Evidence–based Psychiatry ?

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In as yet unpublished work, bona fide research has indicated that in those with ME/ICD-CFS there are more gene abnormalities present than are found in cancer sufferers.

The validity of this remains to be established, but there can no longer be any doubt from both US and UK research that in ME/ICD-CFS there are proven abnormalities in numerous genes and that such abnormalities are acquired as a result of interactions with the environment as opposed to being hereditary.

Gene expression describes the behaviour of certain genes when attacked by an infection or other insult: some genes become over-active and produce chemicals that cause symptoms seen in ME/ICD-CFS, while other genes become under-active or shut down (The Chronic Fatigue Syndrome Research Foundation Newsletter 10, November 2004).

In the UK, Jonathan Kerr of Imperial College, London, is leading the CFS Research Foundation's work in this area: using micro arrays *and* Taqman PCR techniques, his team has found no fewer than 15 genes to be abnormal and these genes showed problems in various body systems including the immune system, in neurological function and in mitochondrial metabolism (ie. in the production of cellular energy). As the CFSRF Newsletter makes plain: "It is clear that in ME/ICD-CFS patients the gene function has changed and these changes can be detected and measured".

In the US Suzanne Vernon and her team have shown that differentially expressed genes are related to energy metabolism, muscle and immune response (T-cell associated chemokines and receptors) and that several of these genes are involved in transcriptional regulation, metabolism and the immune response; Vernon et al have put forward mechanisms possibly associated with exacerbation of symptoms in ME/ICD-CFS and with differences in how patients cope with stress compared with controls (Co-Cure 14th March 2005: http://www.co-cure.org).

The key question associated with genetic abnormalities is whether or not the detected abnormalities are associated with changes in the *function* of the gene that would lead to changes in the gene product(s), so it is the *functional* changes that are critical to understanding the relevance of these observations. It is necessary to understand how the biochemical changes relate to the gene changes because it is the genetic changes that drive the biochemical processes associated with the gene product(s) --- in other words, biochemical abnormalities are a reflection of gene abnormalities.

The work of US immunologist Roberto Patarca-Montero illustrates how changes in just one single gene can have wide-ranging consequences: he has identified an abnormal gene in ME/ICD-CFS patients that is multi-factorial, affecting the immune response to infection *and* the regulation of calcium and phosphate in bone metabolism *and* the expression of autoimmune disease, showing that acquired changes in a single gene can result in a compromised response to infection, to disordered calcium and phosphate metabolism and to

increased susceptibility to autoimmune disease (Chronic Fatigue Syndrome, Genes, and Infection: the Eta-1 /Op Paradigm. Roberto Patarca-Montero, Howarth Medical Press, 2003).

Patarca-Montero's gene studies also reveal consequences within the cardiovascular system in respect of the response to injury of the normal artery wall: endothelial cell migration is stimulated through a co-operative mechanism with other gene products, and these gene products affect vascular permeability, compromising the cardiovascular system and the nerves and tissues it supplies, with potential implications for the ability to exercise without biological consequences that are damaging.

In the UK, John Gow and his team from Glasgow have identified genes which are up-regulated when compared with genes in healthy controls and which prompt an inappropriate up-regulation of the immune system.

Apart from identified gene abnormalities, other researchers have found abnormal immune activity in the pathology of exercise intolerance in ME/ICD-CFS that is consistent with a channelopathy involving oxidative stress and nitric oxide-related toxicity (Exercise capacity and immune function in male and female patients with chronic fatigue syndrome. Snell CR et al. In Vivo 2005:19(2):387-390).

Consistent with the above findings, Jammes et al have shown that in the ME/ICD-CFS patients studied, exercise gives rise to abnormally increased oxidative stress, resulting in patients being quite unable to respond physiologically, which could well account for the reduction in muscle power after exercise as reported by patients and as demonstrated by Paul et al (European Journal of Neurology 1999:6:63-69). The observed changes in markers of exercise induced oxidative stress are considered by the authors to be of real significance, and the paper confirms previous studies that point to positive correlations between muscle symptoms and measures of oxidative stress (Chronic fatigue syndrome: assessment of increased oxidative stress and altered muscle excitability in response to incremental exercise. Jammes Y et al. Journal of Internal Medicine 2005: 257: 299-310).

Clearly, those with ME/ICD-CFS are physically, not mentally, sick: it may be helpful to highlight once again what Professor Nancy Klimas from the University of Miami said in her AACFS in-coming Presidential address: "Our patients are terribly ill, misunderstood, and suffer at the hands of a poorly informed medical establishment and society" (Co-Cure 21st March 2005: http://www.co-cure.org).

Other world-renowned researchers have described ME/ICD-CFS as "a global disablement, nearly comparable to paralysis" (Osler's Web. Hillary Johnson. Crown Publishers Inc, New York, 1996).

ME/ICD-CFS was described in 1992 by Hyde et al (see below) in specific terms: "ME/CFS represents a major acquired CNS dysfunction. This persisting multilevel CNS dysfunction defines the nature of the disease process …..the majority of symptoms can only be attributed to a CNS or muscle pathology".

Since 1938, there have been thousands of published papers in the medical literature that document biological abnormalities in ME/ICD-CFS and there are also many books, both self-help and medical textbooks, some of the best – in addition to Osler's Web, which is essential reading -- being (1) The Clinical and Scientific Basis of Myalgic Encephalomyelitis Chronic

Fatigue Syndrome; edited by Byron M Hyde, Jay Goldstein and Paul Levine, published by The Nightingale Research Foundation, Ottawa, 1992; (2) Myalgic Enephalomyelitis; Celia Wookey; published by Croom Helm Ltd 1986; reprinted 1988 and 1989, Chapman and Hall Ltd – more essential reading, as this book provides numerous case histories that cannot be bettered as teaching material; (3) Postviral Fatigue Syndrome; A Melvin Ramsay; published by Gower Medical Publishing, London, 1986; reprinted as Myalgic Encephalomyelitis and Postviral Fatigue States; Gower Medical Publishing, London, 1988 (soon to be re-issued by the UK ME Association); (4) The Disease of a Thousand Names: Chronic Fatigue / Immune Dysfunction Syndrome; David S Bell; published by Pollard Publications, Lyndonville, New York 1991; (5) Chronic Fatigue Syndrome and the Body's Immune Defense System; Roberto Patarca-Montero; published by Haworth Medical Press, 2002; (6) Chronic Fatigue Syndrome – A Biological Approach; edited by Patrick Englebienne and Kenny de Meirleir; published by CRC Press, 2002 and (7) Post-Viral Fatigue Syndrome; edited by Rachel Jenkins and James Mowbray; published by John Wiley & Sons, Chichester 1991.

No-one who is aware of this wealth of information can credibly doubt the reality, the validity and the devastation of this organic multi-system disease.

At the Second World Congress on ME/ICD-CFS held in September 1999 in Brussels, world-renowned expert Daniel Peterson went on record saying that ten years previously he had believed that this disorder would be resolved by science but he had now changed his mind and believed it could only be resolved by politics.

It seems beyond dispute that it is psychiatric bias and vested commercial interests that drive current politics about ME/ICD-CFS: as Hyde noted in 1992 about the 1988 Holmes et al case definition: "This failure to return to the literature haunts the very basis of their definition", a statement that is equally valid today, because it is the continued failure to heed the literature that underpins the current chaos.

Such an enormous amount of information must not be allowed to be "buried" by Wessely School psychiatrists or by the Government and insurance officials to whom these psychiatrists are advisers, but that this is in fact happening cannot be disputed: as reported in the RiME Spring Newsletter 2005 (www.erythos.com/RiME), there is evidence that the treatments to be offered by the Government-funded new centres are psychiatrically biased and that the clinics appear to make no distinction between those with ME/ICD-CFS and those with other chronic fatigue states. Severely affected patients are not being catered for. One patient has described being put on gym machines and ending up in bed for several months – in a letter to the patient's GP, psychiatrist Peter White from St Bartholomew's Hospital, London, wrote that symptoms were the result of deconditioning, that fear and anxiety prevented the patient from exercising and that psychological factors contributed to the illness. It is reported that in the Greater Manchester area, a psychiatrist unknown to that area has come from nowhere and been made Head of the new "CFS/ME" service, with sufferers being told during cognitive behavioural therapy (CBT) sessions that they have a 'fear of activity' and 'motivation problems'.

It seems that Wessely School psychiatrists continue to attempt to subvert the WHO classification of ME as a neurological disorder and to include it under behavioural disorders, despite the UK Government's acknowledgment that a neurological classification is valid.

How can symptoms that clearly indicate significant pathology be so constantly dismissed and sufferers be so constantly denigrated by certain psychiatrists, given the nature of the problems presented? These include not only the watered-down subjective descriptions of “fatigue”, sore throat, cognitive impairment and altered sleep patterns, but organic symptoms that ought to be unmissable, even by psychiatrists, for example:

extreme malaise; abdominal pain and diarrhoea; post-exertional exhaustion almost to the point of collapse; inability to stand unsupported for more than a few moments – this is absolutely diagnostic of ME; sometimes too weak to walk (different from deconditioning); inability to walk upstairs or to maintain sustained muscle strength, as in repeated brushing of hair with arms elevated, or inability to carry a shopping bag, or dry oneself after a bath, peel vegetables or prepare a meal; neuromuscular incoordination, not only of fine finger movement with clumsiness and inability to control a pen and to write legibly, but also of the larynx and oesophagus -- a frequent complaint is the need to swallow carefully to avoid choking; oesophageal spasm and pain; dysequilibrium ie. loss of balance; staggering gait (ataxia); bouts of dizziness and frank vertigo; difficulty with voice production, especially if speaking is sustained; aphasia (inability to find the right word); muscle cramps, spasms and twitching; black-outs and seizure-like episodes; spasmodic trembling of arms, legs and hands; episodes of angor animi –brought about by abrupt vasomotor changes that cause the sufferer to have uncontrollable shaking, like a rigor, and to think they are at the point of death – it is essential to understand the terror that such attacks induce in a patient, and no patient can fake them; photophobia; difficulty focusing and in visual accommodation, with rapid changes in visual acuity; blurred and double vision, with loss of peripheral vision; eye pain; swollen and painful eyelids, with inability to keep eyelid open; tinnitus; hyperacusis, for example the noise of a lawnmower can cause acute distress and nausea; heightened sensory perception (for example, acute sensitivity to being patted on the back; inability to tolerate lights, noise, echoes, smells, movement and confusion such as found in a shopping mall or supermarket without being reduced to near-collapse); frequency of micturition, including nocturia; peripheral neuropathy; numbness in face; altered sleep pattern, with hypersonmia (in the early stages) and insomnia (in the later stages); alternate sweats and shivers; temperature dysregulation, with intolerance of heat and cold; parasthesias; sleep paralysis; intermittent palindromic nerve pains; tightness of the chest alternating with moist chest; muscle tenderness and myalgia, sometimes burning or vice-like; typically shoulder and pelvic girdle pain, with neck pain and sometimes an inability to hold head up; orthostatic tachycardia; orthostatic hypotension, and symptoms of hypovolaemia, with blood pooling in the legs and feeling faint due to insufficient blood supply to the brain; labile blood pressure; intermittent chest pain akin to myocardial infarct; segmental chest wall pain; subcostal pain; vasculitic spasms, including headaches; cold and discoloured extremities, with secondary Raynaud’s; easy bruising; peri-articular bleeds, especially in the fingers; shortness of breath on minimal exertion; the need to sleep upright because of weakness of the intercostal muscles; pancreatic exocrine dysfunction leading to malabsorption; rashes (sometimes vasculitic in nature); flushing of one side of the face; ovarian-uterine dysfunction; prostatitis; hair loss and mouth ulcers that make speaking and eating difficult. The notable point about symptoms in ME/ICD-CFS is their variability. All these symptoms and more are documented in the literature; they bear little resemblance to “chronic fatigue” or to a “continuum of on-going tiredness”.

It is, of course, the Wessely School psychiatrists’ view that such multiplicity of symptoms confirms their belief that ME/ICD-CFS is a somatoform disorder, but if these psychiatrists do not acknowledge and identify such symptoms, they are either not seeing patients with ME (so

therefore should not describe their studies and results as pertaining to those with "CFS/ME") or are comprehensively failing in their professional responsibilities towards such patients.

As there is an ever-increasing abundance of evidence of an organic pathoaetiology, why do these psychiatrists profess to remain unconvinced that ME/ICD-CFS is an organic disease and insist that it is merely a "mistaken illness belief"?

As David Lees points out: "To work from the assumption that the illness is not primarily organic in origin and must therefore be primarily psychological is unscientific and therefore unacceptable. We should surely have moved on from filling gaps in our medical knowledge with assertions, and the least we should expect from our medical practitioners in the NHS is that their methods and conclusions should be scientific. The diagnosis of 'mistaken illness beliefs' is not – it is itself merely a statement of belief" (Network Mesh West London Newsletter, June 2005 http://networkmesh-westlondon-me.org).

For years, Wessely School psychiatrists (most notably Professor Simon Wessely himself; Professor Michael Sharpe from Edinburgh and Professor Peter White) have attempted to take the moral high ground by insisting on "evidence-based" medicine as the only acceptable evidence of disease in ME/ICD-CFS: this appears to mean to them that only "laboratory-based" evidence is acceptable evidence of disease, and they accord lower evidential weight to objective clinical observation than to laboratory measurements with all their potential unreliability and consequential missed diagnoses.

Now there *is* laboratory evidence of organic disease in ME/ICD-CFS, yet these psychiatrists continue to dismiss or ignore it and intend, at a cost to UK taxpayers of £11.1 million, to pursue their own belief that "CFS/ME" is a functional somatic syndrome that is amenable to behavioural modification techniques.

In a recent debate in the Scottish Parliament (Motion No.2852 in the name of Alex Fergusson), Alex Fergusson asked: "Does the Minister accept that if Dr Gow's research project comes to fruition, all the steps she outlined will be completely unnecessary?" -- in other words, the "services" promoted by Government would become completely unnecessary should genetic research supply an alternative solution, because currently the policy is to service chronic ill-health without providing any route towards finding cause or cure for ME/ICD-CFS. As has been noted on MEActionUK (http://www.meactionuk.org.uk) by the listowner, pressure must be brought to bear to provide research funds for projects like gene research and there must be an end to the present policy that merely perpetuates chronic ill-health.

Michael Sharpe was recently appointed to a Personal Chair in Psychological Medicine and Symptoms Research at the University of Edinburgh. In his inaugural lecture given on 12th May 2005 (attended by Simon Wessely), Sharpe gave a light-hearted delivery; people in the audience noted that his reasoning was full of holes and were quite shocked at how lame it all was. Sharpe spoke on "functional medicine" (in which he includes ME/ICD-CFS) and how to treat diseases with "no pathology". Perhaps it escapes him that no disease had recognised pathology before appropriate research had been carried out.

This is the same Michael Sharpe who is on record as stating about those with ME/ICD-CFS that **"Purchasers and Health Care providers with hard pressed budgets are understandably reluctant to spend money on patients for whom there is controversy**

about the 'reality' of their condition (and who) are in this sense undeserving of treatment. 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" (ME. What do we know (real physical illness or all in the mind?) Lecture given in October 1999 by Michael Sharpe, hosted by the University of Strathclyde).

Physician, heal thyself.