Notes on recent research in ME/ICD-CFS and the Government's policy of denial

September 2003

During August and early September 2003, Stephen Ladyman MP, Parliamentary Under Secretary of State for Health / Community Care in the UK Labour Government of Mr Blair, has been busy responding to letters about what he refers to as "CFS/ME".

In one of his letters (to Dr Liam Fox, Shadow Minister of Health) he wrote the following about the classification of "CFS/ME", which he claims comes from "the WHO Guide to Mental Disorders in Primary Care" (referring to a publication whose correct title is "WHO Guide to Mental Health in Primary Care": 30,000 copies of this Guide have been sold and it is not produced by the World Health Organisation but by the UK WHO Collaborating Centre at the Institute of Psychiatry, London, one of several such Centres which are authorised to use the World Health Organisation name for supposed collaborative work but which are wholly independent from the WHO itself):

"In 1997, WHO published its first edition of treatment guidelines for around 20 mental conditions commonly seen in primary care. They adapted each individual guideline for the UK. Although WHO were initially keen to use the term "neurasthenia", they eventually decided to call the section "Chronic Fatigue and Chronic Fatigue Syndrome (may be referred to as ME)". WHO is aware that members of the CFS/ME lobby are dissatisfied with what they feel is an erroneous classification of CFS/ME as a mental condition. The second edition (of the Guide) is to contain three common neurological conditions: headache (and migraine), stroke and epilepsy ".

In another letter to Dr Fox, the Parliamentary Under Secretary of State wrote:

"The WHO's International Classification of Diseases (ICD) provides a system of categories for international systematic recording. These are not diagnostic criteria. The current version (ICD-10) classifies CFS in two places; as Neurasthenia / Fatigue Syndrome in the mental health chapter (F48.0) and as Post Viral Fatigue Syndrome / Benign Myalgic Encephalomyelitis in the neurology chapter (G93.3). Close examination of the diagnostic criteria in the ICD shows that the WHO has essentially put the same condition in both places".

It is disturbing that someone in the responsible position of Under Secretary of State should promulgate such misinformation on behalf of the UK Labour Government.

In the first letter quoted, Stephen Ladyman (or whoever wrote the letter for him to sign) does not even use the correct title of the publication to which he is referring. Importantly, he then confuses the UK WHO Collaborating Centre at the Institute of Psychiatry, London with the WHO itself in Geneva, when the two are completely separate. It was **not** the WHO, but the Institute of Psychiatry, who produced the Guide to Mental Health in Primary Care and, significantly, the WHO itself has distanced itself from the errors

contained in the Guide, stating (in writing) that the views expressed in the UK Guide are at variance with the WHO's position. It is **not** the WHO who "*were initially keen to use the term neurasthenia*", but certain psychiatrists at the Collaborating Centre at the Institute of Psychiatry, and the WHO is quite specific that the term "neurasthenia" does not relate to ME/ICD-CFS and that ME/ICD-CFS is **expressly excluded** from that classification category.

On the issue of neurasthenia it is particularly notable that in the ICD itself, a cardinal feature of neurasthenia is anhedonia (loss of interest in life), and the Director of the UK WHO Collaborating Centre at the IOP, Professor Rachel Jenkins, is on record as confirming that in ME, there is **no** anhedonia, so it is strange indeed that the Parliamentary Under Secretary of State is officially informing people that (under the Directorship of Professor Jenkins) the UK Collaborating Centre was *"initially eager"* to use the term "neurasthenia".

Professor Jenkins' views on ME are admirably set out in two chapters in the book she co-edited with Professor James Mowbray (Post-Viral Fatigue Syndrome. ed: Rachel Jenkins and James Mowbray. pub: John Wiley & Sons, Chichester, 1991: ISBN 0 471 92846 1): in her Introduction (pp 3 – 39) she provides an excellent review of what ME really is, detailing symptoms and signs which have been completely removed from the case definition of "CFS" formulated by Professor Simon Wessely of the IOP and his like-minded colleagues. Professor Jenkins is quite specific that it is not difficult to recognise and diagnose ME:

"Once one is familiar with the concept, such patients are in practice not too difficult to differentiate from those with true psychiatric illnesses such as depressive illnesses, anxiety, hypochondriasis or hysteria".

Given her published views about ME, it is a matter of conjecture as to how she appears to have been over-ruled by her psychiatrist colleagues at the IOP (where the prime movers are known to be advisers to Government and its Departments dealing with health and social security).

The logic of those psychiatrists at the IOP who intend to include migraine, stroke and epilepsy (as well as "CFS") in the forthcoming second edition of the Guide to Mental Health in Primary Care defies rational explanation but is perhaps indicative of the changes to be anticipated following this Government's much criticised reform of the Mental Health Act, whereby **any** "disability or disorder of the mind or brain, whether permanent or temporary" which results in "impairment of mental functioning" is destined to be classified as "mental", thus affording psychiatrists (and Government) far greater powers to enforce compulsory psychiatric treatment on ever larger numbers of people, including the provision to be able to drug people against their wishes and even children against the wishes of their parents.

In the second quotation , the Parliamentary Under Secretary of State is again in serious error. He states about the ICD classifications that *"These are not diagnostic criteria"*

but immediately goes on to state *"Close examination of the diagnostic criteria in the ICD shows that the WHO has essentially put the same condition in both places"* (ie. he states that the WHO has classified the same disorder as both neurological and as psychiatric). This is erroneous, because the WHO has confirmed that the term Chronic Fatigue Syndrome (CFS) is one of the names by which ME has come to be known; that it is **not the same as states of chronic fatigue** and that ME/ICD-CFS is classified as a neurological disorder, not as a psychiatric disorder at F48.0 and, as mentioned above, **ME/ICD-CFS is *expressly excluded* from section F48.0** (the section which includes neurasthenia).

It does, however, seem that "patient power" has had some positive effect, because even the ill-informed Parliamentary Under Secretary of State has now been forced to concede in writing that *"it is correct that there is a distinction between the World Health Organisation (WHO) and the WHO Collaborating Centre"* but there is still a long way to go for those with ME/ICD-CFS.

Before publication of the Chief Medical Officer's Report on "CFS/ME" in January 2002, a letter in the following terms was sent to the CMO himself:

"Due to the gravity of the misinformation published and distributed by (the UK) WHO Collaborating Centre in their WHO Guide to Mental Health in Primary Care, I would ask if you would ensure, if even only as a damage limitation exercise, that the medical profession, the public, the sufferers, the media, insurance companies, the DSS and those internationally concerned are clearly informed of the correct World Health Organisation ICD-10 classification for CFS and ME within your forthcoming report".

Not only was this ignored, but the CMO's report deliberately set out misinformation (at page 5, section 1.4.1) by stating that *"Currently, CFS and ME are classified as distinct illnesses in the WHO's International Classification of Diseases"*. Such an assertion is blatantly untruthful and is readily shown to be so, but it is in line with Mr Blair's Government "policy" to deny the existence of ME and to classify "CFS" as a mental disorder. This is widely held to be because the incidence of ME/ICD-CFS is increasing alarmingly and it has been shown by US researchers that it can be both virally and chemically induced, so the Government and insurance industry dare not even contemplate the costs and service provision implications and have therefore decided upon a policy of denial (as in Gulf War Syndrome, where the same group of psychiatrists act as Government advisers).

For influential Government bodies such as the CMO's Working Group on "CFS/ME" resolutely to dismiss and ignore the many known biomarkers of significant cell injury in ME/ICD-CFS (and extensive published mainstream evidence was put before them) and to advise in their Report that comprehensive testing is neither necessary nor appropriate for such patients and (together with the recent recommendations of the MRC in their research strategy recommendations of May 2003) to continue to promote cognitive behavioural therapy, including graded exercise therapy (ie. forced exercise regimes) for all people with "CFS/ME" who are able to get to a hospital and even for those who are

too sick to attend hospital, with the claim that psychotherapy is the only "evidence-based" form of management for the condition, has once again been shown to defy scientific credibility.

It is therefore necessary yet again to set out a few relevant facts about ME/ICD-CFS which Government Ministers and the Department of Health officials who decide what is to be Government "policy" (and who compose pro forma replies which consistently fail to address the issues raised by MPs) would do well to heed.

We now have the Under Secretary of State not only defending but perpetrating serious misinformation by asserting that the World Health Organisation classifies "CFS/ME" as a mental disorder and we also have the Department of Health classifying ME/ICD-CFS as a mental disorder and we also have the NHS Information Authority (a body set up in 1999 under the Labour Government to disseminate information throughout the NHS) including ME/ICD-CFS in their Mental Health Data Manual and on their website, all of which is in contradiction to and total defiance of the World Health Assembly's neurological classification, facts which seem of no concern to the two major UK ME charities.

Research update

The key feature of recent ME/ ICD-CFS research is one of compromised immune cells, with significant disturbance to the oxidative pathway and lipid peroxidation.

A team in Dundee within the Vascular Research Unit, Department of Medicine, Ninewells Hospital, University of Dundee Medical School led by **Professor Jill Belch and Dr Vance Spence** has identified specific abnormalities in the biology of the vascular endothelium of ME/ICD-CFS patients:

1. **oxidative stress pathway:** free radicals are attacking lipids, forming isoprostanes and oxidised lipoproteins and are possibly attacking proteins, forming carbonyls

2. **choline pathway:** this pathway is dysregulated both at a level of the cholinergic axis, with free choline in the occipital cortex of ME/ICD-CFS patients **and** also by sensitivity to acetylcholine when it is applied as a vasodilator to the systemic circulation. This latter finding is **unique** to ME/ICD-CFS

3. **apoptosis (programmed cell death):** there is clear evidence of accelerated apoptosis of specific immune cells in ME/ICD-CFS patients, identified as cell surface proteins, activation "cell death" receptors and derangement of the internal cell milieu

4. **biology of the blood vessel endothelium:** many of the symptoms of ME/ICD-CFS can be explained by dysfunction of blood vessels, especially at the level of endothelial cells. Such dysfunction may arise out of either the oxidative stress or

apoptotic pathways mentioned above or as a combination of both factors, but current evidence points to significant injury to this vital organ (ie. blood vessels).

This pattern of results is **specific to ME/ICD-CFS** and is not seen in those with OP poisoning or in Gulf War Syndrome or in controls. The results point to ME/ICD-CFS being a separate and distinct syndrome and the findings are robust.

The evidence clearly points to a **persistent** viral or toxic state (and as mentioned above, US researchers have demonstrated that ME/ICD-CFS can be either **virally or chemically** induced).

Reports on this research have been submitted to various leading medical journals and some of these findings have been published (Prolonged acetylcholine-induced vasodilatation in the peripheral microcirculation of patients with chronic fatigue syndrome Khan F, Spence V, Kennedy G, Belch JJ. *Clin Physiol Funct Imaging 2003 Sept:23(5):282-285*). Some of the data has been presented at various conferences, including the Scottish Society of Experimental Medicine on 22nd November 2002 held at the University of Edinburgh (this being the first time that ME/ICD-CFS received recognised status at such a prestigious scientific meeting in the UK) and also at the international AACFS meeting in January 2003 held in Washington DC.

There is sufficient evidence to conclude that ME/ICD-CFS might well be a vascular disorder, with a specific manifestation of endothelial dysfunction very similar to what the celebrated neurologist Professor Charles Poser from Harvard described in 1969 as a vasculomyelinopathy.

Further evidence of this comes from the numerous reports of vascular dysfunction visualised in the central nervous system by SPECT imaging, with one study highlighting specific blood flow anomalies at the level of the brain stem, this being validated by PET imaging in a further report. These reports, along with the various studies of orthostatic intolerance (an insidious drop in blood pressure on being upright) have never been explained and the work from Dundee goes some way to addressing this vacuum.

In earlier work, the Dundee team found abnormalities in the vasoconstrictor pathways, demonstrating biomarkers of toxicity in RNA expression, with a very high level of significance and indicating an on-going toxicity problem.

What is paradoxical in ME/ICD-CFS is the conflict between the activation of both vasodilator and vasoconstrictor pathways, findings which are intriguing.

Many pathways are being disrupted, not just the endothelium: the **cell biology itself is disrupted.** This disruption impacts on the health of the blood brain barrier (BBB), facilitating an autoimmune vasculitis. Capilliary fragility is known to increase as blood levels of cortisol fall and blood levels of cortisol are known to be lower in ME/ICD-CFS patients; this in turn might lead to an inadequate dampening down of the immune system

and to the emergence of autoimmune disease and allergies, both of which have been demonstrated to occur in this disorder.

Professor Kenny de Meirleir from Brussels presented a paper in Northern Ireland on 2nd November 2002 and a video of the lecture is available.

De Meirleir is certain that ME/CFS is a disorder of the immune system and has demonstrated the presence of small fragments of specific RNaseL nucleotides from the antiviral defence pathway within specific white blood cells; these fragments are ***within*** the cells and cause significant chaos to cellular homeostasis, with the antiviral pathway being continually activated, resulting in serious injury to the cell.

The damage caused by these fragments is not discernible on standard blood tests because the fragments interfere with receptor signalling, with specific cell surface ion channels and with proteins, all of which can only be assessed by specific and sensitive assays.

Such interference gives rise to disturbances to many pathways including oxidative stress, lipid peroxidation and cellular apoptosis, with consequences for the vascular endothelium and the behaviour of blood vessels in relation to stimuli.

The thyroid serves as a good example of this derangement: while T3 and T4 and TSH might be normal in ME/ICD-CFS patients, these standard tests of thyroid function give no indication of action at the thyroid receptor level. The problem is that the thyroid receptors are blocked by RNaseL nucleotides and despite normal test results on basic routine screening, the thyroid **cells** are not working. Whilst nominally euthyroid, ME/ICD-CFS patients may indeed by hypothyroid at a receptor level as distinct from a hormone level.

Also, on routine screening, cholesterol levels are seen to be normal, yet ***inside*** the lipid pathways there is chaos in HDL and LDL status. The EFA pathway is being attacked, with catastrophic cell damage. HDL is very low in ME/ICD-CFS patients (being used up as part of the inflammatory process) and patients may be very ill.

Professor Mina Behan of Glasgow has found very swollen muscle cells in some patients with well-defined ME/ICD-CFS, the cells being disordered and dysfunctional, with clearly visible enlarged and thickened mitochondria. This hypertrophy of the mitochondria is likely to be the result of the cell's continued efforts to get energy.

As **Professor Paul Cheney** of the US has made clear, a defect in mitochondrial function would be exacerbated by exercise, especially aerobic exercise, and this would inevitably lead to further, possibly irreversible, DNA damage. This is best explained as excessive production of free radicals from within muscle cells, leading to the production of metabolic by-products that have consequences on local vasoconstriction, with damage to

muscle and endothelial cells. Inflammation plus exercise induces free radicals, which absorb nitric oxide, which causes vessels to collapse, which results in vasoconstriction, which gives rise to pain and fatigue.

The psychiatric myth: it seems that the psychiatrists who now wield so much power at the Department of Health and who exert such influence upon Mr Blair's Government have difficulty in understanding the significance of these (and numerous other) scientific findings because they continue to assert that ME does not exist and that "CFS" is a somatisation disorder which must be "managed" by brain-washing techniques designed to "correct" the patients' "aberrant illness attributions" that they have a serious organic disorder, and patients must not be granted secondary gain in the form of financial support but must be compelled to return to productive employment.

By its refusal to pay any attention to what has so repeatedly been brought to its attention, Mr Blair's Government seems determined to keep the lid on what is increasingly considered to be another scandal.

As with Gulf War Syndrome, the evidence continues to be dismissed. That patients suffer indescribably and that many are completely abandoned by the State and are so without hope or support that they are driven to suicide seems to be of no consequence when weighed against costs implications to Government and to the industries which fund it, whose ubiquitous chemicals may well play a role in the increased incidence of ME/ICD-CFS.

Despite all the published international evidence that ME/ICD-CFS is a serious, chronic and devastating neuroendocrine-immuno-vascular disorder, UK Government bodies have decreed that ME patients must not be fully investigated and that no research is to be undertaken into the disrupted biology; instead, all that is to be provided for such gravely sick people are more psychiatric "centres of excellence" which will deliver cognitive behavioural therapy and a psychiatric ascription (thereby excluding such patients from essential financial benefits necessary for basic survival).

All statements in this document are supported by authentic references.

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