricter set of criteria. It is possible that a model of ME pathophysiology will dominate and lead to a diagnostic test, but it is more likely that, as with many other illnesses (such as Rheumatoid Arthritis, mentioned above), we will end up with a cluster of bio-markers which, together with an array of symptoms, determine the diagnosis.

The bio-markers that are described in the next level are only a subset of possible bio-markers, but at the moment appear to us to have promise. In particular, immune abnormalities are numerous, and neurological abnormalities are growing in prominence. Two of the most interesting involve apoptotic DNA (controlling cell death) and blood lipopolysaccharide (LPS - finding toxic materials from the outer membranes of some gram-negative bacteria in the bloodstream), but the full papers on these have yet to be published. One of the most well-replicated is low Natural Killer Cell function.

The PACE trial failed to show good results using CBT and GET for the patients in the study, but it also missed a great opportunity. It could have taken enough data, including blood samples for banking, so that the results could be reworked for other definitions at a later date. We must not waste such opportunities in the future, and insist that the data from future studies is made available for reworking as circumstances develop.