

More potential dangers of the UK NICE Guideline on “CFS/ME” for people with ME/CFS?

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Much has been written about the NICE Guideline on “CFS/ME” since its release on 22nd August 2007, mostly noting concern over the Guideline’s recommendations that cognitive behavioural therapy and graded exercise therapy (CBT/GET) should be the first-line (and only) management for “Chronic Fatigue Syndrome / Myalgic Encephalomyelitis” or “CFS/ME”. This concern is unsurprising, given the existence of numerous published papers which all conclude that CBT is of limited and non-lasting benefit, and given that at least four major surveys of over 3,200 patients with ME/CFS have clearly shown GET to be actively harmful.

“CFS/ME” is different from ME/CFS, the former being the psychiatric model which has no abnormal signs or laboratory findings (i.e. chronic somatisation disorder) proposed and favoured by Wessely School psychiatrists who advise Government Departments on “CFS/ME” and who are believed to exert control over the Medical Research Council’s funding agenda, whilst the latter is a nosological neurological disorder (classified as such by the World Health Organisation) which exhibits distinct signs and has an abundance of abnormal laboratory findings, albeit no single, definitive test.

It is a matter of on-going concern that the psychiatric lobby continues to use the terms ME, CFS and chronic fatigue (CF) as if they were interchangeable, when such is not the case.

Virtually none of the peer-reviewed, published biomedical evidence seems to penetrate the consciousness of these psychiatrists and their supporters, who continue to dismiss or ignore the ever-mounting confirmation of abnormal laboratory investigations now known to exist in ME/CFS. What is so curious is that there is such an abundance of easily accessible evidence of abnormal laboratory findings in ME/CFS, so how -- without losing credibility -- can the psychiatric lobby keep asserting that none exists?

Not only is this evidence down-played, its very existence is repeatedly denied: in an in-press article to be published in *Psychoneuroendocrinology*, James Jones from the Division of Viral and Rickettsial Diseases at the US Centres for Disease Control also seems to ignore this body of biomedical evidence, claiming: “*In the absence of overtly abnormal findings in a person with prolonged duration of illness, it is common for practitioners to consider a psychological explanation during clinical evaluation*” (“An extended concept of altered self: Chronic fatigue and post-infection syndromes”. James F Jones. Doi:10.1016/j.psyneuen.2007.11.007).

For Jones to propose in his essay that:

- (i) *“the illnesses in question stem from responses to previous infections and not to ongoing viral or immunologic factors”*
- (ii) interoception is responsible for the illness behaviour exhibited by patients (*“the sensations and consequences of sickness behaviour are remembered”*)
- (iii) *“persistent illnesses such as CFS are due to maladaptive biological (interoceptive) signal recognition”*
- (iv) *“It is of interest that CBT remains an effective therapy for CFS”* and
- (v) *“Chronic illnesses, such as CFS, in the absence of evidence of standard mechanisms of pathogenesis, require new concepts of illness origin”*

seems remarkable, given that in 1996 Jones was one of the authors of a paper that provided laboratory evidence for an autoimmune component in ME/CFS (see below).

Royal Society of Medicine meeting to support the NICE Guideline

It is a matter of acute concern that the Royal Society of Medicine is to host a meeting on 28th April 2008 on “CFS” (reference to “ME” is omitted, which is in keeping with the Wessely School’s documented intention to eradicate the term) at which the psychiatric lobby is to provide most of the speakers; not only do those speakers include Professor Simon Wessely himself (famous for his trenchant belief that ME is a myth and that it does not exist except as an aberrant belief in the mind of those who think they suffer from it), but other devout believers in the psychosocial model of “CFS/ME” such as Professor Peter White; Dr Anthony Cleare; Professor Rona Moss-Morris and Professor Matthew Hotopf. Professor Anthony Pinching is to chair Session Two. Pinching is widely-known for his belief that in ME/CFS, *“over-investigation can [cause patients] to seek abnormal test results to validate their illness”*, that *“fatigue [is] not related to ongoing exertion”* and that *“The essence of treatment is activity management and graded rehabilitation”* (as set out in Prescribers’ Journal 2000:40:2:99-196). Sir Peter Spencer, CEO of the charity Action for ME, is to speak in Session Three (to be chaired by Professor Mansel Aylward, formerly Chief Medical Adviser to the DWP and now funded by the notorious medical insurance company UNUM). Another speaker is Professor Chris Dowrick from Liverpool, who, with Rona Moss-Morris is one of the authors of a study for which the MRC awarded £459,707, the results of which were published in the British Journal of Psychiatry: 2007: December:191:536-542 (*“Cluster randomised controlled trial of training practices in reattribution for medically unexplained symptoms”*). The object of the study was to teach general practitioners that “reattribution” of symptoms provides a psychological explanation for medically unexplained symptoms in disorders such as “CFS/ME”.

Another danger of the NICE Guideline?

Given the wall-to-wall influence of the Wessely School lobby and the choice of members of the Guideline Development Group that produced the Guideline on “CFS/ME”, it is little wonder that NICE got things so wrong.

There can be no doubt that NICE ignored the international evidence that ME/CFS is a biomedical, not psychiatric, disorder, claiming that studying this evidence fell outwith its remit. Such a claim is mystifying, since knowledge of the existing evidence-base ought surely to be mandatory before producing a national Guideline on the management of any disorder, especially given that adherence to such a Guideline is obligatory throughout the NHS (and hence for affiliated agencies such as the Department for Work and Pensions and Social Services).

Not only has the “evidence-base” upon which NICE relied for its recommended management interventions for ME/CFS been exposed as deeply flawed by virtue of the heterogeneous populations studied; the methodological inadequacy; the corrupted data; the high drop-out rates; the undeniable ineffectiveness of CBT/GET as shown by the outcomes measures, and the finding that the claimed benefits may have been illusory (see: “Inadequacy of the York (2005) Systematic Review of the CFS/ME Medical Evidence Base” by Malcolm Hooper & Horace Reid at http://www.meactionuk.org.uk/FINAL_on_NICE_for_Gibson.html) but, just as importantly, the proscribing by NICE of appropriate testing and its stipulation that any vitamin or mineral deficiency must not be corrected by prescription would seem to constitute a real and even life-threatening danger to people with ME/CFS – see below.

The proscribing by NICE of testing for Vitamin D status in patients with ME/CFS

This is particularly problematic in respect of vitamin D status which, according to clinicians who specialise in ME/CFS, is known to be frequently deficient in patients with true ME/CFS. If serum vitamin D levels are low, one might expect the serum calcium level to be low and the alkaline phosphate (ATP) level to be high, but in ME/CFS this seems not to be so. Normal screening rules simply do not apply in this disorder.

It seems that some doctors still believe that vitamin D relates just to the health of bones, and that a lack of vitamin D solely results in osteomalacia or in osteoporosis (a thinning of the bone predisposing to multiple fractures).

Whilst this is indeed so, nothing could be further from the whole truth.

Vitamin D is a misnomer because it is now known that it is more than just a vitamin – it is a precursor of a steroid hormone that affects the entire body. Receptors that respond to vitamin D have been found in almost every type of human cell from brain to bone (see: www.mercola.com).

It should be noted that whilst this website (run by Dr Joseph Mercola MD) is useful and informative in many ways, it is essentially an advertising website and contains some information which some clinicians might challenge.

Vitamin D represents D₂ or D₃. The former is known as ergocalciferol and the latter as cholecalciferol.

Whilst vitamin D₂ occurs naturally in fungal form (usually mushroom), medically prescribed vitamin D₂ is usually a synthetic form, which according to some sources has been shown to cause toxicity and to have greater potential for harm (see “Test Values and Treatment for Vitamin D Deficiency” at www.mercola.com).

Vitamin D₃ is the natural form (i.e. the same vitamin D that the body makes when exposed to sunshine).

Vitamin D₃ is converted 500% faster than vitamin D₂.

Currently there is much debate as to whether recommended levels of vitamin D in the diet are sufficient for people living in northern latitudes, but over-supplementation is dangerous and can lead to vomiting, kidney failure and calcification of the arteries (see www.mercola.com) and it is essential to consult a doctor specialising in the field.

With regard to supplementation, it is perhaps worth mentioning that one GP who specialises in ME/CFS (Dr Sarah Myhill, a leading member of the British Society for Allergy & Environmental Medicine / BSAEM) apparently prescribes 0.5 micrograms of calcitriol (ie. the active form of 1,25 dihydroxyvitamin D – see below) for patients with depleted vitamin D levels, which is manufactured by a company called Teva Ltd (0113 – 238 – 0099).

The Medical Information department of this company has confirmed that they use wholly synthetic products in the manufacture and that in addition to the active (synthetic) ingredient, their calcitriol contains butylated hydroxyanisole (E321, a “red” or dangerous substance [BHA/BHT] to which people with ME/CFS who have hypersensitivities might react badly: BHA has a benzene / phenol ring and was developed to protect petroleum from oxidative gumming, whilst BHT [toluene] is methylbenzene derived from petroleum; it is used as a solvent in aircraft fuels); coconut oil; gelatine for the capsule from a mixture of both porcine and bovine sources; glycerol; sorbitol; titanium dioxide (E171); quinoline yellow (E104, another “red” or dangerous substance and a coal tar dye that has been banned in the US, in Australia, in Norway and in Japan, but not in the UK, even though the UK Committee on Toxicity acknowledged the evidence that it inhibits cholinesterase activity in *in vitro* human red blood cells and plasma, and assays have shown that quinoline yellow is genotoxic); patent blue (E131, another “red” coal tar dye and a dangerous substance). In addition, each capsule contains refined shellac and black oxide used in the printing ink.

Ranges of Vitamin D

Vitamin D from the skin and diet is metabolised in the liver to 25-hydroxyvitamin D (25(OH)D), known as calcidiol. It is this that is used to determine vitamin D status. 25(OH)D is in turn metabolised in the kidney to its active form of 1,25 dihydroxyvitamin D (1,25(OH)₂D, known as calcitriol).

Optimal range is now considered by world experts to be 45-50 ng/ml (nanograms per millilitre). Twenty-five nanograms equates to one International Unit (the measure in which supplementation is usually prescribed).

Below 40 ng/ml is considered sub-optimal; below 30 ng/ml is deficient; below 20 ng/ml is now considered seriously deficient, and below 10 ng/ml places the patient at real risk, requiring prompt intervention. Experts recommend that, ideally, the vitamin D level should never be below 32 ng/ml (see www.mercola.com).

In ME/CFS, levels as low as 8.3 ng/ml have been recorded.

The NICE Guideline on “CFS/ME”, however, is categoric: not only is testing for vitamin D status proscribed, but the prescribing of vitamin supplements to rectify any deficiency is specifically forbidden: the Guideline states that supplements to correct any vitamin or mineral deficiency “*should not be prescribed for treating the symptoms of the condition*” (see the 52 page version of the Guideline, page 24, paragraph 1.4.7.2).

Quite how cognitive behavioural therapy and graded exercise can raise deficient levels of this vital and life-saving hormone that are found in ME/CFS patients is not explained by NICE.

Effects of deficiency of Vitamin D

Deficiency results in chronic illnesses, specifically in symptoms that occur in ME/CFS: deficiency impacts on muscle function (with muscle pain and weakness) and is a risk factor for cardiovascular disease (CVD risk is documented in the ME/CFS literature and was the subject of keynote lectures at the international research conference hosted on 25th May 2007 by ME Research UK in Edinburgh). A deficient vitamin D status is known to result in high blood pressure, with the consequent dangers of heart attack or stroke (see “Vitamin D Deficiency”. Michael F Holick MD PhD; NEJM 2007:357:266-281; see also “Ultraviolet B and blood pressure”. Rolfdieter Krause, Michael Holick et al. Lancet 1998:352:709-710), and in raised triglycerides (see “Prevalence of Cardiovascular Risk Factors and the Serum Levels of 25-Hydroxyvitamin D in the United States”. David Martins et al. Arch Intern Med: 2007:167:1159-1165).

Vitamin D is an essential part of the endocrine system (which is well-documented as being disrupted in ME/CFS) and it controls several of the adrenal hormones, production of enzymes and the growth of cells (www.mercola.com: interview with William B Grant

PhD of the Sunlight, Nutrition and Health Research Centre, one of the top vitamin D researchers).

Deficiency of vitamin D has also been implicated in inflammatory disorders such as ME/CFS is increasingly being demonstrated to be (see “Higher serum vitamin D concentrations are associated with longer leukocyte telomere length in women”. T Spector et al. The American Journal of Clinical Nutrition, 8th November 2007) and in autoimmune disorders such as multiple sclerosis, rheumatoid arthritis and diabetes (see “Vitamin D Deficiency”. Michael Holick MD, PhD: NEJM 2007:357:266-281).

It will be recalled that some experienced ME/CFS researchers – including Professor Kenny De Meirleir from Belgium -- now hold ME/CFS to be an autoimmune disease and that evidence of autoimmunity was presented at the fifth AACFS International Research and Clinical Conference held in 2001 in Seattle. This was a major multi-centre study looking at the presence of autoantibodies to a cellular protein expressed primarily in neuronal cells (MAP2). Initial studies with immunohistochemistry showed a high percentage of (ME)CFS sera reactive to centrosomes and that other proteins besides MAP2 might also be target antigens in (ME)CFS autoimmunity (see “A multi-centre study of autoimmunity in (ME)CFS”. K Sugiura, A Komaroff, E Tan et al. AACFS #037).

Previously, a 1996 paper demonstrated the occurrence of autoantibodies to a conserved intracellular protein (lamin B1), which provides laboratory evidence for an autoimmune component in ME/CFS. The authors found that 52% of patients with ME/CFS develop autoantibodies to components of the nuclear envelope (NE), mainly nuclear lamins, suggesting that in addition to the other documented disturbances of the immune system, humoral autoimmunity against polypeptides of the NE is a prominent immune derangement in ME/CFS. 67% of ME/CFS patients were positive for NE reactivity compared with 10% of normal subjects. No patients with either depression or atopy showed reactivity to NE proteins. Autoantibodies to NE proteins are relatively infrequent and most fall into the category of an unusual connective tissue disease subset characterised by brain or skin vasculitis (see “Autoantibodies to Nuclear Envelope Antigens in Chronic Fatigue Syndrome”. K Konstantinov, James Jones, Eng Tan et al. J Clin Invest 1996:98:8:1888-1896). Many patients with ME/CFS report a vasculitic-type headache which has become known as “the ME headache”.

The paper concluded that such activation “*could be the result of various triggering agents, such as infections or environmental toxins*”. It recommended that: “*Future work should be directed at a better understanding of the autoimmune response of CFS patients to other NE antigens*”.

This important paper has been widely cited in, for example: American Journal of Psychiatry:2003:160(2):221-236 (N Afari and D Buchwald); Clin Vaccine Immunol: 2002:9(4):747-752 (BH Natelson et al); Brain 2001:124(9):1821-1831 (RK Gherardi et al); Rheumatology: 2001:40(7):806-810 (M Nishikai et al) and Journal Watch:1997:314:4.

It therefore surprising that one of the authors (James Jones) now seems to regard ME/CFS as maladaptive interoceptive signal recognition.

Not only is deficient vitamin D implicated in autoimmune disorders, it is also known to be implicated in at least 16 different types of cancer, especially pancreatic, lung, breast, ovarian, prostate and colon cancers (see www.mercola.com). A landmark study from the Moores Cancer Centre at the University of California found that some 600,000 cases of breast and colorectal cancer could be prevented each year, if only vitamin D3 levels were increased.

Quite apart from being implicated in pancreatic cancer, low vitamin D is also known to affect pancreatic function, and pancreatic dysfunction is well-documented in ME/CFS.

As well as being implicated in common cancers, autoimmune diseases and cardiovascular disease, there is evidence that deficient vitamin D levels are implicated in infections: vitamin D can increase the body's production of naturally occurring antimicrobial peptides which destroy the cell wall of viruses and bacteria (see www.mercola.com; see also "Vitamin D Deficiency". Michael F Holick as above) and a deficiency is also implicated in seizures (see <http://news.bbc.co.uk/1/hi/health/7161458.stm>).

Holick, a world expert on vitamin D, states that 1,25 dihydroxyvitamin D controls more than 200 genes, including genes responsible for the regulation of cellular proliferation, differentiation, apoptosis and angiogenesis, and that it is also a potent immunomodulator, as well as increasing insulin production and myocardial contractability. Vitamin D deficiency is associated with congestive cardiac failure and blood levels of inflammatory factors including C-reactive protein and interleukin-10.

Conclusion

Given the immense importance of vitamin D, and given the fact that people with ME/CFS are known sometimes to have inordinately low levels, and given the protean symptomatology arising from a deficiency, it is disturbing that NICE precludes both testing for it and the prescribing of supplements to raise the level if necessary for patients with ME/CFS.

It would seem to be imperative that patients suffering from ME/CFS take charge of their own management and either persuade their GP to act against the NICE Guideline and check their vitamin D status (which in the UK, may mean sending blood to a specialist laboratory in Manchester and is expensive to do) or consult a private clinician specialising in ME/CFS.

For people within travelling distance of London, one such clinician is Dr William Weir, whose details are on the Co-Cure UK Good Doctor List (<http://www.co-cure.org/Good-Doc.htm>). Dr Weir works part-time as a Consultant Physician in the NHS but he also

runs a private ME/CFS Clinic at 10, Harley Street, London W1G 9PF (telephone: 0207 – 467 – 8478) and he now routinely checks vitamin D levels in all his ME/CFS patients.

The Doctors' Laboratory (55 Wimpole Street, London W1G 8YL, telephone 0207 – 460 – 4800) also carries out the 25 (OH)D test. A referral from a medical practitioner is required, but blood can be sent by post in a serum tube and must arrive within two days. If sent by post by a medical practitioner, the cost is £40, but if a patient is referred and attends in person to have blood taken, there is an additional service cost of £29.

There are numerous sources of vitamin D₃ supplements that do not contain excipients; one such company is Biocare (telephone 0121 – 433 – 3727), whose supplement contains only lanolin (the source of D₃) in extra virgin olive oil (but some people with ME/CFS may be unable to tolerate lanolin). There are different strengths of the supplement.

A more efficient way of increasing vitamin D levels may be by using a lamp specifically made for the purpose. One such lamp is the Xiris. It is made in Italy and can be obtained from Allergy Matters (telephone 0208 – 339 – 0029). It comes with full instructions and costs £225.

Alternatively, provided that the support of clinicians can be obtained and for those fortunate enough to have access to an NHS phototherapy unit (within a Dermatology Department), personalised, carefully titrated and monitored phototherapy is available on the NHS.

The NICE Guideline on “CFS/ME”, however, may prove to be a barrier impossible to surmount.

Clarification about the article "More potential dangers of the UK NICE Guideline on "CFS/ME" for people with ME/CFS?"

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