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A FINAL FAREWELL TO THE PSYCHIATRIC FALLACY?

Margaret Williams 13th August 2005

Because of the extreme importance to the international ME community of the latest paper from the Vascular Research Unit at Dundee (Oxidative stress levels are raised in chronic fatigue syndrome and are associated with clinical symptoms. Gwen Kennedy, Vance A Spence, Jill JF Belch et al. *Free Radical Biology & Medicine* 2005:39:584-589) and because it may be quite a challenge for those without the necessary scientific expertise to understand, it seems prudent to highlight the key points in simple terms, especially as the findings could have a significant impact on the safety of the UK Medical Research Council's current PACE trials on "CFS/ME" and on the use of graded exercise that will be the mainstay of the new "Centres of Excellence" for those with myalgic encephalomyelitis (also listed in the International Classification of Diseases as Chronic Fatigue Syndrome).

This is the first time that raised levels of isoprostanes (see below) that precisely correlate with patients' symptoms have been presented.

As Dr Neil Abbot (Director of Operations of the charity MERGE that funded the research) has observed on the MERGE website (www.mereseearch.org.uk), the importance of these findings cannot be understated. To quote Abbot: "Circulating in the bloodstream are highly reactive molecules, known as free radicals, which can cause damage to the cells of the body, a process called oxidative stress. In healthy people, increases in free radicals are neutralised by antioxidant defences, and it is only when these defences are overwhelmed that cell injury results. The source of excessive free radical generation in ME/CFS patients may be associated with a variety of altered biological processes".

Of particular significance, as Abbot makes clear, is that **exercising muscle is a prime contender for excessive free radical generation**, and existing evidence has shown a good correlation between muscle pain thresholds on exercise with various blood markers of oxidative injury in ME/CFS patients. As Abbot says: "recent research has demonstrated that **incremental exercise challenge** induces a prolonged and accentuated oxidative stress that might well account for post-exercise symptoms in ME/CFS patients".

A further pathway for such excessive free radical generation is associated with immune activation, with free radical generation being activated by white blood cells, either as a consequence of infection (viruses are associated with excessive free radical production) or as the result of environmental stressors. The Dundee team has previously reported increased neutrophil apoptosis (apoptosis being programmed cell death) in ME/CFS, and, to quote Abbot again: "it could be suggested that **many patients currently diagnosed with ME/CFS could have an inflammatory condition** and be in a 'pro-oxidant state'".

As Abbot makes clear, the data from the Dundee team are strengthened by the results of recent gene investigations in ME/CFS, especially the findings of Kaushik, Kerr, Holgate et al of upregulation of the genes ABCD4 and PEX16, suggesting enhanced defence to oxidative stress in ME/CFS, and Dr John Gow's recent evidence of alterations to genes controlling the

metabolism of prostaglandin (see below). For details of this gene research and a consideration of the significance of it, see http://www.meactionuk.org.uk/ME_Organic_or_Psychiatric_-_Decision_Time.htm

The latest paper from the Dundee team is but one of a series designed by Dr Vance Spence that aim to unravel, step by scientific step, the organic dysfunction in ME/CFS, which is an impeccably scientific approach to elucidate the aberrant biology that underpins ME/CFS. Many in the series have already been published but have received little attention from the UK ME charities, possibly because their scientific significance has not been understood, or possibly because one of the major ME charities (Action for ME) has aligned itself with the psychiatric lobby (see: Functional Symptoms and Syndromes: Recent Developments. Michael Sharpe. Trends in Health and Disability, UNUM Provident, 2002) and the Dundee findings militate against such an approach, or possibly because this work has been published in mostly non-clinical journals. In contrast, Spence's work has received acclamation from other scientists and the plaudits have been many, resulting in extended connections with other international laboratories, and this will be reflected in MERGE-funded research in coming years.

The Dundee series of research papers into ME/CFS addresses both vascular and immune anomalies and may be summarised as follows: the vascular papers looked at orthostatic problems present in ME/CFS and at the molecular mechanisms within blood vessels that underpin them, such mechanisms involving acetylcholine, nitric oxide, prostaglandins and other chemical mediators. In conjunction with this, Spence was interested in how immune cells interact with blood vessels and his team specifically looked at neutrophils, since these white blood cells cross the endothelium (the inner lining of all blood vessels); Spence's team duly demonstrated that neutrophils are significantly apoptotic in ME/CFS.

The link between both of these dysfunctional pathways may lie with oxidation products, and Spence's latest research has demonstrated high levels of abnormal prostaglandin metabolites known as isoprostanes, which are highly noxious by-products of the abnormal cell membrane metabolism.

Given so much evidence of serious organic pathology in ME/CFS, perhaps psychiatrist Professor Michael Sharpe of Edinburgh needs to re-think his previous pronouncement that "Those who cannot be fitted into a scheme of objective bodily illness yet refuse to be placed into and accept the stigma of mental illness remain the undeserving sick of our society and our health service" (lecture given in October 1999 hosted by the University of Strathclyde).

On a separate but related topic, attention is drawn to a powerful article from PLoS Med 2005;2(8):e206, available online at www.plosmedicine.org by Dan Hoch and Tom Ferguson entitled "What I've learned from E-Patients". This is a refreshing acknowledgment from a neurologist at one of the world's most respected academic and medical institutions (Harvard) of the value of online patient support groups and is in stark contrast to the pontifications of psychiatrists of the "Wessely School" who are on record as being contemptuous of such patient support groups, having claimed that membership of patient associations is a predictor of an adverse outcome and is not to be recommended.

Hoch and Ferguson, however, take a robustly different view:

“I knew that many patients with chronic diseases had been making use of online medical information. I was shocked, fascinated, and more than a bit confused by what I saw. I’d been trained in the old school medical style: my instructors had insisted that patients could not be trusted to understand or manage complex medical matters. I realised that there had always been an unspoken prohibition against groups of patients getting together. I had the uncomfortable sense that by promoting interactions between patients and de-emphasising the central role of the physician, I might be violating some deep taboo. I found dozens of well-informed, medically competent patients sharing information. These patient narratives gave rise to an accumulated body of what my colleagues and I began to think of as an expert patient knowledge base. In 70% of postings, group members provided each other with what amounted to a crash course in their shared illness. I was surprised to learn that many clinicians caring for group members provided considerably less information, guidance and support. We concluded that many professionals have seriously overestimated the risks and underestimated the benefits of online support groups and other online health resources for patients. The most important thing I have learned was that patients want to know about, and in most cases are perfectly capable of understanding and dealing with, everything their physician knows about their disease. While some postings do contain erroneous material, online groups of patients who share an illness engage in a continuous process of self-correction, challenging questionable statements and addressing misperceptions as they occur, and the consensus opinion arrived at by patient groups is usually quite excellent. It now seems quite clear that growing numbers of patients are perfectly capable of empowering themselves, with or without their clinician’s blessing. Physicians and other health professionals should do all they can to support them in this worthy effort”.

Psychiatrists of the “Wessely School” may wish to take note of these developments and to understand that it is time for them to re-think their obviously outdated and potentially damaging approach to those with ME/CFS.