INFORMATION ON MYALGIC ENCEPHALOMYELITIS (ME)

FOR THE USE OF THE MEDICAL RESEARCH COUNCIL (MRC)

AND THE NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE (NICE)

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25th June 2004

Based on the evidence known to have been submitted to each group, there is widespread belief that the arbiters of both the Chief Medical Officer's Working Group Report on "CFS/ME" of January 2002 and the MRC's Research Strategy Plan for "CFS/ME" of May 2003 complied with a pre-determined policy not to clarify in their reports the World Health Organisation classification of ME / CFS as a neurological disorder. Not only was there no clarification, the report for the CMO contained specific misinformation, namely that "**CFS and ME are classified as distinct illnesses in the World Health Organisation's International Classification of Diseases**" (CMO's report, page 5, section1.4.1) and the MRC report stated that it relied upon the CMO's report.

This was notable, since the WHO has classified ME as a neurological disorder since 1969 and in the current ICD (revision 10, 1992) the classification remains unambiguous, with ME/CFS being coded to G93.3 under Diseases of the Nervous System. Specifically, the G93.3 classification captures all listed terminologies for the disorder including ME, CFS and PVFS (postviral fatigue syndrome).

This ambivalence of classification in the CMO's report and the MRC report was further exploited in 2000 by the deliberate inclusion of CFS/ME as a mental disorder in the Guide to Mental Health in Primary Care produced by the UK WHO Collaborating Centre at the Institute of Psychiatry where Professor Simon Wessely works.

It is not permitted under WHO rules to move a condition from one chapter of the ICD to another; moreover the WHO does not classify diseases by practice specialities: they are placed within a chapter according to pathophysiology. It fell to the Countess of Mar to obtain a retraction in the form of a letter dated 11th February 2004 from the Health Minister, Lord Warner, who confirmed that "**the WHO, the WHO Collaborating Centre and the Department of Health have now agreed a position on the classification of CFS/ME. The UK accepts ICD-10 (and) the Department accepts that it might have been clearer to say that chronic fatigue syndrome is indexed to the neurology chapter and fatigues states to the mental health chapter**".

This seemed clear enough, but a letter dated 31st March 2004 from Karen Nicolaysen in the Research and Development section of the Department of Health states that the Department is "**neutral on this issue**". Further, when the Countess of Mar asked the question "**Whether, in the light of their clarification that ME/CFS is a neurological disease and not a psychiatric disorder, (Her Majesty's Government)**

will forward this information to the chief executives of all NHS healthcare trusts", the reply on 20th April 2004 from Lord Warner was semantic: "**The Department of Health did not say that ME/CFS is a neurological disease**".

We are therefore left with confirmation that the Department of Health accepts that ME/CFS is a classified neurological disorder but that the Department does not accept that it ***is*** a neurological disorder.

This is important, because a letter dated 30th March 2004 from Professor Anthony Sheehan, Professor of Care Services at the Department of Health sent on behalf of the Chief Medical Officer, whilst confirming that there will be only one code for CFS/ME and that it is neurological, also stated "**It is not possible for me to say what intentions other parties may have about the classification of CFS/ME. I can only say that the Department of Health has no plans to seek a reclassification of CFS within ICD-10**".

This again is semantic, because it did not address the fact that under the accredited auspices of the UK WHO Collaborating Centre at the Institute of Psychiatry, psychiatrists of the "Wessely School" are endeavouring to secure a reclassification of "CFS/ME" as a functional somatic syndrome in the next revision of the ICD (ICD-11), for which deliberations are in progress.

Mindful of this, and of the MRC's acquiescence with the Oxford (1991) entry criteria for the PACE and FINE trials for "CFS/ME" for which it has agreed funding of £2.6 million, and also mindful of the letter dated 25th May 2004 from Robert Harkins at the Department of Health about the new "centres of expertise" for "CFS/ME" (for which Government has made available £8.5 million) which stated that "**The centres will be headed up exclusively by psychiatrists**", it would surely be naïve to expect that the forthcoming Guidelines commissioned from NICE ("Guidelines on the Diagnosis and Management of Chronic Fatigue Syndrome / Myalgic Encephalomyelitis") might come to a significantly different conclusion from either of the two above-mentioned reports, because NICE is part of the National Health Service, and indeed its views on the allegedly most effective management strategies for CFS/ME are already in the public domain.

There is concern in the ME community that Government and the MRC set the outcome they wish to achieve. This being so, it would be remarkable if NICE were to produce Guidelines that are substantially different from its already known view of the same issue.

NICE funds the publication of "Effective Health Care" bulletins: the Department of Neurology and Psychiatry of the Royal Society of Medicine vigorously promoted (and urged members to disseminate) one particular issue (that of May 2002) which proclaimed cognitive behavioural therapy and graded exercise therapy to be the strategies that have shown the best "evidence of effectiveness" for the management of CFS/ME ("Interventions for the Management of CFS/ME": Effective Health Care Bulletin, 2002:7:(4); RSM reference 43).

In an attempt to prevent the promulgation of more misinformation, it seems imperative that before it is too late, the information on ME contained in a major

medical textbook on ME/CFS should be publicly drawn to the specific attention of both the MRC and of NICE.

The textbook is "Handbook of Chronic Fatigue Syndrome" by Leonard Jason, Patricia Fennel and Renee Taylor and was published in 2003 by John Wiley & Sons, Inc; the ISBN number is 0-471-41512-X. The chapter from which the following quotations are taken is by Byron Hyde and is called "The Complexities of Diagnosis" (chapter 3, pp 42-72). It is particularly relevant to the current disquiet over the entry criteria for the MRC "CFS/ME" trials and to the forthcoming Guidelines from NICE on the management of "CFS/ME".

People may wish to draw this document to the attention of their Members of Parliament and request that MPs take up the matter with both the MRC and with NICE.

Quotations

"Although ME and CFS share many characteristics, the titles often represent two distinct groups of illnesses.

"ME in adults is associated with measurable changes in the CNS (central nervous system) and autonomic function and at times injury to the cardiovascular, endocrine and other organs and systems. It is described as (1) a systemic illness often (with) subnormal temperature; (2) marked muscle fatigability; (3) an acute onset of CNS changes of memory impairment, mood changes, sleep disorder, irritability and reactive depression; (4) involvement of the autonomic nervous system resulting in tachycardia, coldness of the extremities, urinary frequency, bowel changes, pallor, and sweats; (5) diffuse and variable involvement of the CNS leading to severe headaches, visual problems, ataxia, weakness, cramps, and sensory changes; (6) muscular and neck pain, acute fleeting spasmodic pain and tenderness and myalgia.

"The initial period of illness lasts from weeks to up to two years and tends to be more severe. The chronic phase is often sufficient to prevent return to school or work for either long periods or permanently.

"Dr John Richardson of Newcastle (UK) and others have documented significant associated cardiac and cardiovascular injury as well as other organ injuries associated with the usual CNS and autonomic changes in this group of patients.

"The ME descriptions deal with primarily CNS and autonomic changes, with easy fatigability and with poor or delayed recovery of CNS or muscle abilities. Although ME clinical descriptions noted the infectious onset, (in the) history of ME illness, neither pharyngitis nor involvement of lymph glands was ever mentioned (but are core features of CFS in the 1988 (Holmes et al CDC) criteria and in the 1994 (Fukuda et al CDC) criteria).

" (in relation to death), because of their overwhelming illness and the specificity of the end-organ injury, (patients) are never diagnosed as ME.

“Overwhelming fatigue is often a feature of the chronic (not the acute) illness phase. This profound fatigue often changes (and) in this new phase, the patient has rapid fatigability and poor recovery after any stressor.

“Those adults who are still significantly ill at two years can still improve but only a few ever return to any degree of normal function.

“CFS is *not* a disease. It is a chronic fatigue state.

“Where the one essential characteristic of ME is acquired CNS dysfunction, that of CFS is primarily chronic fatigue.

“If in any CFS patient, any major organ or system injury or disease is discovered, the patient is removed from the definition.

“Though the symptoms of CFS resemble those of ME, the differences are so significant that they would exclude ME patients from the 1988 and 1994 CDC (criteria).

“The following features of ME separate it from CFS: the epidemic characteristics; the known incubation period; the acute onset; the associated organ pathology (particularly cardiac); neurological signs in the acute and sometimes chronic phases; the specific involvement of the autonomic nervous system; the frequent subnormal patient temperature; the fact that chronic fatigue is not an essential characteristic of the chronic phase of ME.

“Organ disease in CFS has been avoided. By definition, it does not occur. For this reason, not only have most physicians avoided exhaustive testing but many have decried exhaustive testing as foolish.

“The patient with the diagnosis of ME/CFS is chronically and potentially seriously ill.

“These patients require a total investigation and essentially a total body mapping to understand the pathophysiology of their illness and to discover what other physicians may have missed.

“The chronic ME/CFS patient deserves, at least once, a complete investigation that includes mapping of body structures, organs and systems. Patients routinely come into my office telling me they have had a complete workup but few of these patients have had what I consider to be even basic investigation.

“Though ME/CFS usually represents significant disease processes, the underlying pathophysiologies or physical anomalies causing these processes are so varied that it is unreasonable and perhaps even dangerous to suggest or embark on any uniform treatment.

“Whether this suggested treatment protocol employs pharmaceuticals, cognitive or physical re-training, or alternative medications, these treatment modalities and philosophies are not medically justifiable and are often potentially dangerous to the patient. In the past two centuries, the development of Western medicine was based on

autopsy, physiology, pathology and reproducible tests. To date, however, this approach has largely been missing in the investigation and understanding of ME/CFS. There has been an immoral intervention by the insurance industry into the philosophy of physicians and health workers treating (these patients). This corporate insurance company intervention has used the mechanism of sponsoring medical symposiums to produce a uniform, insurance-friendly policy. Insurance companies have reputedly placed large numbers of (clinicians) under a significant annual retainer, injuring not only patient access but also negatively influencing other physicians who may not be aware of this economic relationship.

“Remember, a patient with ME is a patient whose primary disease is CNS change, and this is measurable. The primary disease of a patient with CFS is fatigue, and fatigue is neither definable nor measurable.

“The gradual onset group is of particular concern to me. It is in this group that vascular injury of the CNS or cardiac system is most frequently observed.

“Whether a patient fell ill abruptly or gradually, or has been ill for many years, is no excuse not to search for a potentially treatable cardiac, vascular, or other organ illness.

“Without being able to understand and measure the nature and degree of the underlying injury or disease, it is impossible to measure the effectiveness of any treatment.

”Patients want to know and have a right to know what has happened to them.

“I often accompany patients for tests in the hospital simply to observe them. Walking with these patients is like walking with a tortoise. They can be slow, clumsy, sometimes walking with a wide-leg stance. These patients have obvious CNS injury.

“A physician who saw some of these patients for only up to an hour would reasonably conclude that (there was) nothing wrong. This is misleading. During the course of a day’s examination, the patient may change from a brighter than normal person to one who resembles a blank-faced zombie, a patient who can talk and walk only with difficulty or not at all. Sometimes their voices become scanning, and they begin verbally to stumble. When I see them on the second day, they have often, in physical and intellectual terms, gone to pieces. A one-hour physical examination will rarely pick up ME/CFS pathology.

“(re):Thyroid disease: It is well known that the thyroid is one of the essential glands that regulate energy and temperature and it is equally well known that ME/CFS patients tend to have both energy and temperature dysregulation. For this reason, I not only do free T4 and TSH on all patients but also do thyroid antibody tests. Even with major thyroid disease, the TSH may be normal. TSH may vary from week to week. Even with all these tests returning as normal, I do a thyroid ultrasound on all ME/CFS patients. Patients with significant thyroid pathology as found on ultrasound and biopsy often have relatively normal TSH, free T4 and relatively normal thyroid antibody tests. Their thyroid pathology, however, is only part of a general autoimmune dysfunction, certainly involving the CNS but undoubtedly other areas as well. NeuroSPECT scans in these patients, as well as their immune tests, tend to be

grossly abnormal. The SPECT immune anomalies tend to persist. For some, this list of tests would already appear to be excessive. However, I cannot count the times that I have found abnormal thyroid and parathyroid function in this group of patients. Most physicians would not find (these) tests alarming unless they believed that ME/CFS is an invented phenomenon.

"(re) Lumbar puncture: during the early days or weeks of the disease, the patient may have a significant increase in intracranial pressure. The second point to remember is that many patients with acute onset ME/CFS may demonstrate IgG oligoclonal bands in their spinal fluid.

"Many acute onset ME patients have incredibly high polio 1, 2, or 3 antibody levels.

"The most important tests that I do are Doppler scans and echocardiograms. They are more productive than MRIs or almost any other group of tests in uncovering pathology in ME/CFS patients.

"I have found that during the first year of acute onset ME/CFS disability, the incidence of pericardial effusion is unusually high.

"Few physicians investigating ME/CFS employ the visual carotid and transcranial Doppler. This is a major error. It is a relatively inexpensive and totally safe procedure (and) it does things that no other type of test can do. Carotid atherosclerosis --- sometimes substantial--- is often found in patients with lipid dysfunction. This is a treatable condition.

"In patients with ME/CFS it is possible to demonstrate spasmodic disease of both major and smaller arteries. With the transcranial Doppler, the operator can measure the velocity of the blood flow. If (the arteries) are in spasm, you can observe this. Like ME/CFS muscles, ME brains are sometimes in significant pathological spasm. Arterial spasm may account for some, but not all, of the SPECT changes that are routinely seen in ME patients. Left middle cerebral arterial field hypoperfuson is typical of ME.

"(re): Ultrasound. Consider the following ultrasound scans: abdominal and pelvic organs and aorta; femoral and popliteal arteries in patients with leg pain.

"Early on in ME/CFS you will find a small number of enlarged spleens.

"Fatty infiltration of the liver is regularly seen.

"Ultrasound is a fairly inexpensive non-invasive type of testing and I do it on every patient. I routinely find pelvic pathology in as many as 30% of females.

"(re) Further Examination of the Heart and Cardiovascular System. Patients with ME/CFS frequently cannot do exercise tests.

"In our hospital we find a wide variety of circulatory changes in relation to surface volume. I have some ME patients with a circulating red blood cell volume of less than 50% (and) a very large number with the range of 60% to 70%. This means that

blood is pooling somewhere in the body and is probably not available to the brain. In effect, there may be a reduced perfusion of oxygen in these patients.

"(re) Diagnostic Tests of ME. Consider the following tests: (1) SPECT; (2) Xenon SPECT; (3) PET and (4) Neuropsychological testing.

"The primary diagnostic criterion for ME is acquired CNS change. SPECT demonstrates the microcirculation of the terminal arterioles in the brain. An ME patient has an abnormal brain SPECT. The typical SPECT change in an ME patient is a decreased perfusion in the cortex in the area of the left middle cerebral artery. Often there are also significant changes in the subcortical regions, specifically in the brain stem, cerebellum and basal ganglia.

"Another finding that we frequently discover is a vasculitis pattern. This change is identical to what one finds in a patient with HIV dementia. Patients with this vasculitis pattern are some of our most severely affected.

"(re) Fundamental Advice. Patients who arrive at the office of a new physician and who have been completely investigated by many excellent physicians are sometimes dismissed as psychiatric. It is in these patients that I find all of the pathology and some of it is obvious. Rarely do physicians do more than a routine series of tests.

"The belief that (ME)/CFS is a psychological illness is the error of our time. Patients are now being diagnosed with CFS as though it were a disease. It is not. It is a patchwork of symptoms that could mean anything".

(30 references).

The ME/CFS community owes Dr Hyde a debt of great gratitude. It remains to be seen if his latest contribution is treated with the same disdain and dismissal by Government bodies as was the case with the seminal 724 page textbook he co-edited with Drs Jay Goldstein and Paul Levine (The Clinical and Scientific Basis of ME/CFS published by.The Nightingale Research Foundation, Ottawa, 1992). This contains contributions from world leaders in the disorder, including at least one Nobel prize nominee, and is one of the most comprehensive textbooks on ME/CFS available.

At considerable personal expense, someone in the UK who is involved in litigation concerning ME arranged for 128 copies of this book to be flown from Canada to the Department of Health Headquarters at Quarry Hill in Leeds because she believed it essential that firstly, the CMO's Key Group members and subsequently the MRC Research Advisory Group members should read it for themselves. After (confirmed) arrival of the books in Leeds, it was the same Robert Harkins mentioned above (whose letter of 25th May 2004 stated that the new centres of expertise would be "headed up exclusively by psychiatrists) who resolutely refused to send copies as requested to the MRC.

Is it coincidence that the Department of Health Headquarters apparently lost track of these volumes and they are "missing", having been dumped at a Cystic Fibrosis unit and now believed to have been trashed? When a written complaint was sent to the CMO, the response received was nothing more than curt disinterest.

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