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ME: the last and the next ten years

Margaret Williams **28th April 2015**

What a difference a decade makes in medicine -- or does it?

The two camps in the ME/CFS "battle" remain as far apart as ever, to the continuing detriment of patients and also to the State's limited resources: it is currently claimed that the cost of "CFS" to the UK economy is up to £3.5 billion per annum.

One camp consists of biomedical scientists and clinicians whose research shows that ME is an organic multi-system neuro-immune disorder with protean symptomatology; some consider it likely to be an autoimmune disease with the target organ being the vascular endothelium.

The other camp consists of a small but influential group of UK psychiatrists and insurance doctors (known colloquially as the "Wessely School") who remain convinced that what they refer to as "CFS/ME" is a psychogenic condition where reported symptoms result not from organic disease but from patients' maladaptive beliefs and behaviour, and that the condition can be fully reversed by graded exercise and cognitive behavioural therapy. These doctors appear to be accountable to no-one for their persistent disregard of advancements in medical science, neither to the General Medical Council (the nominal regulators of fitness to practise), nor to their NHS employers (whose conditions of contract used to require keeping up to date with medical progress).

Currently we are at a tipping point, because the "behavioural" camp is slowly but surely being unseated. In the last ten years the quintessence of the ME battleground in the UK has been the focus on pseudoscience, but there is at last a transition underway from pseudoscience to scientific medicine.

Here are some facts, all easily verifiable:

Since 2005, ME has been included in the UK National Service Framework for long-term neurological conditions.

On 30th January 2006 the then Health Minister, Lord Warner, said on the record: *"There is only one World Health Organisation International Classification of Diseases code for chronic fatigue syndrome/myalgic encephalomyelitis, which is G93.3"* (HL3612).

On 2nd June 2008 the Parliamentary Under-Secretary of State, Department of Health (Lord Darzi of Denham) stated: *"My Lords, the Government accept the World Health*

Organisation's classification of CFS/ME as a neurological condition….My Lords, I have acknowledged that CFS/ME is a neurological condition" (HLPQ: Health: Chronic Fatigue Syndrome/Myalgic Encephalomyelitis).

On 21st November 2011 Lord Freud, Minister for Welfare Reform, confirmed in a letter to the Countess of Mar that the Department for Work and Pensions does not consider ME/CFS to be a mental disorder. The letter was unequivocal: "*The Department of Health has indicated that they have 'always relied on the definition set out by the World Health Organisation in its International Classification of diseases (ICD) under ICD code G93.3, subheading other disorders of the brain'. The DWP is in agreement with this view. Therefore, for the avoidance of doubt, I can be clear that the Department does not classify CFS/ME as a mental health disorder".*

Such official confirmation from UK Ministers of State about the correct status of ME would seem to end any argument but, sadly, the "behavioural" lobby refuse to see the world as is actually is and they remain ruthlessly entrenched in their own ideology, ignoring and/or denying the medical science that vitiates that ideology.

Despite Ministers' clear pronouncements, given that key members of the "behavioural" camp have acquired formidable powers and have secured established positions as advisors on "CFS/ME" to UK Departments of State, including the Department of Health and the Department for Work and Pensions, and also to bodies such as the Medical Research Council (MRC) and NICE (the National Institute for Health and Care Excellence), it is their behavioural modification interventions (ie. "brain-washing") that prevail throughout the NHS, with the risk of serious iatrogenic harm to patients with ME/CFS.

Many informed observers believe that within the next ten years this situation will be seen for what it is – a truly appalling medical scandal of astounding proportions, but it is a scandal that (via the auspices of the Science Media Centre and the UK media) many UK luminaries, including the President of The Royal Society, Sir Paul Nurse, and Professor Sir John Beddington, until 2013 Government Chief Scientific Advisor, have condoned without question, as have influential science reporters such as David Shukman, the BBC's science editor (http://www.sciencemediacentre.org/film/); (http://www.meactionuk.org.uk/The-SMC-and-its-campaign-against-MECFS.htm).

The "evidence" of the "behavioural" camp

The PACE trial (**P**acing, **A**ctivity, and **C**ognitive behavioural therapy, a randomised **E**valuation) is by far the most contentious clinical research study conducted in the field in the last ten years. Conceived and executed by psychiatrists Professors Peter White and Michael Sharpe, assisted by a behaviour therapist, Professor Trudie Chalder, it was funded by the MRC, the Scottish Chief Scientist's Office, the Department of Health and the Department for Work and Pensions. The PACE Trial is the only clinical trial that the DWP has ever funded and it did so because it was assured that cognitive "restructuring" would successfully remove people with ME/CFS from claiming State benefits. Recruiting began in 2004 and finished in November 2008.

Problems with the PACE trial were legion, a particular one being that CBT and GET participants (but not those in other arms of the trial) were instructed to ignore their symptoms. Such advice has previously been described as "*dangerous*" in a Witness Statement for the High Court (http://www.meactionuk.org.uk/Statements-of-Concern-for-High-Court.htm).

After the trial had started the Principal Investigators abandoned the protocol-defined thresholds for fatigue and physical function required for a "*positive outcome*" and "*recovery*" and replaced them with far less demanding criteria. These changes were such that it became possible to leave the trial with greater fatigue and worsened physical function and still meet the newly-defined thresholds of *"the normal range"* (this is not the same as normal health, but the media was encouraged to report it as synonymous with "recovery"). The re-calculating and constructing of their own version of *"the normal range"* allowed the Investigators to claim that participants had "recovered": "*This study confirms that recovery from CFS is possible and that CBT and GET are the therapies most likely to lead to recovery"* (PD White et al: Psychological Medicine: 2013: doi:10.1017/S0033291713000020).

The Investigators initially claimed that the PACE trial was to study "CFS/ME" but after publication in The Lancet of selective results in February 2011, the Chief Principal Investigator (Professor Peter White) wrote to the editor in March 2011 saying that the PACE trial "*does not purport to be studying CFS/ME but CFS simply defined as a principal complaint of fatigue".* This was a cause for concern, because funding and ethical approval had been sought and obtained on the basis that the Investigators would be studying "CFS/ME", not "fatigue".

The PACE trial cost UK taxpayers over £5 million and, despite the desperate and increasingly ludicrous attempts of the Investigators and of the Science Media Centre (a founder member being psychiatrist Simon Wessely) to proclaim its success by feeding inaccurate information to the media, it is widely acknowledged to have failed (http://www.bmj.com/content/350/bmj.h227/rapid-responses) and, far from reducing claims for benefits, participants' claims for benefits due to illness or disability actually increased from baseline to follow-up (McCrone et al PLoS ONE 7(8): e40808. doi:10.1371/journal.pone.0040808).

Numerous FOIA requests for the raw data (which does not belong to the Investigators but to UK tax-payers) to be released have been refused on entirely spurious grounds, lending yet more support to the widespread opinion that release would conclusively demonstrate the failure of CBT and GET as vehicles for recovery from ME/CFS, indicating that their proponents have spent their professional lives in a null field. It must not be forgotten that Simon Wessely insists that "ME" does not exist and is but a myth (12th May 1994) or that Peter White asserts that it is definitely a behavioural disorder (5th November 2007).

A sign of maturity is said to be the ability to learn from experience, but these "behavioural" psychiatrists seem to persist in exhibiting a disturbing inability to learn from experience and they appear to remain detached from reality.

For example, the recently published promotion of a study by one of the PACE trial Investigators (Professor Michael Sharpe) is terrifying for patients with ME. Whilst he was Professor of Psychological Medicine at the University of Edinburgh from 1997 – 2012, Sharpe (now honorary Professor at Oxford) and colleagues looked at a cohort of referrals of patients with "medically unexplained symptoms" to neurology clinics, including people with ME/CFS, concluding that: "*The UoE work challenged the once popularly held view that CFS is an organic disorder".*

He and his co-authors now claim that: *"By showing the benefits of accurate identification and targeted treatment of chronic fatigue syndrome, UoE research has influenced worldwide medical practice and …stimulated medical debate…Guidelines and policy debate have resulted in improved patient treatment, with associated economic benefit….These medically unexplained symptoms…cost the NHS £14K per annum per patient. The cost to the UK economy is up to £3.5 billion per annum for chronic fatigue syndrome alone. In 2011, Sharpe and colleagues published the first definitive randomised controlled study showing superior efficacy of cognitive behaviour therapy for CFS* (note: the PACE trial was not a randomised controlled trial) *….The work has been presented at international meetings, and published in high-impact medical journals with global reach….The work has also led specifically to individual service developments across the UK…and directly to changes in what is considered best clinical practice. The work has fed into the development of the International Classification of Diseases (ICD-11) and the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-V)"* (http://impact.ref.ac.uk/casestudiesapi/refservice.svc/GetCaseStudyPDF/23887).

It is difficult to reconcile such over-confident claims with the facts, but not everyone was persuaded and two major US institutions have revised their position on ME/CFS (see below).

As an example of inconsistency, Professor Sharpe claims superb success and global influence of the PACE trial using CBT and GET interventions, but this contrasts with what he actually said on 18th April 2011 on Australian Radio about the PACE trial: *"What this trial wasn't able to answer is how much better are these treatments, than really not having very much treatment at all"* (http://www.abc.net.au/rn/healthreport/stories/2011/3192571.htm).

Given that there is an acknowledged nationwide lack of basic services for ME patients and that most have no access to NHS consultants and never get to see a neurologist, immunologist, endocrinologist or vascular specialist and even have profound difficulty in seeing a GP, Professor Sharpe's claim that the cost to the UK economy of "CFS" alone is £3.5 billion per annum is questionable (J Psychosom Res. 2012;72:242–7). Patients with ME/CFS experience real difficulty in seeing a GP: not only do many GPs refuse to accept that it is a legitimate disorder, but after the BMJ ran a campaign to list "*non-existent*" diseases that are best left untreated, in which ME features along with big ears and freckles (BMJ 2002:324:883-885) -- a campaign with which Simon Wessely was known to have been involved but which he later denied -- patients with ME were removed from GPs' lists, being tersely informed that: "*This practice does not treat non-existent diseases*".

It is a matter of grave concern that these psychiatrists have such power and influence and, moreover, that they are rewarded and lauded for ignoring medical science. For example, in 2004 Peter White was awarded an OBE for his work on CFS, the citation being "*For services to medical education"*; notices circulating at the time proclaimed him as leading the research into CFS/ME and said his OBE was a *"well-deserved honour and acknowledgement of his contribution to work on CFS/ME"* and in November 2012 Simon Wessely (now Professor Sir Simon Wessely, President of the Royal College of Psychiatrists) was awarded the inaugural John Maddox prize for "*standing up for science"* and for his "*courage"* in facing opposition to his beliefs about ME and Gulf War Syndrome (ie. that they do not exist).

The two major US institutions that -- despite the glowing reports of the PACE trial's claimed success -- have revised their position on ME/CFS are the NIH and the CDC.

(1) The US National Institutes of Health, one of the world's foremost medical research centres, convened a Pathways to Prevention working group which in December 2014 published its draft Statement entitled "Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome". It is an important document, as it signifies a major change in attitude towards ME/CFS and casts further doubt on the claimed success of the PACE Trial. The NIH Statement is unambiguous that the Oxford criteria (formulated by the Wessely School themselves and used in the PACE trial) are flawed and lack reliability, thereby confounding the ability to interpret results drawn from studies which used them to select cohorts and noting that use of the Oxford criteria may impair progress and cause harm. This being so, it can be surmised that all previous psychiatric "research" on ME/CFS that used the Oxford criteria (not just the PACE trial) used groups of people who were not properly characterised and thus those results also lack scientific credibility.

The following quotations from the NIH are particularly significant:

"ME/CFS exists.

"The Oxford criteria (published in the Journal of the Royal Society of Medicine in February 1991) are flawed and include people with other conditions, confounding the ability to interpret the science.

"Often, patients with ME/CFS are labelled as lazy, deconditioned, and disability-seeking; this hampers scientific progress. Both society and the medical profession often treat patients with ME/CFS with disdain, suspicion, and disrespect. Patients are frequently treated with psychiatric and other inappropriate drugs that may cause harm.

"There is reproducible evidence of neurocognitive dysfunction with abnormalities in functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies. Strong evidence indicates immunologic and inflammatory pathologies, neurotransmitter signalling disruption, microbiome perturbation, and metabolic or mitochondrial abnormalities in ME/CFS.

"This is not a psychological disease in aetiology.

"Existing treatment studies (CBT and GET)…(have) not translated to improvements in quality of life. Thus, they are not a primary treatment strategy.

"The focus on exercise programmes has further stigmatised and discouraged research participation.

"Many patients with ME/CFS are misdiagnosed and treated erroneously with potentially toxic therapies that may cause harm.

"Current research has neglected many of the biological factors underlying ME/CFS onset and progression.

"ME/CFS is a chronic, complex condition…with no cure…..Nothing has improved the lives of the patients.

"fMRI and imaging technologies should be further studied as diagnostic tools and as methods to better understand the neurologic dysfunction of ME/CFS.

The Conclusions of the draft report reiterate key findings:

"Specifically, continuing to use the Oxford definition may impair progress and cause harm…Thus, for needed progress to occur we recommend that the Oxford definition be retired".
https://prevention.nih.gov/docs/programs/mecfs/ODP-MECFS-DraftReport.pdf

Since such strong doubts have been raised about the Oxford criteria, the question again arises about the validity and safety of the NICE Clinical Guideline on ME/CFS (CG53) which relies so heavily on Oxford criteria-based research and which promotes directive (not supportive) CBT and GET as the primary intervention for those with ME/CFS. In the light of current knowledge, whether or not clinicians should rely on the NICE Guideline has become ever more imperative, especially in the light of the recent UK Supreme Court ruling that over-turned the long-held Bolam principle (a test used to assess medical negligence; it held that a doctor was not negligent if his actions would be supported by a responsible body of medical opinion; indeed, the accused doctor needed only to find an expert who would testify to having done the same thing). This has now changed: there are new rules of consent and doctors are legally accountable for informing patients of any material risks in any recommended medical interventions (BMJ 2015:350:h1481). This means that psychiatrists who recommend graded exercise therapy for people with ME/CFS must warn them of the potential risks of deterioration with exercise, or be in breach of the law. To many people, it also means that having to inform patients with ME/CFS of the risks of GET (because of the increased cardiovascular risk, which would have to be explained to patients) invalidates the psychiatrists' belief that patients are suffering from a behavioural as opposed to a physical disorder.

The latest NIH draft Statement confirms the long-held belief that the NICE Guideline on ME/CFS should be withdrawn because, as many have claimed from the time it was published in August 2007, it was never fit for purpose, and further doubt must now arise as to how safe it is. Indeed, this has now been acknowledged: in June 2014 Professor Mark Baker, Director of the Centre for Clinical Practice at NICE, said at the

Forward-ME Meeting at the House of Lords that the NICE Guideline was no longer meeting the needs of people with ME/CFS and should be replaced.

(2) After publication on 10th February 2015 of the Institute of Medicine's Committee's report (Beyond ME/CFS: Redefining an Illness), the US Centres for Disease Control decided to archive its CFS Toolkit that recommended CBT and GET as interventions for ME/CFS. The conclusion of the IOM Report states: *"It is clear from the evidence compiled by the committee that ME/CFS is a serious, chronic, complex, and multisystem disease that frequently and dramatically limits the activities of affected patients"* (http://www.cdc.gov/cfs/toolkit/archived.html).

Illustrations of the biomedical evidence that disproves the "behavioural" theory

The "behavioural" school continues to ignore the evidence (not hypotheses) of the following that have been documented in ME/CFS:

- evidence of disrupted biology at cell membrane level
- evidence of abnormal brain metabolism
- evidence of a reduction in grey matter
- evidence of widespread abnormal cerebral perfusion (hypoperfusion)
- evidence of central nervous system / immune dysfunction
- evidence of central nervous system inflammation and demyelination
- evidence of hypomyelination
- evidence of spatial disorientation
- evidence that ME/CFS is a complex, serious multi-system autoimmune disorder (in Belgium, the disorder has now been placed between MS and lupus)
- evidence of significant neutrophil apoptosis
- evidence that the immune system is chronically activated (eg. the CD4:CD8 ratio may be grossly elevated, as seen in multiple hypersensitivities)
- evidence that NK cell activity is impaired (ie. diminished)
- evidence of hair loss in ME/CFS
- evidence that the vascular biology is abnormal, with disrupted endothelial function
- novel evidence of significantly elevated levels of isoprostanes (a marker for oxidative stress, which in ME/CFS goes up with exercise intolerance)
- evidence of impaired proton removal from muscle during exercise
- evidence of cardiac insufficiency and that patients are in a form of heart failure
- evidence of autonomic dysfunction (especially thermo-dysregulation; frequency of micturition with nocturia; haemodynamic instability with labile blood pressure; pooling of blood in the lower limbs; reduced blood volume (with orthostatic tachycardia and orthostatic hypotension)
- evidence of respiratory dysfunction, with reduced lung function in all parameters tested
- evidence of neuroendocrine dysfunction (notably HPA axis dysfunction)

- evidence of recovery rates for oxygen saturation that are 60% lower than those in normal controls
- evidence that the average maximal oxygen uptake was only 15.2 ml/kg/min, whilst for controls it was 66.6 ml/kg/min
- conclusive evidence of delayed recovery of muscles after exercise, with ME/CFS patients reaching exhaustion more rapidly than controls, with this failure to recover being more pronounced 24 hours after exercise (note: there is no evidence of de-conditioning)
- evidence of mitochondrial metabolic dysfunction
- evidence of inability to sustain muscle power
- evidence of greatly increased REE (resting energy expenditure)
- evidence of enteroviral particles in muscle biopsies
- evidence of on-going infection
- evidence that the size of the adrenal glands is reduced by up to 50% (with reduced cortisol levels)
- evidence that up to 92% of ME/CFS patients also have irritable bowel syndrome (80% of the immune system is located in the gut)
- evidence of abnormal gene expression (at least 35 abnormal genes -- acquired, not hereditary), specifically those that are important in energy metabolism; there are more abnormal genes in ME/CFS than there are in cancer
- evidence of profound cognitive impairment (worse than occurs in AIDS dementia)
- evidence of adverse reactions to medicinal drugs, especially those acting on the central nervous system, such as anaesthetics
- evidence that symptoms fluctuate from day to day and even from hour to hour
- there is no evidence that ME/CFS is a psychiatric or behavioural disorder.

None of these can rationally be explained as evidence of a behavioural disorder.

The evidence is now so strong that ME/CFS is a serious multi-system neuro-immune disorder that it becomes intellectually embarrassing for anyone to continue to consider it to be a behavioural disorder.

It is incontrovertible that heart failure is a leading cause of death in patients with (ME)CFS (Jason et al: Healthcare for Women International 2006:27:615-626).

UK research supporting the increased cardiovascular risk for those with ME/CFS includes the work of the prestigious Vascular and Inflammatory Research Unit at The Institute of Cardiovascular Research, Dundee, who in 2008 demonstrated low-grade inflammation in and damage to the blood vessels of people with ME/CFS: the arteries of patients are stiffer than those of healthy controls, and the level of arterial stiffness is related to levels of oxidative stress and inflammation (Spence VA et al. Clinical Science (Lond) 2008:114 (8): 561-566).

In 2012, further research from the same unit found that endothelial function is impaired in ME/CFS, both in large vessels and in the microcirculation; this endothelial dysfunction contributes to increased cardiovascular risk (David J Newton et al. Int J Cardiol 2012:154 (3):335-336).

In 2010, a different UK team demonstrated that patients with (ME)CFS "*have an underlying cardiac abnormality and it is only on performing appropriate examination that these high-risk patients will be identified"*. The study confirmed: "*This impairment is associated with an increase in cardiac contractility on standing* (*ie. the heart has to work harder for the same degree of physiological stress), the severity of which associates with symptoms on standing in those with CFS….These abnormalities were CFS-specific"*. The researchers discussed reduced organ perfusion as a consequence of cardiac impairment (Hollingsworth et al. Eur J Clin Invest 2010; May 20).

The advice about performing appropriate examination stands in stark contrast to the Wessely School's advice to UK policy-makers*: "The Royal Colleges have stressed that approaches to these patients should not be based on simple biomedical models….No investigations should be performed to confirm the diagnosis"* – CR54: Simon Wessely, Anthony David, Peter White et al.

The following year the same team further confirmed impaired cardiac function in (ME)CFS: "*CFS patients have markedly reduced cardiac mass and blood pool volumes…this results in significant impairments in stroke volume and cardiac output compared to controls"* Cardiac output was reduced by 25%. (Hollingsworth et al. J Intern Med 2011: July 27).

Recent research from the US posits that true ME (as distinct from ubiquitous chronic "fatigue") is an autoimmune disorder: "*Our results indicate a markedly disturbed immune signature in the cerebrospinal fluid of cases that is consistent with immune activation in the central nervous system, and a shift towards an allergic or T-helper type-2 pattern associated with autoimmunity….Profiles of ME/CFS subjects also differed from those of MS subjects, with ME/CFS cases showing a markedly greater degree of central nervous system immune activation as compared with those with MS"* (M. Hornig et al; Molecular Psychiatry 31st March 2015: doi:10.1038/mp.2015.29).

In February 2015 perturbations in inflammatory cytokines in the cerebrospinal fluid of patients with CFS/ME were posited to contribute to the observed neurological discrepancies (Peterson, Brenu, Marshall-Gradisnik et al; (http://www.hindawi.com/journals/mi/2015/929720/). This group from the National Centre for Neuroimmunology and Emerging Diseases at Griffith University, Queensland, is a world-class research facility focusing on pathomechanisms of ME/CFS, specifically on NK cell cytotoxicity and signalling dynamics; T- and B-cell phenotype profiles; genomic and proteomic profiling and gene expression in ME/CFS.

Professor Jose Montoya, leader of the US Stanford University ME/CFS Programme, is on record stating: "*Our cytokine data contradicts the erroneous conclusion that ME/CFS is not an inflammatory disease and supports that not only an inflammatory state exists in these patients but it also opens the door for the use of anti-inflammatory drugs as… in other inflammatory diseases whose aetiology is still unknown… including systemic lupus erythematosus"* (http://www.cortjohnson.org/blog/2015/04/01/big-studies-big-possibilities-montoya-and-unger-in-their-chronic-fatigue-programs).

The presence of inflammation was further strengthened by the publication of a UK study supporting the role of cytokine-induced inflammation in ME/CFS as well as mitochondrial dysfunction (Kate Earl, Anne McArdle et al; FASEB Journal, April 2015: 29: no 1 Supplement 1055.34) .

Dr Oystein Fluge and Professor Olav Mella from Haukeland, Norway, have conducted several studies of the cancer drug rituximab (a monoclonal antibody that targets and destroys the body's B cells, which recover once treatment ceases) on ME/CFS patients. Their theory is that ME/CFS is a variant of an autoimmune disease that affects the body's ability to control blood flow. World-class experts like Fluge and Mella would not use anti-cancer drugs like methotrexate, cyclophosphamide and rituximab, all of which carry a black box warning, if they believed ME/CFS to be a behavioural disorder; the difference between Fluge and Mella and the "behavioural" psychiatrists is that the former actually listen to their patients whilst the latter prefer to impose their own beliefs and control their patients' behaviour.

Gambuzza et al considered the role of Toll-like receptors (TLRs): "*Peturbations in immune processes play an important role in CFS/ME…typically affecting a variety of bodily systems…Recent reports have shown that CFS/ME is an inflammatory disorder (that) may be associated with autoimmune responses, mainly characterised by reduced functional activity of most immune cells….Interactions between gut microorganisms and host immune function have been shown to contribute to aberrant inflammation in CFS/ME patients….Commensal and/or pathogen-associated molecular patterns detected by TLRs expressed on intestinal epithelial cells appear to trigger (an) inflammatory signalling cascade leading to neuroinflammation and neurodegeneration"* (CNS Neurol Disord Drug Targets Mar 2015).

In the UK, Professor Julia Newton et al found four main differences in the skeletal muscle cells of ME/CFS patients, pointing to an abnormality at the level of, or upstream of, AMPK. The authors conclude that there are at least two muscle phenotypes in (ME)CFS patients and that: "*the results of the current study further emphasise …the need to fully characterise the muscle phenotypes in CFS before generically prescribing exercise as an effective intervention"* (PLoS ONE 10(4): e0122982.doi:10.1371/journal.pone.0122982).

Lengert and Drossel investigated the reduced capacity for mitochondrial ATP synthesis by looking at metabolic dynamics in skeletal muscle during exercise and recovery; they showed that (ME)CFS simulations exhibit critically low levels of ATP and that in order to stabilise the energy supply at low ATP concentrations, the total adenine nucleotide pool is reduced substantially, causing a prolonged recovery time, and that repeated exercise worsens the situation considerably (Biophys Chem. 2015 Apr 4;202:21-31. doi: 10.1016/j.bpc.2015.03.009.)

Klimas, Hornig, Peterson and Komaroff et al have published findings from a clinical and laboratory database that was developed for the discovery of pathogenic mechanisms in ME/CFS, collecting more than 4,000 pieces of data from each of the 203 subjects, demonstrating that fatigue severity is matched by cognitive, autonomic, inflammatory and neuroinflammatory symptoms as the predominant clinical features,

including gastrointestinal and endocrine symptoms (http://www.tandfonline.com/doi/full/10.1080/21641846.2015.1023652).

The above are merely illustrations of some of the many important biomedical research findings published on ME/CFS in the last ten years.

After almost 30 years of UK health care providers' dismissal and mistreatment -- due in no small measure to what has been described as the Wessely School's malign influence -- patients with ME/CFS are aware that finally, a paradigm shift is occurring and the psychiatrists' stranglehold over their disease is being loosened.

That this is so is thanks to charities like Invest in ME and ME Research UK who, quietly but resolutely, have done so much to bring about that paradigm change.

During the next ten years, it is likely that the link between the immune defects found in ME/CFS and an infectious or environmental trigger will be discovered and, without doubt, ME/CFS will be added to the long list of organic disorders (including epilepsy, myasthenia gravis, MS, diabetes, migraine, pernicious anaemia, ulcerative colitis, gastric ulcer and Parkinsons) which psychiatrists forcefully asserted were psychogenic until medical science proved otherwise.