

## **DENIGRATION BY DESIGN?**

A Review, with References, of the Role of Dr (now Professor) Simon Wessely in the  
Perception of Myalgic Encephalomyelitis

**UPDATE: 1996 - 1999**

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**NOTE**

In the Frontispiece to the 1996 manuscript “Denigration by Design? it was clearly stated that no personal animosity whatsoever was directed at Dr Wessely.

It was noted that there was widespread concern that Wessely’s published papers do not provide a balanced or accurate picture of the available published world literature on myalgic encephalomyelitis (ME).

It was also stated that the aim of the review was to provide a factual record of Wessely’s involvement in the perception, both medical and public, of ME.

It was noted that whilst even the hint of any kind of vendetta against Wessely would be unacceptable and unprofessional, the exposing of a genuine problem (with which Wessely is closely associated) is, however, essential.

Likewise in this 1999 Update, it is re-iterated that there is no personal animosity directed at Wessely.

Rather, this updated literature review seeks only to bring to public attention matters with which Wessely continues to be closely associated and which some believe might indeed amount to scientific misconduct.

## Introduction

In August 1996 we produced a 217 page referenced review in which we attempted to consider the role played by Dr — now Professor—Simon Wessely in the perception (both medical and public) of myalgic encephalomyelitis (ME) in the years 1987 - 1996 (*Denigration by Design? A Review, with References, of the Role of Dr Simon Wessely in the Perception of Myalgic Encephalomyelitis, 1987 - 1996. Eileen Marshall & Margaret Williams, September 1996*). In it, we considered Wessely's status, his tactics, others involved (ie. psychiatrists with whom he frequently and regularly collaborates in publishing his own views), legitimate research findings about ME with which he openly disagrees, illustrations of those research findings, and a review of Wessely's published works on ME/CFS. We considered his lack of balance and his obvious bias, his part in the “organic - v - “functional” debate, the harm done to sufferers of ME by Wessely, some losses sustained by those sufferers as a result of Wessely's denigration of their suffering, and we listed 39 questions which we believe Wessely could usefully be required to address (for example: why does he not visit the more severely affected in their own homes, so that they, too, can be included in his trials; in what percentage of his patients has he carried out a water-loading test; what percentage of his patients show an increased CD4-CD8 ratio; what percentage of his patients have a clear-cut vestibular lesion; what percentage of his patients have undergone muscle biopsies subjected to polymerase chain reaction (PCR); what percentage of his patients have vascular problems; what percentage have positive autoantibodies; why does he assume that people with ME /CFS are invariably *benefitting* by “adopting the sick role” when he has never published any *proof* that this is so, and why has he never attempted to consider the *losses* his patients have sustained).

There was little original material in our literature review and it was never intended for publication but rather as a compendium of ready reference for lawyers and medical practitioners involved in trying to assist patients overcome seemingly insuperable problems (most notably the problem of the credibility of their suffering and disability) with which they found themselves grappling.

The review received some acclaim for what it was: a reasonably comprehensive overview of Wessely's published works on ME / CFS. Copies were requested from all over the UK, America, Australia and the Netherlands.

We would hope that we showed *why* the problem of credibility in ME is such a major issue in medico-legal situations, and that we demonstrated the key role played over that decade by Dr Simon Wessely in the creation of this widespread problem.

Has anything changed in the last three years?

Sadly, it seems that little has changed. Despite excellent international published research papers showing definite neuro-endocrine-immunological deficits in ME, and despite the advances in understanding about ME revealed by nuclear imaging of the brain, problems of definition remain, with the same group of psychiatrists still claiming that ME is merely

a form of somatisation.

Recently, the Lancet carried an article by Wessely and Mike Sharpe (*Functional somatic syndromes: one or many?* S. Wessely, C. Nimnuan, M. Sharpe: *Lancet*: September 11, 1999:354:936-939) in which they claim to review the literature on syndromes such as irritable bowel syndrome, chronic fatigue syndrome, pre-menstrual tension syndrome, fibromyalgia, temporomandibular joint pain, tension headache, atypical chest pain, multiple chemical sensitivity and globus hystericus; they assert that the similarities between all these syndromes (the authors believe that the “similarities” are that they are all “functional” and all occur predominantly in women) outweigh the differences, and urge that all these “functional” syndromes be converged into one diagnostic category of somatisation, which they define as a “functional somatic syndrome, or one that after appropriate medical assessment cannot be explained in terms of a conventionally defined medical disease”. The authors state that “many of these syndromes are dignified by their own formal case definition” and they “question this orthodoxy and ask whether these syndromes represent specific diagnostic entities”, and postulate that “the existence of specific somatic syndromes is largely an artefact of medical specialisation”. The authors urge that the acceptance of distinct syndromes as defined in the medical literature should be challenged, and state that they are currently attempting to do just that. (See pp 130-137 for more details of this paper).

It is perhaps worth mentioning here that the DSM IV (*American Psychiatric Association Diagnostic and Statistical Manual of Psychiatric Disorders*, 4<sup>th</sup> edition, Washington DC, 1994) somatisation disorder criteria do not mention fatigue syndromes.

That's same week, delegates at the Brussels international conference on CFS/ME were told that CFS/ME had finally escaped from the psychiatrists' ascription of somatisation disorder; this would be welcome, but such a view may be over-optimistic, as this present review may demonstrate.

Regrettably, the common usage of the various terms [ME (myalgic encephalomyelitis), CFS (chronic fatigue syndrome), CF (chronic fatigue), PVFS (postviral fatigue syndrome) and CFIDS (chronic fatigue and immune dysfunction syndrome, which is the favoured American term for ME, ie. for those chronically and severely affected by the most severe of all the CFS subsets] as synonymously interchangeable continues to hamper both research and approaches at clinical management.

In the previous review we attempted to include as many as possible of Wessely's published papers in order to demonstrate the sheer *extent* of the onslaught on those with a diagnosis of ME, which he and his like-minded psychiatrist colleagues continue to insist be called Chronic Fatigue Syndrome: it remains a cause of concern that their own criteria for what they term “chronic fatigue syndrome” specifically *exclude* the cardinal neurological problems long documented in the international ME literature. (The 1991 criteria - known as the Oxford criteria arose from a meeting consisting of 21 clinical and scientific researchers of whom 8 (38%) were psychiatrists or psychologists: it was

convened by three psychiatrists and chaired by a fourth, Professor Anthony Clare who, with some exasperation, informed those present that there was only one reason for calling the meeting and that was “a group of patients with a cluster of symptoms who get a lot of publicity”: [*Consensus on research into fatigue syndrome: BMJ 1990: 300:382*]. The 1994 (revised) criteria were issued by the Centres for Disease Control (CDC), in the formulation of which both Sharpe and Wessely were named as being involved. In both these definitions, the psychiatrists extended the criteria to include *all* medically unexplained “fatigue” of at least six months’ duration. In the 1994 definition, it was additionally stipulated that they were dropping all *physical* signs from their inclusion criteria. Both these definitions *specifically include* psychiatric conditions which are *known* to be associated with prolonged fatigue. Further, the 1994 definition advises *against* doing screening tests, but states “we consider a mental status examination to be the minimum acceptable level of assessment”.

In this update, some illustrative examples are provided, with no claim whatsoever to have produced a comprehensive review of Wessely’s published output on CFS / ME over the last three years 1996 -- 1999.

Nevertheless, it is hoped that this update will provide enough examples to show how little has changed in the understanding of medical science by psychiatrists of the “Wessely School”.

For example, 10 years after Wessely was instrumental in getting a child with ME forcibly removed from his parents and taken under police presence into “care”, (see Denigration by Design? Marshall, E & Williams, M. 1996, pp 65 -68, which deals with Wessely’s involvement in the tragic case of Ean Proctor), children and distraught parents are still being placed in that same intolerable situation, as will be shown in a forthcoming BBC Panorama programme scheduled for transmission in November 1999.

Wessely seems to have become confused, for in a Channel 4 News programme broadcast at 7pm on 26th August 1998 in which the case of Child X was being discussed, when asked by the presenter Sheena McDonald if there can ever be a case for a coercive approach in situations involving forcible removal of a child with ME from the parents, he stated (verbatim quote) “You know very well,

I know nothing about these cases.....’ and when Sheena McDonald interposed by saying “So you would agree that unless there is criminal abuse there is never a case for a coercive approach to take children away from parents?”, Wessely replied (verbatim quote) “I think it’s so rare; I mean it’s never happened to me. We’ve seen lots of children and families and it’s just not on the agenda”. This contrasts markedly with what Wessely wrote in a letter dated 3<sup>rd</sup> June 1988 to the Principal Social Worker in Ean’s case (Mrs Jean Manson), in which he states that he is “Approved under Section 12 of the 1953 Mental Health Act” and in which he wrote (quote): “I feel that Ean needs a long period of rehabilitation, part of which will involve very skilled management of separation from his parents. - ..For this reason, I support the application made by your department for wardship”.

This letter was written by Wessely in his capacity as Senior Registrar in Psychiatry at The National Hospital for Nervous Diseases, London, and unequivocally reveals that despite his ardent assurances to Sheena McDonald on national TV that he had never been personally involved in cases of children being forcibly removed from their parents and being subjected to psychiatric treatment, Wessely *has* been personally involved, and that he personally advised the local authorities to take the action they did.

Moreover, just a short time after his denial on the Channel 4 broadcast, Wessely once again repeated on air his denial of personal involvement in the forcible removal of children with ME from their parents: on 13th September 1998 Radio 5 Live broadcast a programme entitled “Child Abuse by Professionals” (Brian Hayes, Sunday 13th September 1998, 10am -12 noon), and Wessely again claimed never to have been involved in such cases.

(Copies of Wessely’s letters and audio / video tapes available if required).

In the original review, we provided for comparison a short selection of published papers which revealed aspects of ME which differed from the extensively proclaimed views of Wessely; likewise in this update, we provide a random selection of other people’s work on ME which has been published in the same period as the one under review (1996-1999). No attempt has been made to classify these illustrations into sections (for example, neurological, endocrinological, immunological, cardiac, neuropsychological, virological etc); all are merely listed according to the year of publication.

**Illustrations of research findings and opinions about ME / CFS which Wessely seems to dismiss, trivialise or completely ignore**

1996

Randomised, double-blind, placebo-controlled study of fluoxetine in chronic fatigue syndrome. Jan H M M Vercoulen, Caroline Swanink et al: *Lancet*, 1996:347:858-861

“Antidepressant therapy is commonly used (in CFS). However, there has been no randomised, placebo-controlled double-blind studies showing the effectiveness of antidepressant therapy in CFS. We have carried out such a study to assess the effect of fluoxetine (*Prozac*) in depressed and non-depressed CFS patients”.

“There have been anecdotal reports that fluoxetine is poorly tolerated by patients with CFS. In our trial, 15% of fluoxetine-treated patients withdrew because of side effects, a higher withdrawal rate than in fluoxetine trials in depressed patients on the same regime”.

“In our study, fluoxetine was no better than placebo in treating depression”.

“Fluoxetine in a 20 mg daily dose does not have a beneficial effect on any characteristic of CFS”.

“We conclude that prescription of 20mg fluoxetine in CFS is unwarranted, irrespective of whether depressive symptoms are present; it does not lead to improvement in any area of the patient’s functioning”.

Chronic Fatigue Syndrome: is total body potassium important? Burnet RB et al. *Medical Journal of Australia*, 1996:164:6:384

The authors found that total body potassium (TBP) was lower in patients with CFS and they suggest that abnormal potassium handling by muscle in the context of low overall body potassium may contribute to fatigue in CFS.

Lung function test findings in patients with chronic fatigue syndrome.  
De Lorenzo et al. *Australia and New Zealand Journal of Medicine*, 1996:26:4:563-564.

The authors found that compared with controls, patients with CFS showed a significant reduction in all lung function parameters.



Abnormality of adrenal function in the patients with chronic fatigue syndrome.

Yamaguti K et al. *JCFS*, 1996;2:2/3. Abstract of presentation at The Proceedings of the First World Congress on CFS, Brussels, November 9-11, 1995.

“The level of DHEA decreases in some patients and the level of DHEA - S decreases in most patients with CFS. These abnormalities found in CFS are quite different from those found in patients with mental and physical diseases reported previously”.

Eosinophil cationic protein serum levels and allergy in chronic fatigue syndrome. Conti F et al. *Allergy*: 1996;51:124-127

“ECP serum levels were significantly higher in CFS patients than in controls. In CFS patients, the prevalence of radio-allergosorbent (RAST) positive responses to one or more allergens was 77%, while no control showed positive RAST”.

Chronic Fatigue Syndrome: evaluation of a 30-criteria score and correlation with immune activation. Hilgers A and Frank J. *JCFS*, 1996;2:4:35-47.

The aim of this study was to develop a score to evaluate the severity of CFS and to correlate the degree of severity with parameters of immune activation; five hundred and five patients were studied using a 45-criteria score and basic laboratory programmes, together with immunological profiles. In most of the patients, further tests of complement system, immune activation markers, hormones and viral serology were evaluated.

385 patients fulfilling the 1994 CDC criteria showed significant differences to healthy controls in 40 of the 45 symptoms assessed. Thirteen symptoms corresponding to CDC criteria were all significant, but 17 further significant criteria were added to improve precision:

respiratory infections; palpitations; dizziness; dyspepsia; dryness of mouth / eyes; allergies; nausea; paraesthesia; loss of hair; skin alterations; eczema; dys-coordination; chest pain; personality changes; general infections; urogenital infections; twitches.

A correlation between the 30-criteria score and immunological parameters could be evaluated in 472 of the 505 patients.

Significant positive correlation was found in numbers of CD8+ T lymphocytes, HLA DR+ lymphocytes, gamma globulins, IgM, IgG, and for the numbers of types of autoantibodies (mainly ANA, ACA, antithyroid and antiparietal cell antibodies).

Significant negative correlation was found in albumin-globulin ratio, eosinophils and IgE.

Most of these parameters also correlated with one another.

“In increasingly larger groups of patients with CFS and related constellations we often see clinical signs and longer anamnesis of other symptoms beside the classical criteria of CFS, especially a high prevalence of local and general infections and hints to prolonged inflammation processes...A reduced or unstable immune control can lead to a chronic neuro-immune activation state and autoimmune disorders. Hypersensitivity symptoms of the patients might not be mediated by classical allergies alone but also result from a type IV hypersensitivity”.

The neuroendocrinology of chronic fatigue syndrome. Scott LV, Dinan TG.  
*JCFS: 1996;2:4:49-59*

The authors note that there is an increasing volume of evidence to support the view that patients with CFS have unique neuroendocrinology patterns.

Central to this endocrine dysfunction is altered hypothalamic-pituitary-adrenal axis (HPA) activity.

The cardinal findings include attenuated adrenocorticotrophic hormone (ACTH) responses to corticotrophin-releasing hormone (CRH) and low 24 hour urinary cortisol. These are compatible with a mild central adrenal insufficiency.

Adrenal steroids have widespread impact in the brain, and of particular importance is their dense concentration on serotonergic and noradrenergic neurotransmitter pathways.

The authors propose that the disruption of the HPA axis (which may be triggered by a number of stressors) may represent a primary phenomenon, and that neurotransmitter abnormalities (serotonin and noradrenalin) are in fact secondarily heralded by prolonged HPA dysregulation.

Evidence that abnormalities of central neurohormonal systems are key to understanding Fibromyalgia and Chronic Fatigue Syndrome. Leslie J.Crofford and Mark A.Demitrack.  
*Rheum Dis Clin North America:1996;22:2:267-284*

The concept that disorders such as fibromyalgia (FM) and chronic fatigue syndrome (CFS) are associated with subtle and undetectable disturbances in the central nervous system was introduced in 1869 by Beard. Great strides have been made in recent years towards defining neurochemical abnormalities in FM and CFS, and both FM and CFS fall into the spectrum of what might be termed *stress-related illnesses* by virtue of the clinical observation that the onset of both is coincident with physical or emotional stress. The article focuses on abnormalities of the HPA axis and sympathetic nervous system (SNS), ie. the major stress response systems, and the authors point out that it is important to

keep in mind that activity of stress response systems is determined by genetic and environmental factors.

The authors present data which supports the view that FM and CFS could represent different forms of insufficient stimulation of the HPA axis, with both syndromes expressing low hypothalamic CRH but with FM being characterised by *increased* exposure of the corticotrophs to AVP, while CFS patients have *decreased* AVP levels. Patients with a longer duration of disease tend to have more severe basal abnormalities in cortisol levels.

When estrogenic stimulation diminishes, relative hypo-function of the HPA axis could follow, contributing to the development or maintenance of FM / CFS.

Further research into the nature of the neurohormonal perturbations in FM and CFS may elucidate treatment strategies for these disorders.

Neuroimmune mechanisms in health and disease. Part 2: Disease. Anisman H. et al. *Can Med Assoc.J*: 1996;155(8) 1075-1082

In the second part of their article on the emerging field of neuroimmunology, the authors present an overview of the role of neuroimmune mechanisms in defence against infectious disease and in immune disorders. Profound neuroendocrine and metabolic changes take place: acute phase proteins are produced in the liver; bone marrow function and the metabolic activity of leukocytes are greatly increased, and specific immune reactivity is suppressed. Defects in regulatory processes (which are fundamental to immune disorders and inflammatory diseases) may lie in the immune system, the neuroendocrine system or both.

Defects in the HPA axis have been observed in autoimmune disease, chronic inflammatory disease, chronic fatigue syndrome and fibromyalgia.

Defective neural regulation of inflammation is likely to play a pathogenic role in allergy and in gastrointestinal inflammatory disease.

A better understanding of neuroimmunoregulation holds the promise of new approaches to the treatment of immune and inflammatory disease with the use of hormones, neurotransmitters and neuropeptides and drugs which modulate these newly recognised immune regulators.

Prevalence of irritable bowel syndrome in chronic fatigue. Gomborone JE et al. *JRCP Lond* 1996;30:6:512-513

The purpose of this study was to determine the prevalence of irritable bowel syndrome in chronic fatigue sufferers.

A questionnaire about bowel symptoms was sent to 4,000 members of Action for ME self help group, and was returned by 1,797 (45%).

The people with chronic fatigue reported more bowel symptoms including the Manning criteria than the general population.

Seventy three per cent qualified for the diagnosis of IBS, which greatly exceeds estimates of IBS prevalence of up to 22% in the general population.

The researchers suggest that CFS and IBS may overlap in pathogenesis.

Decreased vagal power during treadmill walking in patients with chronic fatigue syndrome. Cordero DL, Natelson BH et al. *Clin Auton Res*: 1996;6:(6):329-333

The purpose of this study was to determine if patients with CFS have less vagal power during walking and during rest periods following walking.

Patients had significantly less vagal power than the control subjects, despite there being no significant group-wise differences in mean heart rate, tidal volume, minute volume, respiratory rate, oxygen consumption or total spectrum power.

Notably, patients with CFS had a significant decline in resting vagal power after periods of walking.

These results suggest a subtle abnormality in vagal activity to the heart in patients with chronic fatigue syndrome.

Autoantibodies to Nuclear Envelope Antigens in Chronic Fatigue Syndrome  
K.Konstantinov, D.Buchwald, J.Jones et al. *J.Clin Invest* 1996;98:8:1888-1896

The authors identified and partially characterised the autoantibodies in sera of 60 patients with CFS. The autoantibodies were of the IgG isotype.

The occurrence of autoantibodies to a conserved intracellular protein like lamin BI provides new laboratory evidence for an autoimmune component in CFS.

The immunological abnormalities described are in accordance with a growing body of evidence suggesting chronic, low-level activation of the immune system in CFS.

The authors found that 52% of patients with CFS develop autoantibodies to components of the nuclear envelope (NE), mainly nuclear lamins. Their findings suggest that in addition to the other disturbances of the immune system, humoral autoimmunity against polypeptides of the NE is a prominent immune derangement in CFS.

67% of CFS patients were positive for NE reactivity, compared with 10% of normal subjects in control groups I and II. In addition, none of the patients with chronic depression or atopy showed reactivity to NE proteins.

These results confirm that the NE reactivity of some CFS sera is against lamin B. Autoantibodies to NE proteins are relatively infrequent in routine ANA serology, and most of these fall into the broad category of an unusual connective tissue disease subset characterised by.... brain or skin vasculitis.

The authors state that future work should be directed at a better understanding of the autoimmune response of CFS patients to other NE proteins.

Randomized, double-blind, controlled placebo-phase in trial of low dose phenelzine in the chronic fatigue syndrome

Benjamin H.Natelson et al. *Psychopharmacology* 1996;124: 226-230

The authors investigated the possibility that CFS was a disorder of reduced central sympathetic drive; their study allowed the authors to evaluate patients for a placebo effect: no evidence for this was found, suggesting that CFS is not an illness due to patients being overly suggestible, and negating the proposal by some investigators that CFS is not a disease at all but simply a form of aberrant illness behaviour related to the suggestibility of the patient.

The authors conclude that their results are certainly not consistent with what might be expected in suggestible patients with psychogenic illness.

The authors state that “no clear effect of any commercially available treatment has ever been demonstrated in this devastating illness”.

1997

Evidence for enteroviral persistence in humans

Daniel N.Galbraith, Carron Nairn and Geoffrey B.Clements. *Journal of General Virology* 1997: 78:307-312

The authors present for the first time evidence for enteroviral persistence in humans based on sequence comparison of serial PCR products from the 5' non-translated region (NTR).

A group of CFS patients was being followed prospectively, and showed closely related enteroviral sequences containing a unique shared pattern detectable in sera of individual patients for up to 24 months, providing good evidence for viral persistence.

The sequences from the CFS patients form a group demonstrating a close genetic

relationship with each other, and fall into a subgroup that is related to Coxsackie B viruses.

The authors point out that co-existence of populations of different enteroviral sequences has been shown in poliovirus where reversion of attenuated vaccine strains to a neurotropic type can occur in an individual.

Biochemical Evidence for a Novel Low Molecular Weight 2-5A-Dependent RNase L in Chronic Fatigue Syndrome

Robert J.Suhadolnik, Daniel L.Peterson, Paul R.Cheney, Kenny de Meirleir et al  
*Journal of Interferon and Cytokine Research* 1997;17:377-385

Previous studies from this laboratory have demonstrated a statistically significant dysregulation in several key components of the 2' 5'A synthetase / RNase L and PKR antiviral pathways in CFS. The 2-5A synthetase / RNase L pathway is part of the antiviral defence mechanism in mammalian cells.

An accumulating body of evidence suggests that CFS is associated with dysregulation of both humoral and cellular immunity, including mitogen response, reactivation of viruses, abnormal cytokine production, diminished natural killer (NK) cell function and changes in intermediary metabolites.

Marked and striking differences have been observed in the molecular mass and RNase L enzyme activity of 2-5A binding proteins in extracts of PBMC from individuals with CFS compared with healthy controls.

The authors present biochemical evidence for an RNase L enzyme dysfunction in CFS, in particular for an upregulated RNase L activity associated with CFS.

The biochemical and immunological data presented in this paper have identified a potential subgroup of individuals with CFS with an RNase L enzyme dysfunction that is more profound than previously observed in CFS, and which the authors believe is related to the severity of CFS symptoms.

Elevation of Bioactive Transforming Growth Factor- $\beta$  in Serum from Patients with Chronic Fatigue Syndrome

Adrienne L.Bennett, Dedra Buchwald, Anthony L.Komaroff et al. *Journal of Clinical Immunology*: 1997;17:2:160-166

The authors provide evidence that patients with CFS had significantly higher levels of bioactive TGF- $\beta$  levels compared to the healthy controls, to patients with major depression, patients with SLE, patients with relapsing/remitting multiple sclerosis and patients with CP MS, ie. that in patients with CFS, the levels were significantly higher

compared to patients with various diseases known to be associated with immunologic abnormalities and *I* or pathologic fatigue.

The authors state that perhaps of greatest relevance to CFS are the effects of TGB- $\beta$  on cells of the immune and central nervous systems, and the evidence that it may play a role in autoimmune and inflammatory disease.

Elevated apoptotic cell population in patients with chronic fatigue syndrome: the pivotal role of protein kinase RNA

A.Vojdani, CW Lapp et al. *Journal of Internal Medicine* 1997;242:465-478

The authors state that a prominent feature of CFS is a disordered immune system and recent evidence indicates that induction of apoptosis (*programmed cell death*) might be mediated in a dysregulated immune system by the upregulation of growth inhibitory cytokines.

The authors' results are in agreement with previous reports on abnormal cytokine production in CFS patients.

Quantitative analysis of apoptotic cell population in CFS patients has shown a statistically significant and marked increase compared with healthy controls.

Such an abnormality in cell cycle progression is an indication of abnormal mitotic cell division.

Activation of PKR can result in inhibition of protein synthesis and induction of apoptosis, and activation of the PKR pathway could result from a dysregulated immune system or from chronic viral infection.

Blunted serotonin-mediated activation of the hypothalamic-pituitary-adrenal axis in chronic fatigue syndrome

Timothy G.Dinan, Tahir Majeed, Peter Behan et al  
*Psychoneuroendocrinology* 1997;22:4:261-267

The authors state that CFS is a clinically defined syndrome in which serotonergic activation of the HPA axis is defective, with the release of ACTH (but not cortisol) in response to ipsapirone challenge being significantly blunted, and that patients with CFS show disturbances of HPA function which differ markedly from those seen in melancholic depression.

The authors note that an increase in peripheral turnover of the major metabolite of 5HT might explain the heightened allergic responsiveness, as well as the musculoskeletal pain seen in CFS patients.

Politics, Science, and the Emergence of a New Disease Leonard A. Jason, Karen M. Jordan et al. *American Psychologist*: 1997;52:9:973-983

This paper states that many physicians minimised the seriousness of CFS and interpreted the symptoms as being equivalent to a psychiatric disorder; the authors state that these attitudes have had negative consequences for the treatment of CFS.

They point out that use of the original case definition of CFS and the type and scoring of psychiatric tests appear to have produced erroneous estimates of the extent of CFS comorbidity with psychiatric disorders.

The authors specifically mention the work of Wessely, pointing out that he was “influential”, and also pointing out that Wessely’s findings have led some to conclude that CFS is solely a psychiatric disorder.

The authors comment on “unfortunate biases” having been introduced, and they point out that the DIS (a structured psychiatric instrument designed for use in community surveys) has frequently been used to assess psychiatric comorbidity in CFS, when that instrument was not designed for use with *medically* ill populations.

The authors point out that high or low psychiatric rates in CFS samples may relate to whether symptoms are attributed by physicians to psychiatric or non-psychiatric cause.

The authors consider methodological problems with the “broadened” case definition (as advocated by Wessely et al to include all cases of unexplained “fatigue” lasting for at least one month), and point out that by broadening the CFS definition, it is important to ensure that those patients with solely a psychiatric disorder are not erroneously included within the CFS rubric, as to do so could seriously complicate the interpretation of epidemiological and treatment studies.

Professor Jason points out that some CFS investigators would not see this as a confounding problem because they believe that high rates of psychiatric comorbidity indicate that CFS is mainly a psychiatric disorder.

The authors urge caution with graded exercise regimes in CFS, saying that for those CFS individuals who do not have psychologically mediated reductions in activity, such a directed approach would be inappropriate and could even be counterproductive.

The authors point out that differences observed by investigators (named as Sharpe et al, a UK psychiatrist and close collaborator of Wessely) could well be due to Sharpe’s focus on illness beliefs, so Sharpe’s sample of CFS patients might have been less impaired than a severely ill group.

The authors re-iterate that biases in the scoring and selection of psychiatric tests



contributed to high levels of psychiatric comorbidity in CFS claimed by this group of psychiatrists, and that these findings were possibly due to the psychiatrists' belief that CFS was predominantly a psychiatric rather than a medical disorder, and that the findings were influenced by "flawed epidemiological research".

The papers states "Other investigators, such as Wessely et al, believe that CFS represents an arbitrarily defined end point and that there are no clear cutoff points separating those with severe fatigue from CFS".

"Psychiatrists and physicians have also regarded fatigue as one of the least important of presenting symptoms (Lewis and Wessely, 1992). These biases have been filtered to the media, which has portrayed CFS in simplistic and stereotypic ways".

The authors comment on the disregard of the *severity* of CFS symptoms; they conclude by commenting "We believe that it is crucial for CFS research to move beyond fuzzy recapitulations of the neurasthenia concept and clearly delineate precise criteria for diagnosing pure CFS".

Cognitive functioning is impaired in patients with chronic fatigue syndrome devoid of psychiatric disease

John de Luca, Benjamin H.Natelson et al  
*JNNP 1997;62:151-155*

The authors conclude that impaired cognition in CFS cannot be explained solely by the presence of a psychiatric condition and is contrary to expectations based on a model of "depression - induced" cognitive impairment in CFS.

"The results of the present study suggest that at least in a subgroup of patients, CFS is not simply a manifestation of a primary psychiatric disorder".

Neuroendocrine correlates of chronic fatigue syndrome: a brief review

Mark A.Demitrack. *J Psychiat Res 1997;31:1:69-82*

The author begins his review by stating "Over time, it has not escaped the view of clinical authors that CFS and its historical antecedents shares many characteristics with endocrine disease states... contemporary clinical research efforts have clearly documented that neuroendocrine disturbances are evident in patients with CFS".

"In almost all studies, at least 25% of subjects show no evidence, either past or current, for formally diagnosable psychiatric illness".

"Indeed, the accumulating body of evidence is contributing to a view of CFS as a disorder which is, in part, characterised by a novel dysregulation of the stress response".

The author surveys the published literature of neuroendocrine abnormalities in patients with CFS; he provides confirmatory support for an impairment of the HPA axis (consistent with the view that adrenocortical function is impaired); he notes the overall observation of reduced adrenocortical activation is a common feature to both fibromyalgia and chronic fatigue syndrome; he underlines the role of stress in the onset and course of CFS, and provides concluding remarks on the implications of this work.

Epidemiological Advances in Chronic Fatigue Syndrome. Paul H. Levine *J Psychiat Res* 1997;31:1:7-18

The author begins by noting that “Epidemiologic studies of CFS have been hampered by the absence of a specific diagnostic test...working case definitions have not always been utilized precisely by various investigators...the separation of those patients with and without pre-existing depression and other psychologic diagnoses that are not exclusive to CFS continues to be of major importance”.

The author comments specifically on the fact that all physical findings were dropped from the CDC 1994 case definition of CFS (*note that UK psychiatrist Michael Sharpe is a named co-author of this revised definition and that Wessely is listed as being a member of the International Chronic Fatigue Syndrome Study Group, who produced the CDC 1994 definition*)

The author states “Not surprisingly, the differences among these and earlier studies persist due to the different populations evaluated”.

This author (as others) notes that “The effect of stress on the neuroendocrine and immune function is being increasingly well characterised”.

He states “The data suggest a poorer prognosis in those with more severe debilitation for a prolonged period of time”.

This author is another to comments specifically that “The importance of the definition of subgroups is apparent. The heterogeneity of the disorder clearly highlights their existence”.

The author points out that “The most important risk factors for CFS continue to be gender and a recent history of severe stress”.

Precipitating Factors for the Chronic Fatigue Syndrome.  
Irving E. Salit. *J Psychiat Res* 1997;31:1:59-65

This author also points out that “Stressful events were very common in the year preceding the onset of CFS”.

He concludes by stating “Even more compelling is the evidence that CFS can and does occur after physically traumatic events such as motor vehicle accidents”.

The Quality of Life of Persons with Chronic Fatigue Syndrome

JS Anderson & CE Ferrans. *The Journal of Nervous and Mental Disease*  
1997;185:5:359-367

The purpose of this study was to explore the quality of life (QOL) of persons with CFS.

Over all scores on the quality of life index, people with CFS were significantly lower than for other chronic illness groups.

The authors conclude that “The findings suggest that quality of life is particularly and uniquely disrupted in CFS”.

The authors note that there has been little research into this aspect, and their study revealed that 90% of their sample group experienced frequent feelings of isolation, alienation and inadequacy due to CFS.

The authors are aware that what may be considered a disability for one person may be merely a nuisance for another, and they point out that the QLI is one of the few available instruments which takes account of this phenomenon, and that the reliability and consistency of the QLI is well established.

All participants stated that CFS had had a profound impact on every aspect of their lives in ways they had never imagined possible.

All participants related profound and multiple losses, including the loss of jobs, relationships, financial security, future plans, daily routines, hobbies, stamina and spontaneity, and even their sense of self because of CFS. Activity was reduced to basic survival needs in some subjects.

These profound losses significantly affected the participants’ mental health and outlook for the future.

Participants had difficulty in describing their illness because of the marked variability in symptoms. Symptoms were reported to be multiple, diverse, variable and pervasive. Participants reported that symptom variability tended to impede diagnosis and credibility and made it difficult for them to adjust and cope with the illness. Symptom variability also made it impossible for those with CFS to predict their level of functioning, which interfered with efforts to plan activities. For this reason, symptom variability was regarded as an especially frustrating aspect of CFS, and the uncertainty was one of the most difficult aspects of CFS to deal with.

Patients reported that they were exhausted and could not function, and that “it never goes away”.

All participants (100%) felt that CFS had devastated social relationships and activities: “Friends of 15 years stopped returning my calls and quietly disappeared”. A third reported that they had lost most, if not all, of their previous friendships; 18% currently had no friends whatsoever. Several participants reported that they had no family.

The authors conclude that the extent of the losses experienced in CFS was devastating, both in number and in intensity.

Participants described a sense of hopelessness that was integral to the illness due to symptom variability, length of illness and repeated relapses. Over time, those who were initially optimistic became emotionally exhausted.

Patients were particularly concerned about their longterm financial needs.

The authors note that such fatigued patients may lack the energy to seek out social support, and they may lack the energy to maintain existing relationships.

The authors found that the impact of CFS on patients’ life was so total and so devastating that participants had difficulty in accepting their illness and its consequences.

The authors conclude by stating “CFS is a poorly understood and often trivialized illness, which in reality causes marked disruption and devastation”.

A 56 year old woman with Chronic Fatigue Syndrome: Clinical Crossroads:Conference Report. Anthony L Komaroff. *JAMA*, 1997; 278:14:1179-1185

*(This conference took place at the Medicine Grand Rounds of the Beth Israel Deaconess Medical Center, West Campus, Boston, Mass. on June 11th 1997. Dr Komaroff is Professor of Medicine, Division of General Medicine, Brigham & Women’s Hospital, Harvard Medical School, Boston, Mass. He is a world acclaimed expert on ME/CFS)*

Dr Komaroff told the Conference that two themes emerge: (I) the enormous frustration of suffering from an illness that is poorly understood and (ii) the loss of legitimacy that a patient with CFS / ME feels.

He explained that CFS is not just a state of chronic fatigue (such as many people experience), but a truly debilitating state, associated with impaired memory / concentration, sore throat, adenopathy, myalgias, arthalgias, new headache, unrefreshing sleep, postexertional malaise, anorexia, nausea, drenching night sweats, intolerance of alcohol and pharmaceuticals that affect the central nervous system, and dizziness.

He reminded those present that objective, biological abnormalities can be found in patients with CFS, and that the medical literature of the past decade indicates that there are indeed such abnormalities.

Komaroff made the point that it is now evident that this illness is not simply an imaginary one, nor the result of anxiously amplifying normal bodily sensations. Komaroff dealt with the evidence of central nervous system (CNS) involvement in CFS: in his experience, a majority of CFS patients have symptoms which could reflect an underlying CNS process, for example, difficulty with memory, concentration and balance; photophobia and paraesthesias; in addition, substantial objective evidence of abnormalities in the CNS is now available: MRI scans have revealed areas which may represent inflammation and *I* or demyelination.

Komaroff told the Conference that the signal abnormalities in CFS patients “most closely resemble those seen in AIDS encephalopathy”.

Autonomic nervous system testing “frequently reveals abnormalities of the sympathetic and parasympathetic systems”.

He then dealt with the evidence of chronic immune activation in CFS: Komaroff discussed this evidence, and concluded that a state of chronic immune activation could lead to the production of cytokines that disrupt neurotransmitter function, resulting in the symptoms of CFS.

He made the point that the state of chronic immune activation in CFS suggests the possibility of a chronic infectious process, saying that some physicians (including himself) believe that infectious agents may trigger and even perpetuate the symptoms of CFS; he referred to the evidence for a chronic viral infection as demonstrated by Suhadolnick, which showed an abnormality in an antiviral lymphocyte enzyme system (2-5A pathway), which is found to be chronically activated in patients with CFS.

Komaroff referred to the findings that many CFS patients have experienced atopic symptoms from childhood, and that the atopic symptoms often flare up in CFS.

Komaroff stated that perhaps the most important nonpharmacologic intervention was to encourage patients to avoid physical or emotional stress, and to pace themselves.

He stated that it is antitherapeutic for the clinician to dismiss any patient’s symptoms out of hand, especially in CFS, which is a “de-legitimizing illness”, as “patients often experience rejection by family, friends and physicians.. ..The illness is hardly ‘imaginary’”.

Derek Pheby (Director, Unit of Applied Epidemiology, University of the West of England, Bristol, UK) *Physiotherapy: 1997;83:2:53-56*

“No-one who has experienced this illness, or who has had the responsibility of caring for a family member who has had the misfortune to suffer from it, can have any doubt not only about the extent of the real pain, suffering and distress that it can cause, but also as to the disastrous effect it can have on social relationships and life in the community”.

“The most seriously affected individuals may be bed-ridden..., most or all of the time and can do little or nothing for themselves”.

“In this illness, ‘recovery’ is very much a relative term: in follow-up studies.... after 48 years, eight out of ten patients continued to have some form of disability (Hyde & Bergman 1991). This is in line with Ramsay (1986) who wrote that complete recovery is confined to one third of cases”.

“Recent research has made it clear that the view that there were no specific changes demonstrable in patients with CFS has become untenable”.

“The disturbances to the HPA axis in CFS differ markedly from those found in depression, as do brain vascular perfusion patterns”.

“The overall costs associated with the syndrome are likely to be around £90 million per year (National Task Force Report, 1994, page 21). Given the tendency to chronicity. . . much of this cost is due to the need for long - term supportive care of patients”.

“CFS/ME is a major challenge to all health care professionals”.

#### Chronic Fatigue Syndrome —aetiological aspects

Dickinson CJ. *Eur J Clin Invest: 1997;27:4:257-267*

“There is some evidence both for active viral infection and for an immunological disorder in the CFS. Many observations suggest that the syndrome could derive from residual damage to the reticular activating system (RAS) of the upper brain stem and / or to its cortical projections”

“Regional blood flow studies by SPECT have been more consistent (and) have revealed blood flow reductions in many regions, especially in the hind brain. Similar lesions have been reported after poliomyelitis and in multiple sclerosis —in both of which conditions fatigue is characteristically present”.

Cardiac Involvement in Patients with Chronic Fatigue Syndrome as Documented with Holter and Biopsy Data in Birmingham, Michigan, 1991 - 1993 A.Martin Lerner et al. *Infectious Diseases in Clinical Practice 1997;6:327-333*

This study reports the prevalence of abnormal oscillating T-waves on Holter 24 hour monitoring in a consecutive case series of 67 CFS patients.

Resting 12 lead ECGs were normal, with the presence of labile T-wave abnormalities coming to light only with 24 hour Holter monitoring.

Repetitive T-wave flattening was a sensitive indicator of the presence of CFS, as every CFS patient (but only 22.4% of the controls) showed abnormal flattening or inversion on Holter monitoring.

Abnormal cardiac wall motion (at rest and on stress), dilatation of the left ventricle and segmental wall motion abnormalities were present. (Normal left ventricular resting ejection fraction is 50%, but in CFS, the left ventricular ejection fraction — at rest and with exercise — of as low as 30% was seen).

Abnormal T-wave oscillations ( T-wave flattening or inversion) of at least 25 normally conducted beats were necessary to be considered abnormal; they frequently appeared only with the advent of sinus tachycardia.

Two cardiologists unaware of the position of the patients reviewed the Holter tracings.

“This study confirms our earlier report (see *following item*) that CFS patients uniformly have abnormal oscillating T-wave flattenings and T-wave inversions by Holter monitoring...as described here, abnormal Holter monitoring is important to the explicit diagnosis of patients with CFS (and) are a characteristic of CFS (and) appear to be an essential element to the pathologic physiology of the cardiomyopathy of the CFS”.

New Cardiomyopathy: pilot study of intravenous gangiclovir in a subset of the chronic fatigue syndrome.

Lerner AM et al *Infectious Diseases in Clinical Practice* 1997;6:2:110-117

This study involved a subset of CFS patients with oscillating repetitively abnormal aberrant T waves on Holter 24-hour electrocardiogram (ECG) recording. None of these patients could work or manage a household.

The type of abnormalities documented in the cardiac study “are not seen in normal persons leading a sedentary life”.

Does the chronic fatigue syndrome involve the autonomic nervous system?

Freeman R and Komaroff AL *American Journal of Medicine* 1997;102:4:357-364

The aim of this study was to investigate the role of the ANS in the symptoms of CFS patients (selected if they had one of three criteria indicating ANS dysfunction).

The CFS subjects had significant increase in baseline and maximum heart-rate on standing and tilting.

Tests of the parasympathetic nervous system function were significantly less in the CFS group, as were measures of sympathetic nervous system function.

Deconditioning alone did not fully explain the documented ANA abnormalities.

89% of patients reported that an infectious illness had preceded the onset of CFS, and in 46%, the ANS symptoms occurred within four weeks of the infection: “a temporal pattern that is consistent with a postviral, idiopathic autonomic neuropathy”.

Symptoms of ANA dysfunction are not related to psychiatric disorder.

#### A population-based incidence study of chronic fatigue

Lawrie SM, Pelosi AJ et al *Psychological Medicine* 1997;27:343-353

Longitudinal studies using appropriate measures have shown that physical attributions do not affect outcome.

#### Exercise limits in chronic fatigue syndrome

Lapp C. *American Journal of Medicine* 1997;103:83-84

This reports a trial involving 31 consecutive new CFS patients, which allowed them to reach their maximum oxygen consumption within 8 - 10 minutes of exercise.

The results showed that 74% of patients experienced worsening fatigue. None improved.

The average relapse lasted 8.82 days, although 22% were still in relapse at 12 days (when the study ended).

These findings suggest that, pushed to maximal exertion, patients with CFS may relapse.

Lapp advises his CFS patients to limit exercise to less than 5 minutes, followed by rest. This work-rest cycle may be repeated several times daily in order to maintain strength, flexibility and conditioning.

1998



Cardiovascular responses during a cognitive stressor before and after exercise in chronic fatigue syndrome versus sedentary healthy subjects

SA Sisto, B Natelson et al

*Presented at the Fourth International AACFS Research & Clinical Conference on CFIDS, Mass. USA 1998: Abstract:page 48*

Patients with CFS complain of cognitive difficulties that worsen after exercise.

The purpose of this study was to determine if patients with CFS have similar cardiovascular responses (compared with sedentary controls) during a cognitive test battery, both before and after exercise.

The CFS group demonstrated a significantly lower change in systolic blood pressure compared with the sedentary controls.

Exercise produces the expected attenuation of the cardiovascular responses in the healthy group, but not so for the CFS patients.

This hyporesponsiveness may, in part, be responsible for CFS patients reporting detrimental effects of periods of psychological stressors or excess physical exertion.

CFS severity is related to reduced stroke volume and diminished blood pressure responses to mental stress

Arnold Peckerman, Benjamin Natelson et al

*Presented at the Fourth International AACFS Research & Clinical Conference on CFIDS, Mass. USA 1998: Abstract page 47*

One plausible hypothesis of the pathophysiology of CFS is a disorder of circulation.

The present study examined whether cardiovascular homeostasis at rest and centrally-mediated haemodynamic responses to behavioural challenges are altered in CFS,

The results showed that in CFS patients, a lower stroke volume was highly predictive of illness severity: across three different postures, the most severely affected CFS patients were found to have a lower stroke volume and cardiac output compared with those with more moderate illness.

These findings suggest a low flow circulatory rate in the most severe cases of CFS; this may indicate a defect in the higher cortical modulation of cardiovascular autonomic control.

In the most severely affected, situations may arise where a demand for blood flow to the brain may exceed the supply, with a possibility of ischaemia and a decrement of function.

Respiratory symptoms and lung function testing in CFS patients

P de Becker, K de Meirleir et al

*Presented at the Fourth International AACFS Research & Clinical Conference on CFIDS. Mass. USA 1998: Abstract page 104*

The purpose of this study was to report the prevalence of respiratory symptoms in a cohort of CFS patients. The following respiratory symptoms were observed: cough, chest tightness, medical history of allergy, new onset of allergy; the major respiratory complaint was found to be a pronounced exercise-induced dyspnea.

In 60% of CFS patients, a marked bronchial hyper-responsiveness was present. (Bronchial hyper-responsiveness was defined as PD 20 *his* < 2 mg histamine).

CFS patients show a significant decrease in vital capacity (VC), possibly due to a significant increase of residual volume (RV).

The incidence of bronchial hyper-responsiveness in this group is remarkably high.

These observations can, at least partially, explain the respiratory symptoms in these patients.

#### Chronic Fatigue Syndrome: An Update

A.L.Komaroff D.S.Buchwald *Annu Rev Med* 1998;49:1-13

Studies indicate that the illness is not simply a manifestation of an underlying psychiatric disorder, but rather is an illness characterised by activation of the immune system, various abnormalities of several hypothalamic pituitary axes and reactivation of certain infectious agents.

The most robust findings are increased numbers of CD8+ cytotoxic T cells that bear antigenic markers of immune activation on their cell surface, and depressed function of natural killer lymphocytes.

Other reported findings of immune activation are elevated levels of circulating immune complexes and immunoglobulin G, and higher frequencies of various autoantibodies.

More circumstantial evidence of a chronic viral infection in many CFS patients comes from reports of an abnormality in an antiviral lymphocyte enzyme system (the 2-5A pathway) which appears to be chronically activated in patients with CFS.

These reports provide strong evidence that CFS can be triggered by an acute infection that has the capacity to produce a chronic infection.

This paper concludes by affirming that “there is growing evidence that abnormal, objective biologic processes are present in many patients with CFS -- in particular, subtle

abnormalities of the CNS, chronic activation of the immune system, and reactivation of several latent viruses”.

Muscle fibre characteristics and lactate responses to exercise in chronic fatigue syndrome  
Russell JM Lane, Leonard C Archer et al *JNNP* 1998;64:362-367

The object of this study was to examine the proportions of types I and II muscle fibres and the degree of muscle fibre atrophy and hypertrophy in patients with CFS in relation to lactate responses to exercise, and to determine to what extent any abnormalities found might be due to inactivity.

Muscle fibre histometry in patients with CFS did not show changes expected as a result of inactivity

The authors note that one of these patients had an inflammatory infiltrate, and it would seem that inflammation and class I MHC expression may occur in biopsies from patients with CFS.

The authors note that this is of some interest, as they have argued previously that some forms of CFS may follow a previous virally-mediated inflammatory myopathy.

On symptoms and life events surrounding the onset of chronic fatigue syndrome  
Evengard B et al  
*Presented at the Fourth International AACFS Research & Clinical Conference on CFIDS, Mass. USA: 1998: Abstract page 32*

This study was aimed at describing the sequence of psychosocial events and infections preceding the onset of CFS (related to the temporal development of crucial symptoms).

Sixty seven percent of the CFS patients had a clearly negative life event preceding infection, which preceded CFS onset.

Gastrointestinal Manifestations of Chronic Fatigue Syndrome: Symptom Perceptions and Quality of Life  
Herbert Hyman Thomas E Wasser *JCFS* 1998;4(1):43-52

The authors conclude that the classification of irritable bowel syndrome (IBS) should be modified to include a subset of patients who have a combination of CFS and IBS.

They enumerate not only functional gastrointestinal (GI) complaints, but also other abdominal complaints, particularly neurologic.

They point out that in CFS, immunologic abnormalities are regularly found, and that there are more lymphocytes associated with the GI tract than any other site in the human body.

Since the gut mucosa contains immunologically active lymphoid tissue, the authors believe that a pattern of immune dysfunction exists in CFS in which immune products are transmitted to the gut via the lymphatic system, reacting on both the luminal contents and intestinal motor system, and that the GI lymphatic system not only has an effector function, but also transmits characteristic CFS immune dysfunction to other organs.

The authors also suggest that oral antigens could be similarly effective in CFS patients by way of the immunological activity of the gut mucosa.

Some CFS patients had abdominal wall pain due to unilateral segmental neuropathy.

In summary, this study demonstrated three primary findings: (I) CFS patients showed significantly more symptom dysfunction than those in the functional bowel disease (FBD) group; (ii) CFS patients had significantly lower Quality of Life scores than the FBD group and (iii) since differences occur between CFS and FBD patients, the classification of IBS should be modified to include a subset of patients who have a combination of CFS and IBS.

#### Chronic Fatigue Syndrome in Children and Adolescents: A Review.

Karen M Jordan, Leonard A Jason et al

*Journal of Adolescent Health* 1998;22:4-18

The majority of studies concerning CFS have concentrated on adults, but the illness does strike younger individuals, and the case definitions do not address the appropriateness for the paediatric population. The lack of specificity to the unique characteristics of children and adolescents is pervasive in much of the research literature.

Several authors reported a preponderance of acute onset with viral-type illness in children and adolescents.

Many previous epidemiological studies (one of Wessely's studies is cited) have relied on physician referral, when (those) physicians are sceptical of the validity of CFS as a true illness.

Repetitive treatment-seeking is often necessary before a diagnosis of CFS is made: children may be less able to seek care persistently, so the prevalence rate in those under 18 years has undoubtedly been minimised.

The authors describe the Cheney proposition (*Cheney PR. Proposed pathophysiological*

*mechanism of CFIDS. CFIDS Chronicle: 1994:7: 1-3*) that the common symptoms of CFS (eg. hyperreflexia, abnormalities of vestibular function, palpable and slightly enlarged discoid shaped lymph nodes, predominantly left-sided tender posterior and cervical lymph nodes) suggest a connection between immune activation and central nervous system injury: as alpha-interferon can be neurotoxic, particularly to the limbic structure and the serotonergic pathways (via opioid receptors), this may account for the abnormalities in corticotrophin-releasing hormone (CRH), and these deficiencies then contribute to a positive feed-back loop which maintains immune activation.

In addition, the decrease in TRH production could lead to reduced cellular metabolism, including impaired oxygen consumption during exercise, which is consistent with mitochondrial dysfunction.

The authors note that there has been minimal controlled study of psychiatric status for children and adolescents with CFS. However in one study, adolescents with CFS received higher scores of psychiatric comorbidity, but on further examination of the somatic complaint items, it was found that this scale was confounded by the presence of many items related to CFS symptoms (eg. headaches, pain and feeling sick).

The authors state that the overlap of CFS symptoms with those of psychiatric disorders has been found to lead to an overdiagnosis of psychiatric disorder in adult CFS populations.

The authors note that a list first supplied by Komaroff provides four discriminating characteristics of fatigue and symptoms which should assist the clinician in distinguishing between CFS and malingering or somatoform disorders, and these include symptoms which are rarely found in paediatric general practice.

The authors note that the perceived causal role of depression in CFS may have been inflated in some studies owing to frequent errors.

They note that the DSM IV criteria for depression do not include any of the primary complaints of patients who present with CFS.

Further, the DSM IV criteria for somatisation do not mention fatigue symptoms. The DSM IV states that individuals with somatisation disorder describe their complaints in a colourful, sensational and emotional manner, with specific factual information missing.

On the contrary, people with CFS describe their symptoms clearly and concisely.

Minimal work has been done in the formal assessment of coping with illness, level of disability or quality of life issues in children and adolescents with CFS.

Paediatric patients may require assistance obtaining special services or accommodations from their school.

The authors note that several authors (Sharpe and Wessely are named) have proposed the use of cognitive behavioural therapy (CBT), and note that while the Sharpe study may be criticised for its poor subject selection methods, no other studies have reported the effectiveness of CBT with child or adolescent populations.

Several authors have conducted follow-up studies with paediatric CFS patients; most reported improvement or recovery in over 50% of the patients studied, but the present authors note that some children continued to experience significant disability, and that it is possible these children who do not improve represent a unique subset of paediatric CFS, perhaps having a more severe form of the illness, including more severe neurologic symptoms such as myoclonus, paraesthesia and seizure-like episodes.

Much of the current literature is confused by the lack of paediatric case definition.

CFS in children and adolescents remains dramatically understudied.

It is imperative that criteria specific to children and adolescents be adopted and used as a standard in future research.

#### Brain SPET in Chronic Fatigue Syndrome

D.di Giuda, D.Racciatti et al

*Presented at the Fourth International AACFS Research & Clinical Conference on CFIDS, Mass. USA: 1998: Abstract page 112*

CFS is a severely disabling illness; this study was designed to investigate possible changes in the brain perfusion of patients with CFS.

Regional brain perfusion impairment ( mainly hypoperfusion) was found in 83.9% of CFS patients. In 30.8%, a concurrent fibromyalgia syndrome was present. A total of 147 brain regions showed abnormal 99mTc-HMPAO uptake.

This study confirmed previous reports of brain perfusion impairment in CFS, providing objective evidence of central nervous system dysfunction.

#### Impaired associative learning in chronic fatigue syndrome

Servatius RJ, Natelson BH et al *Neuroreport: 1998;9:1153-1157*

The researchers tested patients with CFS in protocols designed to measure memory reactivity and acquisition of the classically conditioned eyeblink response.

The authors conclude that their data suggest organic brain dysfunction within a defined neural substrate in CFS patients.

#### Relationship between SPECT scans and buspirone tests in patients with ME /

CFS

Richardson J and Costa DC *JCFS* 1998;4:3:23-38

The SPECT scans revealed that all CFS patients studied had hypoperfusion in the brain: 62% in the brain stem and 51% in the caudate nuclei.

According to the researchers, these findings provide “actual evidence of neurological dysfunction” in ME / CFS.

Brain positron emission tomography (PET) in chronic fatigue syndrome: preliminary data

Tirelli U. et al *American Journal of Medicine* 1998;105:3A: 54s-58s

The PET images examined 22 cortical and subcortical areas. PET is better than SPECT at detecting small structures such as the brain stem.

The scans revealed significantly reduced glucose metabolism in the brainstem of patients with CFS compared with depressed patients and healthy controls. The area particularly affected in the brainstem was the pons. There was also significant hypometabolism in the right mediofrontal cortex in the CFS patients.

Hypometabolism of the brainstem has not been documented in any psychiatric disorder assessed to date.

Neurally Mediated Hypotension and Chronic Fatigue Syndrome

Peter C Rowe & Hugh Calkins *Am J Med* 1998;105: (3A):15S-21S

This article discusses selected issues in the clinical overlap of CFS and autonomic dysfunction.

The authors note that frequently in CFS, patients have symptoms of lightheadedness (88%); cognitive difficulties / problems thinking and concentrating (47%); blurred vision (47%); tremulousness (38%); pallor (31%) and anxiety (29%), and that these neurocognitive symptoms have been attributed to cerebral hypoperfusion.

That fatigue can be associated with neurally mediated hypotension has been appreciated since 1932, when Sir Thomas Lewis demonstrated that a long period of fatigue could follow a single episode of vasovagal (or neurally mediated) hypotension.

One of the patients who prompted the authors' investigation was a 16 year old girl who described becoming tired, shaky, lightheaded and pale after walking more than 10 minutes: one notable physical finding was that her legs and arms developed a purple discolouration after a short period of quiet standing, which is indicative of abnormal venous pooling.

In this study, all the CFS patients but none of the controls developed orthostatic symptoms during the first stage of the testing, suggesting that orthostatic intolerance may be a defining feature of CFS.

Three factors which predispose to the development of NMH are a low resting blood volume, excessive pooling of blood in the dependent vessels, and excessive loss of plasma volume during upright posture, all of which can decrease venous return to the heart.

In those with abnormal responses to upright tilt, when cardiac output is consequently decreased, there seems to be a failure to mobilize blood effectively from the dependent splanchnic and limb vasculature: several groups have identified impaired vasoconstrictor responses in the forearm and splanchnic bed, and in microvascular flow to the skin.

Among the neuroendocrine changes that accompany the orthostatic intolerance are an increase in epinephrine, vasopressin,  $\beta$ -endorphin and vasoactive intestinal polypeptide.

Factors that can contribute to early activation of the vasovagal reflex include stress and sodium depletion.

Conditions with an increased histamine release can also cause a decreased return of blood to the heart.

Such an inappropriate venous return could provoke worse orthostatic tolerance in response to common everyday cognitive stress, which could provide an explanation for why some patients describe worse fatigue after reading or concentrating.

Virtually *all* CFS patients (regardless of their haemodynamic response) have their symptoms provoked by standing upright.

The authors note that there is a high prevalence of allergic disease in those with CFS, and suggest that with an association between CFS and NMH, one would expect to find a mechanism by which allergic disease increases the activation of this reflex pathway: other workers have shown that both viral infection and allergic reactions to food antigens increase the excitability of mechanically sensitive vagal afferents in the airway.

The ability of allergen exposure to enhance the discharge of mechanically sensitive fibres, including C-fibres, provides a potential link between these clinical situations and the development of NMH in CFS patients with allergy, suggesting that efforts to prevent activation of NMH would need to prevent exacerbation of food and inhalant allergies in those with CFS.

Low levels of serum acylcarnitine in chronic fatigue syndrome and chronic hepatitis type C. but not seen in other diseases.



Kuratsune H et al *International Journal of Molecular Medicine* 1998;2:1:51-56

This study found significantly lower serum acylcarnitine (ACR) in CFS patients but not in controls.

It was not present in other medically ill populations such as patients with haematological malignancies, chronic pancreatitis, hypertension or diabetes.

ACR may have an effect as an antioxidant and may be linked to the production of cytokines.

These findings indicate that serum ACR deficiency may be a characteristic of CFS.

Secretion of growth hormone in patients with chronic fatigue syndrome Berwaerts J et al *Growth Hormone and IGF Research* 1998;8:127-129

Serum IGF-I was significantly lower in patients with CFS than in controls.

Adrenal size in chronic fatigue syndrome

Teh J, Scott L, Dinan E et al *Radiology* 1998;209P (Suppl):411-412

A CT scan revealed that the right and left adrenal glands of CFS patients were reduced by 50% when compared with healthy people.

Increased resting energy expenditure in the chronic fatigue syndrome

Watson WS, Chaudhuri A, Behan PO et al *JCFS* 1998;4:4:3-14

When individual resting energy expenditure (REE) was predicted on the basis of total body potassium values, 45.5% of the CFS patients tested had resting energy expenditure above the upper limit of normal, suggesting that there is upregulation of the sodium-potassium pump in CFS.

There was no evidence that the results were due to lack of activity (which would have affected total body water estimates).

Parallels between post-polio fatigue and chronic fatigue syndrome: a common pathophysiology?

Bruno RL et al *Am J Med* 1998; 105 (3A) 66S-73S

Post-polio fatigue is characterised by subjective reports of difficulty with attention, cognition, and maintaining wakefulness. These symptoms resemble those reported in nearly two dozen outbreaks of post-viral fatigue syndrome (PVFS) that have recurred this century and which are related clinically, historically, anatomically or physiologically to polio virus.

This article reviews studies which relate the symptoms of post-polio fatigue and chronic fatigue syndrome to clinically significant deficits on neuropsychologic tests of attention, histopathologic and neuroradiologic evidence of brain lesions, impaired activation of the HPA axis, increased prolactin secretion, and EEG slow-wave activity.

A common pathophysiology for post-polio fatigue and CFS is described.

Alteration of spatial-temporal parameters of gait in Chronic Fatigue Syndrome Saggin R et al *J Neurol Sci* 1998;154:1:18-25

CFS has been widely studied and a lot of information is available in the literature regarding immunological, virological, neuroendocrinal and psychiatric aspects of this disease, and great attention has been paid to the alteration of muscular function in CFS.

The aim of this work was to study the gait of CFS patients to see if there are objective measures which can better characterise the pathology.

Comparison with reference data from healthy controls revealed significant abnormalities.

The abnormalities were present as from the beginning of the gait, which indicates that they are unlikely to be caused by rapidly increasing fatigue.

These findings strengthen the notion of direct involvement of the central nervous system in CFS.

A preliminary placebo-controlled crossover trial of fludrocortisone for chronic fatigue syndrome

Peterson PK et al *Arch Intern Med* 1998;158: (8):908-914

At baseline, study participants reported symptom severity greater than 5 for most symptoms and all had evidence of marked functional impairment.

Five patients withdrew from the trial.

The incidence of adverse experience was similar in patients and controls.

The authors conclude that low dose fludrocortisone (0.1 - 0.2mg for six weeks) does not provide sufficient benefit to be evident in a blinded trial of unselected patients with CFS.

Low-dose hydrocortisone for treatment of chronic fatigue syndrome: a randomised controlled trial

Mckenzie R, Dale J, Demitrack M et al *JAMA* 1998;280: (12): 1061-6

The object of this study was to evaluate the efficacy and safety of low-dose oral hydrocortisone as a treatment for CFS (oral hydrocortisone, 13 mg /m<sup>2</sup> of body surface area every morning and 3 mg /m<sup>2</sup> every afternoon for approximately 12 weeks).

The authors conclude that the degree of adrenal suppression precludes the practical use of hydrocortisone in CFS.

Immunological Status Correlates with Severity of Physical Symptoms in Chronic Fatigue Syndrome Patients

S.Wagner, N.Klimas et al

*Presented at the Fourth International AACFS Research & Clinical Conference on CFIDS 1998: Mass. USA. Abstract page 28*

The purpose of this study was to investigate the relationship between immunologic status and physical symptoms in CFS patients.

The findings suggest that the degree of cellular immune activation is associated with the severity of CFS physical symptoms.

Specifically, elevations in the T-helper / inducer cells, activated T-cells, activated cytotoxic / suppressor T-cells, and CD4 / CD8 ratio are associated with greater disease severity.

Furthermore, reductions in T-suppressor / cytotoxic cells also appear related to greater severity of CFS physical symptoms and illness burden, suggesting that greater symptoms are associated with lower availability of regulatory T-cells.

A study of the Immunology of the Chronic Fatigue Syndrome: Correlation of Immunologic Parameters to Health Dysfunction

I.S.Hassan, W.Weir et al. *Clin Immunol Immunopathol* 1998;87:60-67

Surface and intracellular immunologic and apoptotic markers and functional lymphocyte assays after stimulation with anti-CD3 / anti-CD28 antibodies or phytohaemagglutinin (PHA) were studied.

Patients with increased HLA-DR expression had worse pain and poorer physical functioning scores.

The increased expression of Class II antigens and the reduced expression of the co-stimulatory receptor CD28 (which is a marker for terminally differentiated cells) lend further support to the concept of immunoactivation of T-lymphocytes in CFS and may be consistent with a viral aetiopathogenesis in CFS. The authors demonstrated changes in different immunological parameters, each of which correlated with particular aspects of disease symptomatology and measures of disease severity.

Co-incidental splenectomy in chronic fatigue syndrome

Brian J Miller et al *JCFS* 1998;4(1): 37-42

The authors describe the removal of a ruptured spleen in a female with CFS following a road traffic accident.

At operation, the splenic parenchyma was unusually spongy and friable.

There was a generalised infiltration of the splenic sinuses by atypical lymphoid cells. These cells appeared blastic and had large, vesicular nuclei, multiple large nucleoli and a moderate amount of dense, eosinophilic cytoplasm.

In immunohistochemical studies, they were strongly reactive for the Tlymphocyte markers CD45RO and CD43.

In addition to this cellular infiltrate, there was a reduction in the volume of the white pulp.

Histological examination of the spleen revealed chronic inflammatory changes of uncertain aetiology.

These histopathological changes in the spleen of a patient with CFS have not been described before.

The reduction in white pulp and infiltration of the splenic sinuses by atypical lymphoid cells are not features of traumatic rupture, and suggest a chronic inflammatory process likely to be associated with CFS.

*(At the Second World Congress on Chronic Fatigue Syndrome and Related Disorders, Brussels, 9-12<sup>th</sup> September 1999, Dr L Lambrecht from Belgium spoke on "Chronic Fatigue Syndrome: Clinical, Immunological and Neuroimaging Correlations in 500 Patients", noting that splenomegaly was reported in 29% of CFS patients, saying that this finding has not previously been reported).*

T-Lymphocytes in CFS -- in vitro reaction to mutagens

I Hauspie, K de Meirleir et al

*Presented at the Fourth International AACFS Research & Clinical Conference on CFIDS 1998: Mass. USA. Abstract page 70*

Many studies in CFS patients suggest a virally-triggered onset, associated with an abnormal immune function.

The results from this study add information to the existing knowledge of intracellular abnormalities in CFS, and point towards abnormalities in intracellular protein metabolism, with increased sensitivity to alcohol.

The authors believe that lymphocytic cell membrane permeability is altered in CFS.

Lymph node morphology and phenotype in chronic fatigue syndrome

Nancy Klimas et al

*Presented at the Fourth International AACFS Research & Clinical Conference on CFIDS 1998: Mass, USA. Abstract page 73*

CFS is an illness which is associated with immune dysfunction, including abnormalities in the function and activation status of peripheral blood lymphocytes. There has been no study of the lymph node compartment in this illness.

The authors conclude that the distribution of lymphocyte subsets in the lymph nodes in CFS patients offers confirmation regarding the immunopathogenesis of CFS.

The data here presented indicate a preponderance of activated T-cells that is even higher than that reported in peripheral blood.

The findings are compatible with a chronically activated immune status in this patient group.

CD4 T Lymphocytes from Patients with Chronic Fatigue Syndrome have Decreased Interferon -  $\gamma$  Production and Increased Sensitivity to Dexamethasone

Jeroen Visser et al *The Journal of Infectious Diseases* 1998;177:451-4

To the authors' knowledge, this study was the first to compare properties of purified CD4 T cells from CFS patients with those of cells from healthy controls.

The CD4 cells were studied to determine whether they have an altered sensitivity to dexamethasone (DEX).

CD4 T cells from CFS patients produced less interferon - $\gamma$  than did the cells from controls, indicating an increased sensitivity to DEX.

The authors suggest that their observation of low interferon -  $\gamma$  production in CFS might be due to an increased sensitivity of the CD4 T cells for glucocorticoids, which are known to modulate T cell responses.

Decreased immunoreactive beta-endorphin in mononuclear leucocytes from patients with chronic fatigue syndrome

Conti F et al *Clinical & Experimental Rheumatology* 1998;16:6:729-732

Beta-endorphin concentrations were measured in peripheral blood mononuclear cells (PBMC) by radioimmunoassay performed with antibodies specific for the C-terminal portion of human beta-endorphin.

Beta-endorphin concentrations in the PBMC of CFS patients were significantly lower than in the healthy subjects.

Beta-endorphin concentrations in PBMC seem to mirror the central nervous system homeostasis of the opioid, thus the fatigue and weakness typical of CFS could be related to low beta-endorphin concentrations at the CNS level.

The in vitro immunomodulatory effects of glyconutrients on peripheral blood mononuclear cells of patients with chronic fatigue syndrome

See, DM et al *Integrative Physiological and Behavioural Science* 1998;33:3: 280-287

A glyconutrient compound was added to PBMC isolated from 90 normal controls and 91 patients with CFS.

Cell surface expression of the glycoproteins CD5, CD8 and CD11a were significantly lower in patients with CFS compared with normal controls.

Furthermore, natural killer (NK) cell function was reduced in CFS patients.

Importantly, apoptosis was significantly higher in patients with CFS, but the percentage of apoptotic cells was significantly decreased in PBMC of CFS patients which had been incubated for 48 hours with glyconutrients.

Thus glyconutrients improved immune parameters in vitro in patients with CFS.

Chronic fatigue in overlap syndromes

Abhijit Chaudhuri Peter Behan *Neurology* 1998;1:2:16-20

The authors state that CFS is a disabling neurological illness which may be precipitated by infections, toxins, and physical and mental stress.

They point out that only when a poliomyelitis epidemic swept California in the summer of 1934 was CFS distinguished as a separate epidemic illness, when it was called 'atypical poliomyelitis'.

Most CFS cases now occur sporadically; clinical symptoms include generalised muscular aches and pains (fibromyalgia), weakness, sleep disorder, impaired memory and mental concentration, paroxysmal (usually nocturnal) sweating, intermittent dysequilibrium, mild myoclonus, cervical adenopathy (early in the illness), vertigo, palpitations and angina-like chest pain.

The authors state that the organic nature of CFS soon became apparent from detailed study of symptoms and from neuroendocrine tests.

The authors state that in a number of diseases, fatigue similar to that in CFS may be the only symptom before other signs become apparent: multiple sclerosis (MS), chronic inflammatory demyelinating polyneuropathies (CIDP), sarcoidosis and haemachromatosis are common examples where fatigue can antedate other symptoms; such CFS-associated or CFS-overlap syndromes can be grouped into four divisions:

syndromes commonly associated with postviral or idiopathic CFS  
(eg. dysequilibrium syndrome, Gilbert's disease, atopic disorders, including gluten sensitivity, syndrome X and irritable bowel syndrome)

CFS-like syndromes following exposure to chemicals (eg. after ciguatera fish poisoning, or following exposure to low dose organophosphate compounds, organochlorine exposure, multiple chemical sensitivities, fatigue induced by medication, including anaesthetics)

medical or neuropsychiatric diseases where the severity of the fatigue is independent of the underlying illness (eg. sarcoidosis, Sjogren's syndrome, SLE and other vasculitides, demyelinating neuropathies, Parkinson's disease, metabolic myopathies, HIV infection, post-head injury)

other CFS-like syndromes, where the precipitating factor is uncertain (eg. Gulf War syndrome, sick building syndrome, a CFS-like syndrome following silicone breast implants).

The authors state that Syndrome X is characterised by typical anginal chest pain but with a normal coronary angiogram. Angina-like chest pain, similar to Syndrome X, is a common symptom in CFS patients: the two syndromes share many similarities, including an identical clinical course.

A similar exaggerated GH-release response is seen in patients with chronic low-dose exposure to OPs, who develop a neurobehavioural syndrome identical to CFS.

The irritable bowel syndrome which occurs in CFS is identical to 'idiopathic' IBS.

Cases of CFS may develop after physical trauma.

CFS has been reported in multiple chemical sensitivity, and over-trained athletes may develop a syndrome indistinguishable from CFS.

In summary, CFS should be considered multifactorial in origin, with infection and stress being the two most common triggers.

The mechanism of fatigue in various neurological disorders, including CFS, may be related to an abnormal cell membrane ion channel and / or membrane-associated ATPase function.

## 1999

### Demonstration of delayed recovery from fatiguing exercise in chronic fatigue syndrome

Lorna Paul, Leslie Wood, Wilhemina M.H. Behan & William M. Maclaren  
*European Journal of Neurology* 1999;6:63-69

The purpose of this study was to try to confirm the observations that patients with CFS complain consistently of delay in recovery of peripheral muscle function after exercise.

The use of <sup>31</sup>P-nuclear magnetic resonance (<sup>31</sup>P-NMR) has now provided positive evidence of defective oxidative capacity in CFS.

Patients with CFS reach exhaustion more rapidly than normal subjects, in keeping with an abnormality in oxidative metabolism and a resultant acceleration of glycolysis in the working skeletal muscles.



When the rate of resynthesis of phosphocreatinine (PCr) following exercise is measured, this abnormality is confirmed

The authors' study provides a conclusive demonstration that recovery is significantly delayed in patients with CFS.

It also supports the fact that patients with CFS produce maximum voluntary contractions during exercise. The authors are confident that the differences observed in recovery in this study represent true effects.

The results demonstrate that patients with CFS fail to recover properly from fatiguing exercise and that this failure is more pronounced 24 hours after exercise.

Some of the patients demonstrated more severe effects than others.

Indeed, while the recovery of force in the controls was complete by 200 minutes post-exercise, "an even further decline in force" was observed among the CFS group at 24 hours post-exercise.

This delayed recovery is unlikely to be the result of de-conditioning.

The findings support the clinical complaint of delayed recovery after exercise in patients with CFS.

The authors note that recent experiments by others (*Bouwer & Packer: Corticospinal excitability in patients in patients diagnosed with CFS. Muscle Nerve 1994: 1210-1212; Samii et al. Decreased post-exercise facilitation of motor-evoked potentials in patients with CFS or depression. Neurology 1996:1410-1414*) have demonstrated a significant reduction in motor evoked potentials following exercise in CFS patients compared with controls. This is in keeping with a reduction in the excitability of the motor cortex and could account for a reduction in voluntary motor output leading to the decline in muscle force observed in this study.

#### Chronic Fatigue Syndrome is a Acquired Neurological Channelopathy

Abhijit Chaudhuri & Peter Behan *Hum Psychopharmacol Clin Exp 1999: 14:7-17*

Review article noting that the fatigue in CFS is distinct from the fatigue of neuromuscular disorders but similar to that found in disorders of the central nervous system such as multiple sclerosis, Parkinson's disease and multiple system atrophy.

The authors note that many symptoms of CFS, including severity of fatigue, may be induced by physical trauma and stress.

In this paper, the authors propose dysfunctional ion channels in the cell membrane as the key abnormality in CFS, which may also be responsible for the altered neuroendocrine function found in CFS.

A significant proportion of patients with CFS suffer from irritable bowel syndrome.

Autonomic dysfunction in CFS is also well recognised.

CFS patients have a supersensitivity of cortisol response to exogenous ACTH: both physical trauma and emotional stress (such as bereavement) can precipitate CFS, directly activate the HPA axis and modify the immune system. Chronic activation of the HPA axis may cause a relative decrease by the adrenals of delta 3 - adrenal androgens. This process, in turn, may alter the helper Tcell phenotype in chronically affected patients.

Cytokine levels increase during stress: it has been shown clearly that breakdown of the blood-brain barrier (BBB) can occur during periods of stress.

At the cellular level neurochemicals use second messengers and ion channels for their desired actions.

It is therefore possible that neurochemical abnormalities can lead to alterations in the normal receptor and ligand-gated ion channel function.

Abnormal ion channel functions as the mechanism of neurological disorders now constitute a new group of diseases termed *channelopathies*.

Changes in the ion channel function from time to time offer a rational basis to explain the fluctuating fatigue and related symptoms in CFS. Known channelopathies provide excellent examples of neurological conditions where the symptoms are periodic, fluctuating, and are induced by physical activities, stress and fasting.

If the sodium channels are blocked in the open mode, this causes entry of sodium into neural tissues and muscles. This ingress of sodium is followed by water, which in turn leads to swelling of the neural tissues, a phenomenon observed both electron microscopically and by laser scanning microscopy.

Acquired ion channel abnormalities in myocardium could explain the pathogenesis of Syndrome X and may form the basis of cardiac dysfunction in both Syndrome X and in CFS — a highly significant proportion of CFS patients

have cardiomyopathy, as shown in the epidemiological study by Lerner et al (see pp 22-23 above).

Ion channel abnormality leading to selective neuronal instability may be the common disease mechanism in CFS and other disorders affecting brain function such as migraine and epilepsy.

The authors believe that CFS is *acquired* rather than inherited, making any therapeutic attempts to correct an ionophoric defect difficult.

#### Dehydroepiandrosterone (DHEA) response to i/v ACTH in patients with chronic fatigue syndrome

De Becker P, de Meirleir K et al *Hormone and Metabolic Research* 1999;31:1: 18-21

In order to investigate the dynamic response of the adrenal glands, the researchers measured serum levels of DHEA at intervals during 60 minutes after ACTH stimulation. The patients were severely affected, with no psychiatric illness.

The patients had a blunted serum DHEA response curve to i/v ACTH injection.

This observation adds to the large amount of evidence of endocrinological abnormalities in CFS.

Relative glucocorticoid deficiency might contribute to the overall clinical picture in CFS, and could explain some of the immunological disturbances observed in this syndrome.

#### Chronic fatigue syndrome

Pagani M and Lucini D. *Clinical Science* 1999;96:1:117-125

In CFS there are reported disturbances in autonomic activity and in other homeostatic mechanisms, such as hormonal and immune systems.

There are alterations in cardiovascular autonomic control, as can be assessed by spectral analysis of R-R interval and systolic arterial pressure variability.

Indices of sympathetic modulation could provide quantifiable signs of the interaction between the patients' efforts and their environmental demands, independently of self description; this could provide convenient measurable outcomes, both for diagnosis and treatment titration.

Chronic fatigue syndrome: assessing symptoms and activity level

Jason LA et al *Journal of Clinical Psychology* 1999;55:4:411-424

Current approaches to the diagnosis and assessment of CFS rely primarily on scales which measure the occurrence of various symptoms in CFS.

Such approaches do not provide information on either the severity of symptoms or on the fluctuations in symptom severity, or on activity level over time.

As a result, these measures do not reflect the complexities and the inter-reactions among symptoms.

The present study compared patients with CFS on a fatigue scale and a symptom severity scale; there were notable differences between the patients and controls, and information was obtained by assessing symptom severity during current and worst periods.

By obscuring the fluctuating nature of CFS and its high variability, commonly used assessment procedures may prevent health care professionals from understanding the complexities of this disease.

## **WESSELY'S WORDS 1996-1999**

1996

Chronic fatigue in the community: 'a question of attribution' Chalder T. Power MJ.  
Wessely S *Psychol Med* 1996;26:4:791-800

Thirty eight subjects in a large community survey were found to attribute their fatigue to 'myalgic encephalomyelitis' (ME).

The relationship between psychological distress, specific illness attributions and prognosis are discussed.

The authors claim that attributing fatigue to social reasons appears to afford most "protection".

Chronic fatigue, chronic fatigue syndrome, and fibromyalgia

Wessely S and Sharpe M

In: Mayou R, Bass C and Sharpe M (eds) Treatment of Functional Somatic Symptoms (Chapter 16): Oxford University Press 1995: 285-312 (Reviewed in 1996)

A summary of the authors' personal view of these conditions, supported by their own selection of the available literature describing patients' attitude to their illness and discussing factors which the authors believe might be helpful to recovery.

The authors state "Patient organisations now supply sufferers with digests of professional journals. Such information may have a considerable and often unhelpful influence on patient attributions of illness, which ... can be a major determinant of a patient's willingness to accept psychological treatment" (page 299).

Chronic fatigue syndrome: an adult perspective

Wessely S. *Association for Child Psychology and Psychiatry* 1996;12:37-54

A review focusing in particular on evidence that CFS is a neurobiological disorder, and focusing on the author's belief that the perpetuation of the illness is associated with psychological factors such as maladaptive attitudes.

*(The following section deals with the joint Royal Colleges' Report on CFS: the chronological review resumes on page 77)*

*Chronic Fatigue Syndrome: report of a joint working group of the Royal Colleges of Physicians, Psychiatrists and General Practitioners, October 1996 / CR54*

Ostensibly claimed to have been prepared at the request of the UK Chief Medical Officer (and therefore was commissioned by the CMO) as a response to the 1994 Report of the UK National Task Force on CFS / ME, and that it was the Presidents of the three Royal Colleges who nominated the expert committee, this report constituted a landmark in that, unlike most such reports, it received massive public exposure, and it was widely believed (and conceded by some) that Wessely himself was the instigator and prime mover.

In his CMO's Update 13 (February 1997), which is a communication from the Chief Medical Officer to all UK doctors, the CMO (then Sir Kenneth Calman) specifically endorsed CR54 by drawing its findings to the particular attention of all doctors in the UK. Had he not endorsed those findings and conclusions, the CMO could have chosen not to promote CR54 in his Update 13.

Somewhat surprisingly, in a letter dated 22<sup>nd</sup> December 1997 to The Countess of Mar, the Minister of State for Health ( Baroness Jay of Paddington) implied that the Department of Health claimed total dissociation from CR54, which may possibly have had something to do with the volume and quality of the scientific evidence which by then had been sent to the CMO, showing how biased CR54 was. One immediate criticism was the fact that 10% of the Report's 256 references were authored by just one member of the Working Group — Simon Wessely. Also, nine of those references had not even been published or peer reviewed.

Certainly Wessely was an adviser to the UK Government Department of Social Security, and what is also certain is Wessely's close relationship with virtually all the other members of this "expert committee".

Indeed, out of the 15 medical members, eight (53%) are psychiatrists well known for their published views which deny the reality of ME (as distinct from CFS, which they claim as a psychiatric disorder).

What is also certain is that six of these members were also signatories to the much-criticised Oxford consensus criteria on CFS in 1991.

Expert committees are usually held to be just that; complete impartiality is required as de rigueur: in this case, even the most cursory appraisal reveals that this "expert working group" might not be quite as impartial as is usual.

Of the psychiatrists involved, Dr Anthony David believes:

"A diagnosis of depressive illness would be appropriate. Unfortunately this is not good enough for the patient" (*Postviral fatigue syndrome and psychiatry. A. S. David. BMJ 1991;47:4:966-988*)

“Doctor behaviour, such as sick certification, emerged as a significant contributor to the risk of chronic fatigue” (*Predictors of chronic “postviral” fatigue. Helen Cope, Anthony David, Anthony Pelosi, Anthony Mann. Lancet 1994:344:864-868*).

Dr Sean Lynch believes:

“The original criteria for the chronic fatigue syndrome would exclude patients with any concurrent psychiatric symptoms... as few patients would then meet this definition... these criteria are widened to include psychiatric morbidity.

“There is no evidence to date of a higher than normal risk of adverse drug reactions in this group of patients”. (*Antidepressant therapy in the chronic fatigue syndrome. Sean Lynch, Ram Seth, Stuart Montgomery. British Journal of General Practice 1991:41:339-342*).

Dr Anthony Pelosi believes:

“The closer cases fulfil the definition of chronic fatigue syndrome, the closer the association with emotional morbidity.

“The only significant prognostic predictors... were a primary psychiatric diagnosis... and a strong conviction that the illness represented a physical disease.

“Recovery from syndromes of chronic fatigue has now been shown to be independent of virology and immunological measures, and a poor outcome to be related to psychological morbidity”. (*Chronic fatigue syndrome: prevalence and outcome. Psychological factors are important for management. SM Lawne, AJ Pelosi. BMJ 1994:308:732-733*)

“The myalgic encephalomyelitis societies should not try to set the research agenda or shout down views with which they disagree”. (*Chronic fatigue syndrome and myalgic encephalomyelitis. SM Lawrie, AJ Pelosi. BMJ 1994:309:275*).

Dr Simon Wessely is well known for his much-published belief that:

“Perpetuating factors include ... illness beliefs and fears about symptoms, symptom focusing, and emotional states.

“There lies at the heart of CFS not a virus (or) immune disorder, but a distortion of the doctor-patient relationship”. (*Chronic fatigue syndrome: an update. Anthony J Cleare, Simon C Wessely. Update 1996:61-69*).

Dr Peter White believes:

“Psychiatric diagnoses were particularly associated with a duration of symptoms longer than four months.

“The commonest diagnosis . . . was major depressive disorder in half the patients with a further 15% having a somatisation disorder”

“If symptoms persist... psychiatric disorders will be found in two-thirds of patients”.  
*Fatigue syndromes: neurasthenia revived — psychiatric illnesses are worth considering.*  
*Peter White. BMJ 1989;298:1199-1200).*

Of the non-psychiatrists on this working group, Sir Peter Baylis believes:

“Many of the symptoms in the chronic fatigue syndrome are identical to those seen in psychiatric disease, notably a depressive illness. “Furthermore, many patients with the chronic fatigue syndrome improve in response to anti-depressive pharmacological therapy... about 70% of those treated in this way return to work with a good quality of life”. (*Medico-legal Report prepared for a High Court action in The Royal Courts of Justice, London. R.I.S.Bayliss. 8” July 1991).*

Professor Richard Edwards believes:

“Many of the . . . symptoms of these patients could be a consequence of reduced habitual activities.

“The dizziness and disturbances. .of vision, and the gastro-intestinal problems experienced by patients after relatively mild exercise..., are also experienced by normal controls” (*The metabolic consequences of reduced habitual activities in patients with muscle pain and disease. Anton JM Wagonmakers, John H Coakley, Richard HT Edwards. Ergonomics 1988;31:11:1519-1527).*

Dr Tim Peto believes:

“Illness beliefs and coping behaviour previously associated with a poor outcome changed more with cognitive behaviour therapy.

“Adding cognitive behaviour therapy to the medical care of patients with the chronic fatigue syndrome is acceptable to patients and leads to a sustained reduction in functional impairment”. (*Cognitive behaviour therapy for the chronic fatigue syndrome: a randomised controlled trial. Michael Sharpe, Tim Peto et al. BMJ 1996;312:22-26).*

Dr Leonie Ridsdale believes:

“Doctors may help some patients reattribute symptoms which may prevent unnecessary referrals”. (*GPs and patients disagree over causes of fatigue. Pulse 24 September 1994: 15).*



At least five member of this working group all have connections with Wellcome, the pharmaceutical giant who in 1989 sold Coopers Animal Health, a company it had set up in 1985 in partnership with ICI to produce organophosphates (OPs) (*Dirty Medicine. Martin J Walker. Slingshot Publications, London, 1993, p.219*).

Perhaps of note is the fact that Peter Behan, formerly Professor of Neurological Sciences at Glasgow, UK, has found farmers who have been exposed to low doses of OPs to have a neurological condition indistinguishable from ME / CFS.

*(Chronic Fatigue Syndrome as a Delayed Reaction to Low Dose Organophosphate Exposure. Peter O. Behan. Journal of Nutritional and Environmental Medicine 1996:6:4:341-350).*

Is it purely by chance that these particular doctors who are known to have links with Wellcome should be so unrelenting in their efforts to ensure that ME / CFS is nothing more than an aberrant belief held only by suggestible people, and to promulgate the notion that it is only those doctors who have not learnt to deal effectively with suggestible patients who endorse the existence of ME? (*Old wine in new bottles: neurasthenia and 'ME'. Simon Wessely. Psychological Medicine 1990:20:35-53*).

In a letter dated 14th October 1996 submitted to the BMJ, Dr Charles Shepherd, Medical Director of the UK ME Association, pointed out that many of the disagreements about this Report could have been resolved if the Royal Colleges' working group had agreed to meet with representatives of the National Task Force during the preparation of CR54, but this was not the case: any such collaboration was refused by the members of the CR54 working group, so an opportunity to create a real consensus was lost.

Whilst the Report of the National Task Force concluded that ME is a distinct and particularly severe sub-group of CFS, this Report (CR54) seemed to have as its main agenda a determination to "de-recognise" ME as a nosological entity: indeed, two members of this working group have already tried to get the World Health Organisation neurological classification revoked (*Chronic Fatigue, ME, and ICDIO. Anthony David, Simon Wessely, BMJ 1993:343:1247-1248*).

To co-incide with the publication of CR54, Wessely's like-minded colleague from the USA, Stephen E Straus, Chief of the Laboratory of Clinical Investigation at the NIH, Bethesda, Maryland, (who seemingly can always be relied upon to provide an obligingly supportive stance for Wessely's efforts) wrote in the BMJ about CR54 as follows:

"This week a joint working group of the Royal Colleges of Physicians, Psychiatrists and General Practitioners in Britain issued a report on chronic fatigue syndrome. The report constitutes, arguably, the finest contemporary position statement in the field, and physicians and patients are well advised to read it".

From the outset, the working group addressed inappropriate imperatives; some of these are considered below, and in summary are as follows:

- (i) the report equates ME with CFS: they may be related syndromes, but they are not the same (ICD classifies ME as a neurological disorder - ref G 93.3, whilst fatigue syndromes are classified as other neurotic disorders - ref F48.O) and the National Task Force report classifies ME as the most severe subgroup of the overall term CFS
- (ii) the advice on children with ME / CFS is gravely inappropriate
- (iii) there is a total disregard of the available evidence in disciplines other than psychiatry, eg. virology, neuroendocrinology, immunology.

The present author compiled observations on the joint Report and on 17~'~ November 1996 these were sent to the Chief Medical Officer and to the Presidents of the three Royal Colleges; main issues included the following:

## Chapter 2 / Background

The joint report states *“There is a tendency to over-investigate using laboratory and imaging techniques”*: the reality is that patients with ME frequently find it impossible to be taken seriously by their doctors, who regularly strike ME patients off their list, treating them with obvious disdain and lack of basic courtesy.

*“In clinical practice we have noted that the label of ME has been used by doctors and others for the following situations, emphasising an unacceptable diversity of use: severe, unexplained fatigue and exhaustion”*~ It will be recalled that it was these very psychiatrists who formulated their own “Oxford” criteria, and it is their own criteria which stipulate that all categories of medically unexplained “fatigue” be encompassed in the case definition of CFS, so it was they themselves who advocated such a dilution of critical definitions. It is certain that ME is over-diagnosed, but it is the broadened criteria which have contributed to this over-diagnosis. On page 9 of the joint Report, an incidence of 2.6% of the UK population is claimed, but this is generally believed to be a gross over-estimate, and that the figure for true ME is 0.1 % (ie. one per thousand), which gives a strike rate of 55,000 in the UK. Even if the figure is taken as being 0.2% of the UK population (ie. two per thousand), the figure would then be 110,000 in the UK. This differs from the Report’s estimate of more than one million in the UK (of which they claim that 75% have a psychiatric aetiology).

## Chapter 3/ Definitions

The problem of definition continues to bedevil ME /CFS and it is not helped by the reluctance of these psychiatrists to address the urgent need to differentiate the various sub-groups of chronic fatigue syndromes, with the result that patients with distinctive and defined “true” ME have become submerged under the umbrella term

of “CFS” (which is bad science, as it ignores the disorders of cholinergic transmission and the damage to the receptor chemistry found in ME, together with the evidence of an up-regulated immune system consistent with an on-going response to viral activity).

It is a matter of concern that the authors of the joint Report seem unaware that in ME, “fatigue” is not the major symptom: the over-riding symptom is incapacitating exhaustion together with post-exertional muscle fatiguability, almost always accompanied by profound malaise and a burning, vice-like pain in the affected muscles (myalgia).

The term “chronic fatigue syndrome”, far from being “*the most appropriate term for the syndrome*”, is neither appropriate, accurate, nor descriptive; it excludes core symptoms and is abhorred by patients and physicians alike, who believe it implies a benign state of trivial importance, suggesting that people with CFS lack motivation to get on with life. Little consideration is given by this Report to such commonly found symptoms as ataxia, vertigo, diplopia, rashes, easy bruising, severe and recurrent mouth ulcers, non-androgenous hair loss, pancreatic dysfunction, vascular changes, cardiac problems and autonomic dysfunction resulting in insecure bladder and bowel control.

At paragraph 3.4, the authors state “*Patients may wish to keep a particular term (ie ME) because only with that label are they eligible to call upon the welfare state for help*” In the UK, it is the very label “ME” which has **stopped** patients from getting welfare benefit: even those who on clinical grounds have been awarded such benefits for life have subsequently had those benefits withdrawn on the grounds that “ME is not a pathology in its own right” (*Internal Memorandum from Dr A.E. Fumiss, Medical Officer to the Benefits Agency Medical Services, 4” April 1995*). Those directives come from BAMS, to whom Wessely is an adviser on ME / CFS (*Letter dated icP January 1997 from Dr Simon Wessely to Dr Manse! Aylward at The Department of Social Security, The Adeiphi, 1, John Adam Street, London WC2 6NT*).

#### Chapter 4/ Epidemiology

Paragraph 4.2 states “*At least 25 studies exist concerning the prevalence of chronic fatigue in the communit/*” it is the constant and indiscriminate use of the different terminologies as interchangeable which has contributed to the present obfuscation of case definitions, and this factor is the one which so hinders research (*Report from the National Task Force on Chronic Fatigue Syndrome (CFS), Postviral Fatigue Syndrome (PVFS) and Myalgic Encephalomyelitis (ME). Westcare, Bristol, September 1994*).

## Chapter 5 / Virology

This chapter on virology in CFS is only 21/2 pages in total; it has no less than 12 self-references of the joint report authors (who have long been known for studying “fatigue” as distinct from ME, and then for ascribing their results to all chronic fatigue syndromes, including “pure” ME / CFIDS).

The report authors state at paragraph 5.9 that “the risk.. .was increased if there was evidence of . . . psychological morbidity before acquiring an infection” and at paragraph 5.10 the authors state “Another primary care study using very similar patients found that chronic fatigue after clinically defined common viral infection was associated with the patient’s somatic attributional style (a person’s tendency to see him or herself as suffering from a physical illness) and. . .sick certification”

On 2~ March 1997 an independent ME researcher (D.Jones MSc) sent her own observations on CR54 to the CMO, noting about this chapter that it is beyond comprehension how any professional review panel such as this so-called “expert” working group could have ignored the findings of impaired 2-5A synthetase / RNase L antiviral and anti-proliferative pathways (first reported by Suhadolnik at the 1990 First World Symposium on ME / CFS held at the University of Cambridge, UK and subsequently in the medical literature, for example: *Changes in the 2-5A Synthetase I RNase L Antiviral Pathway in a Controlled Clinical Trial with Poly (!)-Poly(CI2U) in Chronic Fatigue Syndrome. Robert J. Suhadolnik, Daniel L. Peterson, Paul Cheny et al: In Vivo: 1994:8:599-604*), which is perhaps the most important evidence of viral involvement in ME / CFS. This work was well-documented in 1992 on pages 613-617 in the major 724 page textbook on ME. (*The Clinical and Scientific Basis of Myalgic Encephalomyelitis Chronic Fatigue Syndrome* edited by Byron Hyde, The Nightingale Research Foundation, Ottawa, 1992).

An equally incomprehensible omission is any mention of the work by Daniel Peterson et al (*Clinical Improvements with Ampligen in Patients with Severe Chronic Fatigue Syndrome and Associated Encephalopathy, idem pp634-638*). Ampligen has benefitted patients with HIV / AIDS, hepatitis B and certain types of cancer (*HEM Research. Ampligen — Background on an experimental drug for the treatment of HIV infection and AIDS, CFS, several forms of cancer, chronic hepatitis B. NY:Broadgate Consultants Inc., 1990*). Mismatched double-stranded RNA molecules correct the impaired antiviral pathway: these findings alone should give credence to a viral aetiology in many cases of ME / CFS, but this research is not once mentioned by the authors of CR54.

Given that until 1955, ME was known as “atypical polio” and given the known link between the post-polio syndrome and ME (*The Clinical and Scientific Basis of ME! CFS, ed B.Hyde, as above, page 113; Myalgic Encephalomyelitis and*

*Postviral fatigue states. AM Ramsay. Gower Medical Publishing, 1988)* the failure of these authors even to consider whether polio immunisation renders people more vulnerable to enteroviruses and subsequent ME/ CFS is notable.

Such deliberate attempts to classify ME /CFS as a somatisation disorder and such consistent selectivity is inexcusable in a supposedly authoritative publication from the three joint Royal Colleges.

#### Chapter 6 / Muscle dysfunction and immunology

This chapter consists of less than one full page, and contains six self-references by the report authors.

There is an extensive literature on both muscle pathology in ME / CFS and there is an even greater literature on the immunological aspects of ME / CFS; both are very important areas in ME / CFS, but are here treated as quite inconsequential.

#### Chapter 7 / Psychiatry and neuropsychiatry

It can be no coincidence that this chapter takes prominence.

Even in this chapter, the same concern arises, in that the authors are not being careful enough and are not controlling for selection bias.

At paragraph 7.3 the authors claim that *“Approximately half of those.. with a diagnosis of one or other form of CFS fulfill criteria for affective disorder. . . Many studies find that a further quarter fulfil criteria for other psychiatric disorders, chief amongst which are anxiety and somatisation disorders”*

At paragraph 7.7 the authors claim *“Psychological factors are thus one component of a multifactorial view of the aetiology of CFS. Other factors. . .include . . .altered health perception (and) deconditioning”* The authors seem unable to understand that if people become seriously ill, it is normal for them to “perceive” their health status differently, because it *is* different. By what mode can normal perception figure in the *aetiology* of the disorder?

At paragraph 7.9 the authors claim *“Patients with long histories of multiple somatic symptoms (such as) unexplained abdominal pain, headaches, chest pain, food allergies, chemical sensitivities (and) unresolved gynaecological problems. . .may fulfil. . .established criteria for somatisation disorder”*.

Paragraph 7.11 expressly states *“In CFS, as with fibromyalgia, the greater the number of somatic symptoms, the greater the probability of psychiatric disorder”* No mention is made about spectrum disorders, which involve the whole body, most probably at cell membrane level.

It is worth noting that multi-symptomatic patients who may well be victims of medical ignorance and / or arrogance (not to mention medical prejudice) would be abnormal if they were **not** despondent: diagnostic uncertainty is itself associated with increased anxiety (*Diagnosis in chronic illness: disabling or enabling — the case of chronic fatigue syndrome. Woodward R et al; JRSM 1995:88:315-319*) and the authors of the joint Report are here confounding the predictors and the criteria of psychiatric disorder.

This short paragraph attempts glibly to explain away as somatisation many of the symptoms commonly found in ME, and it obscures a huge hidden, but very important agenda. (*see The Lancet article referred to in the present Introduction*).

On neuro-imaging, paragraph 7.13 states “*neuro-imaging is a sensitive technique and may reveal “abnormalities” of little consequence*” In their attempt at discussing the value of neuro-imaging in CFS, the authors adopt their usual dismissive stance, and suggest that neuro-imaging studies are of limited value on the grounds that confounding factors (such as co-existing depression and anxiety) have not been taken into account in the interpretation of the findings. The authors of CR54 are unequivocal that “*there is no justification*” for the use of neuro-imaging studies other than as part of “*carefully conducted*” research (but do not most researchers believe that they conduct their research “carefully”?)

At the Annual General Meeting of the UK ME Association held in London on 5th October 1996, Dr D.C.Costa of the Institutue of Nuclear Medicine at UCL Medical School, London, the foremost ME researcher in nuclear medicine in the UK, gave a lecture in which he explained that hypo-perfusion of the brain stem is the main characteristic apparent on neuro-imaging in ME, and that it is more severe than in AIDS encephalitis, or indeed in any other brain disease he has examined since 1985 in some hundreds of patients.

## Chapter 8 / Presentation, assessment, investigation and prognosis

At paragraph 8.9 the authors advise that there is little point in looking at parameters of anti-nuclear factor, immune complexes, immune subsets or cholesterol levels, claiming that “*revealed changes*” are “*rarely substantial*”

In Appendix 4 (Summary of the Report), the authors spell this out again: they direct that “*No investigations should be performed to confirm the diagnosis*”

At paragraph 8.12 the authors include the following as “aims of assessment”:  
*“to elicit the beliefs and fears of patient and family to identify psychological distress. .  
 .to formulate the problem in terms of predisposing (and) perpetuating factors”*: There is scant acknowledgment of the need for adequate clinical screening but, inevitably, there is over-emphasis on the authors’ perceived importance of the need to change the patients’ *beliefs* about this illness.

This arbitrary (or possibly expedient) rejecting of the significance of parameters found by other researchers to be abnormal in ME / CFS requires detailed consideration. On every front except the psychological, the Report authors urge against “over-interpreting the abnormalities described to date” (6.5). Not only do they urge this in relation to muscle pathology, but to immunological abnormalities (8.9), to virological evidence (5.5) and to neuro-imaging abnormalities also (7.13).

In many illnesses, patients present with multiple non-specific symptoms such as fatigue, joint pains, irritable bowel, altered micturition: such symptoms may well be due to hypothyroidism, SLE, MS, Addison’s disease, chronic brucellosis, rheumatoid arthritis or to other autoimmune overlap syndromes.

Contrary to what the authors of CR54 advise, even supposing that it was certain that no medical explanation for the patient’s “fatigue” had been established, it is imperative to carry out detailed laboratory investigations and not to rely on the personal assumptions of the examining doctor; if such an approach is curtailed as non-essential, one must ask what are the prospects of scientific advancement in medicine. Could it be that if ME patients are refused investigation, then no evidence will readily come to light which challenges the psychiatrists’ stance, so their position will thus be maintained and (at the expense of some very sick people) their need to exercise power and control will continue to be gratified?

At paragraph 8.16, the authors of the joint Report state *“Several studies suggest that poor outcome is associated with social, psychological and cultural factors. These include the strength of belief in a solely physical cause for symptoms .and the use of avoidant coping strategies”*.

At paragraph 8.17, it states *“Chronicity is likely to be associated with perpetuating factors. which may include unaddressed psychosocial issues”*: One must ask if these psychiatrists would look at “perpetuating factors” or “unaddressed psychosocial issues” in multiple sclerosis, or in the post-polio syndrome, or in lupus, or in AIDS. If not, then why the special pleading in ME / CFS?

It seems that such is the joint Report authors’ fanaticism to secure a primary psychiatric aetiology for ME / CFS that they are immoderate in their determination to dismiss any possibility of an organic aetiology.

Their message is clear: only the ill-informed or the naïve would allow themselves to be influenced by “premature” indications of an organic causality: this is a powerful psychological tool which the Report authors are exploiting to effect their own ends.

## Chapter 9/ Management

Yet again, the authors of CR54 declare themselves: at paragraph 9.2 they state “*We have concerns... about the dangers of labelling someone with an ill-defined condition which may be associated with unhelpful illness beliefs*”:

ME is hardly “ill-defined” (though the psychiatrists’ own definition of CFS is less than a paradigm of excellence) and ME is formally classified by the World Health Organisation as a **neurological disorder** (ICD 10: G 93.3), so it is hardly an “unhelpful illness belief”.

At paragraph 9.6 the authors allude to “*pre-existing personality*”~ at paragraph 98 comes the advice that the best way to modulate Such attitude problems is by using cognitive behaviour therapy (CBT), even though there is no evidence of phobic avoidance of activity in ME / CFS and even though evidence superior in design construct confirms that CBT is of no benefit whatsoever in ME / CFS (*Immunologic and psychologic therapy for patients with chronic fatigue syndrome. Lloyd A et al. Am J Med 1993;94:197-203*). Notwithstanding, at paragraph 9.9 the authors of CR54 eulogise that “*CBT is a promising and cost-effective approach that has been recommended for the . . . management of CFS. . . the treatment is safe and acceptable*”

Inevitably, the report authors state at Paragraph 9.20 “*We have concerns about the use of complementary therapy and dietary interventions*”: It might be prudent to reflect that Healthwatch (formerly known as The Campaign Against Health Fraud, with which Weilcome has known and documented associations and for which from its inception in 1989, Wessely has been a leading activist (*Dirty Medicine. Martin J Walker, Slingshot Publications 199~3: page 334*) states that its aim is to promote publicly the view that “valid clinical trials” (ie. **drug trials**) are the best way of ensuring public protection”, and to oppose “diagnoses that are misleading or false, or that may encourage unnecessary treatment for ... **non-existent diseases**”. (*Healthwatch subscription form valid up to 1st May 1990*).

It might also be prudent to reflect that Healthwatch exists to attack anything and anyone who challenges the monopoly hold of the chemical industry on food production and pharmaceuticals (*Dirty Medicine as above, page 340*) and that many people with ME have a chronically up-regulated immune response, which means that they can react badly to common substances, particularly to medical drugs: (i) *The presentation, assessment, investigation and diagnosis of patients with Postviral/ Fatigue Syndrome in an Infectious Diseases Clinic. W. R. C. Weir. IN: Postviral/ Fatigue Syndrome. Eds. Rachel Jenkins and James Mowbray. John Vvi/ey & Sons, 1991*; (ii) *Allergy and the chronic fatigue syndrome. Stephen E. Straus et al. J Allergy Clin Immunol 1988;81:791-795*; (iii) *The Disease of a Thousand Names. D. S. Bell. Pollard Publications, Lyndonville, New York, 1991*; (iv) *The Florence Nightingale Disease: A Multisystem Experiment of Nature. In:*



*The Clinical and Scientific Basis of Myalgic Encephalomyelitis*, ed. B. Hyde, Ottawa 1992; (v) *The Role of Food Intolerance in Chronic Fatigue Syndrome*. Loblay RH. *In idem*, pp 521-538; (vi) *Chemical Sensitivity: The major cause of ME?*. Rea WJ. Public Lecture, Birkbeck College, London, 3<sup>rd</sup> December 1993; (vii) *The Differential Diagnosis between Chronic Fatigue Syndrome and Multiple Sclerosis*. C. M. Poser. Presentation at the International Conference on Chronic Fatigue Syndrome, Dublin, 18-20 May 1994; reported in *Perspectives*, June 1994)

Professor Poser said that a paradoxical or inappropriate response to medication was one of the most important criteria in CFS, and that it was virtually pathognomonic.

**Because** of adverse reactions to so many substances, including medicinal drugs, patients with hypersensitivities may of necessity turn to “complementary therapy and dietary interventions” provided by clinical ecologists or allergy practitioners, who tend to advocate non-drug therapies and who thus become the target of Healthwatch activists (*Dirty Medicine as above*, p 341).

At paragraph 9.23 (management by drug therapy), the Report authors state that “we see no role for immunotherapy. There is no compelling evidence linking immune dysfunction with disability”:

However, in the Summary, the Report authors specifically recommend “controlled clinical trials of antidepressants for CFS sufferers **without** symptoms of depression” - Appendix 4:12.

#### ChaDter 10/ Children and CFS

At paragraph 10.2 the report authors state “CFS in children covers a broad spectrum of problems. . . perhaps even.. . Munchausen’s by Proxy Syndrome”:

The authors are against home tuition and at paragraph 10.12 they advocate “immediate return to school”:

At paragraph 10.14, they advise of the need to remove children forcibly from their home and parents, if this is “in the best interest of the child”: (Compare this with Wessely’s assurances documented on page 4 in the Introduction to this review).

This chapter is perhaps the most disturbing of any in the joint Report. Yet again, the tenor of this chapter relies heavily on selectivity and bias, with no attempt to present a balanced overview of the available literature reviewed by experienced physicians.

#### Chapter 11 / Future Research

The authors state that they “are satisfied that the normal processes of supporting sound research are adequate”: What is ~ mentioned is that in 1992, the Medical Research Council granted £1 million for research into “CFS”, or that this grant was available ~ to

The Institute of Psychiatry, or that ~ applications for funding had to be made to Dr Simon Wessely (personal communication, and it was also announced publicly at medical meetings).

#### Chanter 12/ Facilities and service provision

Predictably, the Report authors state “*we see no reason for the creation of specialist units*”, at paragraph 12.4 the authors state “*we do not think that specific guidelines on the management of CFS should be issued for general practitioners*”:

#### Chapter 13/ Conclusions

ME is dismissed.

At paragraph 13.3 the authors state “*Previous studies have counted people with ME, but these studies reflect those who seek treatment rather than those who suffer the symptoms*”.

How curious then that in the ICD, the World Health Organisation should have overlooked this and should have formally classified ME as a **neurological** disorder.

#### Summary of concerns about CR54

What is particularly objected to about the joint Report is the relentless assertion that the more severe subgroup (ie. those with “true” ME as distinct from CFS) does not exist as a disease entity, and that antidepressant therapy, together with CBT, is an effective measure which should be used to modulate sufferers’ maladaptive “perception” of their suffering.

Since 1987, this onslaught has been unremitting from this group of psychiatrists, so no matter how disingenuously they use their Report to promote the view that psychiatric illness is just as legitimate as “organic” illness, people are not deceived, because the published evidence of what they **really** believe is there for all to see. (*The Views of Dr Simon Wessely on ME: Scientific Misconduct in the Selection and Presentation of Available Evidence?* E. Marshall & M. Williams. *CFIDS Chronicle*, Spring 1994:14-18).

These same doctors have assiduously and relentlessly denigrated patients who are desperately sick with this syndrome, some of whom are so incapacitated that they have to be fed via a nasogastric tube. Many cannot look after themselves and require 24 hour care.

Despite their lip-service about the need for strict operational case definitions, these authors do not heed their own advice in that they do not study those who are the most severely affected, preferring instead to study patient cohorts who will not disrupt their

own analyses.

It is no wonder that some psychiatrists are despised and held in contempt, when they refuse to accept that a conviction of physical disease in ME / CFS may ~ be dysfunctional thinking or psychosocial denial, but may arise from severe physical symptoms which are indeed organic in origin.

Doctors who have set views regardless of the facts might *themselves* qualify as dysfunctional thinkers, the effect of which is their determination to psychologise illnesses which they do not understand.

ME sufferers' iatrogenic distress will end only when truth becomes as important as power and politics, and when inaccurate labelling no longer serves as a cloak for ignorance, prejudice and misguided beliefs.

The promotion of bad science is unacceptable and for the members of the joint Royal Colleges' working group to have presented ~ their own selective and biased choice of references from the enormous body of available medical literature can hardly be anything other than bad science.

The joint Report is thus not a scientific re-appraisal at all.

Many of the studies on which the authors of CR54 relied have been shown to contain major flaws, whilst studies which do not bear out the psychiatrists' views are ignored, dismissed, or misleadingly quoted (*Response of the ME! CFS Charities Alliance, page 7: sent to the CMO on 31~ January 1997*).

For example, whilst a paper by Buchwald, Gallo and Komaroff is mentioned (reference 128 in the joint Report), the authors of the joint report dismiss it (on page 16), stating a *White matter abnormalities occur in a number of settings, and their significance remains to be determined*", whereas the paper itself concludes that patients with CFS "**may have been experiencing a chronic, immunologically mediated inflammatory process of the central nervous system**" and that the MRI scans revealed punctate, subcortical areas of high signal intensity consistent with oedema or demyelination in 78% of cases.

This is a clear illustration of the biased and misleading personal interpretation presented by the joint Royal Colleges' working group.

A paper by Bombadier & Buchwald is listed (reference 173 in CR54), but again, the authors of the joint Report convey that this papers *supports* their own stance, whereas the paper itself actually states "**The fact that the same prognostic indicators were not valid for the group with CFS challenges the assumption that previous outcome research on chronic fatigue is generalizable to patients with...chronic fatigue syndrome**" (which is exactly what Anthony David and Simon Wessely of the joint report invariably do).

Again, at paragraph 7.21, a paper by Curt Sandman is listed (reference 153 in CR54) in apparent support of the joint report's claim that the results of neuropsychological testing have been "*inconsistent*" this is another illustration of deliberate mis-information being propagated by the joint report authors., because the paper itself clearly concludes "**The performance of the CFIDS patients was sevenfold worse than either the control or the depressed group.. These results Indicated the memory deficit in CFIDS was more severe than assumed by CDC criteria.. a pattern emerged of brain behaviour relationships supporting neurological compromise in CFIDS**".

One would never know this from the way the authors of the joint Royal Colleges' report downplay this important research.

Yet again, there seems to be a quite deliberate intention to mis-inform: a very important illustration of this can be found in the fact that the joint report authors entirely fail to mention that, as mentioned above, the ICD 10 formally classifies ME under "Diseases of the Nervous System"; instead, the joint report authors chose to emphasise at para 3.2 that *aThe World Health Organisation International Classification of Diseases (ICD-10) category of neurasthenia also has considerable overlap with CFS*". This is particularly misleading in that the ICD category which contains "neurasthenia" comes at Section F 48.9, which is Mental and Behavioural / Neurotic Disorders.

For the avoidance of doubt, the advice of WHO is unequivocal: **ME must be in Section G 93.3 (Diseases of the Nervous System)**, whereas neurasthenia / fatigue syndromes *must be in Section F 48*.

Again, one would never know this from the authors of the joint report, as they have been so wilfully misleading. One can safely say "wilfully", as there is published evidence which confirms the authors' full awareness of the separate classifications (*Chronic fatigue, ME and ICD 10. David A, Wessely S. Lancet 1993;342:1247-1248*);

It is inconceivable that the authors of the joint report are unaware that the earliest definitions of ME / CFS were concise and descriptive and were based on a good history and on good patient observation: Wallis (1955) provided a concise list of symptoms (with appropriate variations in children and adolescents) whilst Ramsay (1956) introduced the descriptive name "myalgic encephalomyelitis" which has stood the test of time for over 40 years in the UK, Australasia, Canada and elsewhere. (*An investigation into an unusual disease in epidemic and sporadic form in general practice in Cumberland in 1955 and subsequent years. Wallis AL. University of Edinburgh. Doctoral Thesis, 1957; Encephalomyelitis simulating poliomyelitis. Ramsay AM, O'Sullivan E. Lancet 1956;1:761-766*). Moreover, it is acknowledged that ME / CFS has a unique neuroendocrinological profile, and that molecular biology provides documentation of associated viral infection, and that radiobiology points to specific anatomical areas of brain damage. (*Does a chronic fatigue adequately describe myalgic encephalomyelitis? E. G. Dowsett, December 1997*)

It is surely a matter of acute dismay that a substantial report, purporting to emanate from three prestigious Royal Medical Colleges of the United Kingdom, has been allowed to bring such opprobrium on the Academy of Medical Royal Colleges.

In issue number 9033 dated 12th October 1996, The Lancet ran an editorial entitled “Frustrating survey of chronic fatigue”, which stated

“The sixteen - strong committee was top heavy with psychiatric experts, so the emphasis on psychological causes and management (introduction of graded exercise and cognitive behaviour therapy) is no surprise.

“Charles Shepherd, medical director for the ME Association, told us that ‘the Committee was rigged, with dissenting voices excluded’.

“Certainly, the expert committee describes no attempt to collect external opinions, and the report is little more than a literature survey.

“Psychiatry has won the day for now. A decade hence, when an organic cause for at least some cases of CFS may have emerged, it would be tempting to ask the committee to reconvene.

“We believe that the report was haphazardly set up, biased, and inconclusive, and is of little help to patients or their physicians”.

Some weeks later, the Editor of The Lancet, Richard Horton, wrote a telling piece about the Royal Colleges’ joint report in Observer Life on 23~ March 1997, in which he noted

“The college representatives interpreted every piece of evidence pointing to a biological cause —for instance, a virus — in a negative light.

“Indeed, the evidence shows a total failure of antidepressants in these patients.

“Surprisingly, though, the Royal Colleges endorse the use of antidepressants.

“Intelligent discussion is seen as an attack on the physician. And any success for complementary therapies is attributed to the ‘charisma of the practitioner’.

“Medical paternalism seems alive and well in Britain today.

“... the larger lesson — namely, that doctors should listen more and pronounce less — has been missed.

“It is interesting to note that the last word in an American review on chronic fatigue is ‘compassion’. One struggles to find this word in the UK report”.

It is perhaps worth considering the American report to which the Editor of The Lancet refers. It is entitled Chronic Fatigue Syndrome: Information for Physicians and was produced by the National Institutes of Health (National Institute of Allergy and Infectious Diseases), Public Health Service, US Department of Health and Human Services in September 1996, barely one month before the publication of the UK joint Royal Colleges' report.

The American report is very different from the UK joint Royal Colleges' report.

On page 3, it states *"It is important to note that about 20-40% of carefully evaluated CFS patients do not have depression or another psychiatric illness"*, which is substantially different from the UK report, which claims that 75% of all CFS patients have a psychiatric illness.

On page 3, the American report advises that *Some studies have found a significantly greater prevalence of allergy in CFS patients. . . many CFS patients have a history of allergies years before the onset of the syndrome. Sometimes patients report a worsening of allergic symptoms or the onset of new allergies after becoming ill with CFS*", whilst on page 9 it refers to *"the high prevalence of allergies in the CFS population"*. The UK report, in comparison, states "Patients with long histories of . . . food allergies (and) chemical sensitivities... may fulfil established criteria for somatisation disorder (page 16: 7.11). Also, the UK report refers to "food allergy" in inverted commas (page 3:2.7), thereby conferring the authors' non-acceptance of food allergy.

The American report states on page 6 *"Patients with CFS should be treated with compassion"* In the UK, "compassion" involves the withdrawal of state benefits on the advice of Wessely.

On page 7, the American report states that *"a reasonable laboratory workup"* should be performed in cases of CFS, whilst the UK report categorically states "No investigations should be performed to confirm the diagnosis" (page 45).

In discussing children with CFS, the American report states on page 7 that it advocates a *"supportive approach"*, whereas the UK report states that children may need to be forcibly removed from their home and parents.

On page 8, the American report further states *"the physician should work with the school to limit class time, if necessary, and to resume school attendance gradually"*, but the UK report urges "an immediate return to school" (page 31: 10.12).

The American report states *"Home tuition may be an alternative"*, but the UK report asserts "We discourage home tuition" (page 31: 10.12).

The American report recognises (on page 8) and accepts that *"Some patients benefit from participation in CFS support groups"*, but the UK report authors are well known

for their view that membership of such support groups is unhelpful (Outcome in the chronic fatigue syndrome: Simon Wessely. BMJ 1992:365).

The American report states on page 8 “*Referrals to professionals who can help patients with practical matters, such as applying for disability and obtaining home health care.. .can help.. .patients and their families better manage this illness*”, the UK report instead advocates that the best way to manage this illness is to alter the patient’s (and the family’s) view about the illness, and in particular, to brain wash them into accepting that the illness is merely “a belief that they are ill.

The American report states on page 9 “*CFS patients often report that antidepressants given in full therapeutic dose exacerbates their fatigue. . .Many CFS patients are extremely sensitive to these drugs*”, but the UK report unambiguously and vigorously urges the use of “antidepressants for CFS sufferers~(even those) without symptoms of depression” (page 45).

The American report states on page 10 “*A variety of common viruses can be re-activated in some CFS patients most investigators believe virus reactivation could be occurring secondarily to some immunologic disturbance*”~ but the UK report states “Some use the results of immunological tests as evidence for a so-called ‘organic’ component in CFS... such abnormalities should not deflect the physician from the biopsychosocial approach... and should not focus attention ...towards a search for an ‘organic’ cause” (page 13: 6.4).

The American report states on page 11 that, if confirmed, central nervous system research would support the theory that “*CFS is a multisystem illness with prominent central nervous system involvement*” but the UK report concludes that “chronicity is likely to be associated with... unaddressed ~psychosocial issues” (page 21: 8.17), and states “Many of the current findings may be epiphenomena relating to ... psychological distress...or... inactivity”. (page 37:13.7).

The above illustrations are just some examples of the difference in approach to the understanding of ME / CFS by the American and UK physicians.

When an American medical scientist (Dr Terry Hedrick) sent a careful critique of the Royal Colleges’ report (*The Royal Colleges’ Report on Chronic Fatigue Syndrome: Insidiously Biased and Potentially Harmful: CF!DS Chronicle: Winter 1997(ie.January 1997):Vol. 10:1:8-13*) to the President of The Royal College of Psychiatrists (Dr R.E.Kendell), in his defence of Wessely, he responded *not* to the legitimate criticisms, but instead chose to denigrate Dr Hedrick’s professional standing, writing to her on 5<sup>th</sup> March 1997 as follows:

“I do not think it is particularly surprising that you and British doctors generally should take so different a view of the report of the Working Party set up by our Colleges of Physicians, General Practitioners and Psychiatrists. The members of that working party were carefully picked by the three colleges for their extensive experience of treating patients suffering from the chronic fatigue syndrome and for their personal contributions

to the literature on the subject. The report, in other words, was written by doctors and primarily for doctors. Your background, as I understand it, is not in either treatment or medical research, but in the evaluation of review articles.

“You may be interested, therefore, to read the report... produced ... by the National Institute of Allergy and Infectious Diseases at NIH.

“The conclusions of that report are virtually identical to those of our report...”.

In her reply to Kendall, Dr Hendrick wrote:

“I am disappointed that you chose only to question my professional qualifications and did not deal with the substance of my concern.

“Although you stated that the Royal Colleges’ report was written by doctors for doctors, I do not believe it is necessary to be a physician in order to have legitimate criticisms of this report. In fact, the time is long past when one should expect to write reports on controversial illnesses and confine the readership only to physicians. Multi-disciplinary perspectives always enrich the research process.

“In my last position I was a member of the US government’s Senior Executive Service, with the title of Assistant Comptroller General for Program Evaluation, heading a technical division of 70 MA and PhD interdisciplinary researchers ...on.. medical topics.

“Researchers in this division frequently worked closely with physicians... we also worked with biologists, lawyers, economists, educators, welfare researchers, statisticians, evaluation specialists, information technologists, biotechnologists etc.

“I view interdisciplinary collaboration as desirable rather than as something to be avoided.

“The fact that I have an MA in clinical psychology with a PhD in social psychology and postdoctoral specialization in research methodology probably provides me with more background in mental health measurement issues than is typically provided in the usual psychiatrist’s educational programme.

“I have tutored medical students.

“I am a member of the American Psychological Association, the American Evaluation Association (twice elected to the board), the American Statistical Association, the American Association for the Advancement of Science, Sigma Xi (a scientific honorary) and Phi Beta Kappa; I have served on journal editorial boards... I have published journal articles and a 1993 textbook on applied research design for MA level students that is now in its 5th printing.

“Your letter characterizes me as someone who only reviews other peoples’ articles and research. Let me correct this impression. While I did not choose to do clinical work after receiving my degrees, I have personally conducted research studies in university, private



and governmental settings.

“Your letter implied that British doctors generally support the Royal Colleges’ report, yet I have learned that there are a number of on-going disputes regarding

the report’s . . . abrupt dismissal of the more physiologically-oriented CFS research.

“I also understand that at least a couple of US officials who were asked to review the draft report cautioned of the danger of relying so heavily on a single individual’s work.

“Let me correct your misunderstanding of my concerns about the report. The psychiatric literature summarized was not representative of the full spectrum of credible research.

“The working group, by allowing this one viewpoint to dominate., violated basic scientific norms essential to doing objective work.

“To have one working group member’s research constitute 10 percent of the references is a red flag for bias.

“Please be open to criticisms from persons who share a goal of fostering a better understanding of CFS.

“I remain willing to talk with whomever might be interested and look forward to any opportunity provided”.

The uncritical support provided by the President of the Royal College of Psychiatrists for Wessely and the joint report does not stand up to scrutiny.

At the press release to launch the joint Royal Colleges’ report, Dr Robert Kendell, as President of the Royal College of Psychiatrists, was quoted as saying “To try to distinguish between a physical illness and a psychological illness is not just wrong, it’s meaningless” (*Press Launch, Royal College of Physicians, London, 2<sup>nd</sup> October 1996*); this fallacy was encapsulated in a letter to the Guardian newspaper which said “Try telling that to someone with terminal cancer” (*Letter: H.J.H.Berger, Guardian, 5<sup>th</sup> October 1996, page 16*).

Like Wessely, Kendell seems to have become confused: he seems not to recall that when he was a senior registrar, he published a paper entitled “*The Psychiatric Sequelae of Benign Myalgic Encephalomyelitis*” (*R. E. Kendell. Br. J Psychiat 1967;113:833-840*) in which he concluded

“*The psychiatric disturbances occurring during the acute phase.. of ME were so widespread and so similar. . .that the presence of a specific underlying disturbance of cerebral function can hardly be doubted*”.

**The impact of Wessely's input in the Joint report of the three Royal Colleges**

As the CMO had announced the availability of the joint Royal Colleges' report in his Quarterly Update to all UK doctors, (February 1997), the much criticised and flawed report was widely circulated and the consequences of the implementation of its' recommendations became ever more apparent:

- (i) Chronically and severely ill ME / CFS patients had their state benefits withdrawn. If such cases fight that decision and opt to appear before a Tribunal, their benefits are usually re-instated on obvious clinical grounds, but this represents a considerable ordeal for those who are severely sick.
- (ii) On the official assessment form required to be used by the medical advisers to the NHS Pensions Agency, it is drawn to the specific attention of the NHS medical advisers (at section 15.1.5, in large print and bold type) that **"The Royal College Joint Working Party has stated that "No-one should be regarded as permanently impaired until they have had the opportunity of participating in all sensible efforts at rehabilitation.** Accordingly, this information should be sought before a decision on permanence is given. The Chief Medical Advisor's Expert Group's Report lists criteria that are good and bad prognostic indicators. These have been detailed in Assessment Form II reproduced below'.
- (iii) ME / CFS patients are threatened with loss of benefits unless they subject themselves to mental health assessment by psychiatrists well-known for their view that ME / CFS is a wholly psychiatric disorder.
- (iv) Some patients have even been threatened with being sectioned under the Mental Health Act unless they comply with recommended psychiatric treatment and procedures.
- (v) ME / CFS patients have been forced to have anti-psychotics or antidepressants, which have resulted in those patients having epileptic fits and hallucinations, requiring prolonged hospitalisation. Medical evidence in substantiation of this (s available from various general practitioners, who are known to be very concerned at the treatment forced upon their patients.
- (vi) Some patients have committed suicide, as the pressures and new problems they had to face became unbearable.
- (vii) Extra-contractual referrals (ECRs /OATs), which previously enabled some severely ill patients to obtain helpful assessment and support from ME

experts outside the area of their own NHS Trust are threatened with being withdrawn; if so, this would inevitably lead to more unnecessary suffering.

- (viii) Children with ME / CFS have been forcibly removed from their parents and taken into care. (This issue was raised at the CMO's Childrens' sub-group meeting in April 1999: consultant paediatrician Dr Nigel Speight reported pressure on children to attend school and the mandatory involvement of a child psychiatrist, with rejection of input by a paediatrician, and a frequency of psychiatrists diagnosing Munchausen's Syndrome by Proxy which amounted to an epidemic. (*Perspectives: 1999:72:9*)
- (ix) The truly severely ill are left to perish or survive as best they can; they are simply forgotten about, and receive no help or support. Those who have no family to call upon are in quite desperate straights. There are documented cases where Social Services have failed to supervise the Agencies to whom they have delegated community care, with the result that "carers" supplied by Agencies have ill-treated the "clients"; have threatened extremely vulnerable sick people, have raided their homes, or have failed to turn up at all. In one case, a woman was locked in her bathroom. In another particular case, a severely sick and incapacitated woman with ME was left alone in her bed for four days with no food.
- (x) There is virtually no provision, nor any proposed provision, for specialist referral for the most severely ill.
- (xi) Patients with ME / CFS reported a change in attitude by doctors and hospital consultants, and even in the attitude of their own relatives.
- (xi) The Department of Health has not commissioned any research in this area and has no plans to do so
- (xii) ME / CFS is no longer covered by some private medical insurance

Wessely and his co-authors of the joint Royal Colleges' Report CR54 would naturally seek to dissociate themselves from all these consequences of their published Report, but due consideration of the facts and the evidence reveal that Wessely is the common denominator.

The woefully inadequate response from the now retired President of the Royal College of Physicians (Professor Sir Leslie Tumberg) to the many detailed and justified criticisms of CR54 gave rise to further concern: on the principle that if a product is shown to be faulty, it can be taken back to the vendor or supplier for replacement, why should the Royal Colleges and / or the Chief Medical Officer not be equally accountable for the distribution of material which can be shown to be faulty, flawed and misleading?

## **Further Direct Consequences of the Report of the Joint UK Royal Colleges**

### **1. A Petition to Her Majesty's Government**

The published criticisms of CR54 and the many informed critical responses were ignored or were met with dismissive and patronising rebuttal by the Presidents of the three Royal Colleges.

Patients, their families and friends were outraged, as were medical practitioners who were experienced in helping those with genuine ME.

A group of people who were involved with ME came together to organise a petition that the joint Royal Colleges' Report should be withdrawn.

That petition was called "Fighting For Truth" or "ForT" and it was signed by 12,500 people.

Those signatures, together with supportive documentary evidence (in triplicate) were presented to the Countess of Mar on College Green outside the House of Lords in London on 26<sup>th</sup> November 1997.

At 2.38 pm that same day, the Countess of Mar rose to ask the following question:

"What is the current advice upon which general medical practitioners base their diagnosis and treatment for the illness myalgic encephalomyelitis (ME) or, as known by some psychiatrists, chronic fatigue syndrome".

This was followed by six supplementary questions from supporters in the House of Lords.

The Minister of State for Health ( Baroness Jay of Paddington —the former Margaret Jay, daughter of the former Labour Prime Minister James Callaghan) responded in negative and evasive terms, saying that she was unaware of the petition.

This was untrue, as she had previously personally responded to various letters about the petition; Lady Jay subsequently had to apologise and to concede (in writing) that she had indeed mislead the House of Lords; this was deemed by MPs and others to be a very serious matter.

At 3.07 pm, the Countess of Mar presented the petition, extracts of which are as follows:

"To the Right Honourable the Lords Spiritual and Temporal in Parliament assembled

"The humble petition sheweth "that, on behalf of the organisation Fighting For Truth (ForT) she has received a petition calling for the rejection and withdrawal from

circulation of the Royal Colleges' Report on Chronic Fatigue Syndrome (CR54).

“that CR54 advises that all patients suffering from chronic fatigue should be rehabilitated by re-education, that is, by psychological therapy, which aims at changing the patients' belief that they are ill, that the Report stipulates antidepressants should be given even to those who are not depressed and recommends participation in programmes of graded exercise, no matter how severely ill the patient, and that it claims a successful recovery rate from such programmes, despite the fact that international published evidence concludes that such programmes are ineffective and sometimes harmful;

“that a diagnosis of ME should only be made when fatigue of a wholly incapacitating nature is present and is unequivocally accompanied by neuro-immunological components which together form a consistent, reproducible, well-defined and recognisable pattern for medical practitioners who are familiar with the specific sub-category of ME;

“This claim is based upon a considerable body of published material which demonstrates organic abnormalities in the brain, muscle, vascular system, gut, immune and endocrine systems of those with ME, and that these areas are virtually ignored, trivialised or dismissed in CR54;

“that medical experts in these areas were actively prevented by the Royal Colleges' Working Party from participating in the preparation of this Report, and that any input from medical experts involved with the ME Charities Alliance was deliberately excluded by members of the CR54 Working Party;

“that eight out of sixteen members of the CR54 Working Party were psychiatrists and seven were physicians well known for their bias towards a psychiatric diagnosis of ME;

“that extensive published medical evidence supports the view that to diagnose “CFS” without full investigations (a course recommended by CR54) is potentially damaging; and prays that the House of Lords will take note of the Petition organised by Fighting for Truth which calls for the rejection and withdrawal of the Royal Colleges' Report on Chronic Fatigue Syndrome (CR54) which has been signed by 12,500 people and further prays that the House of Lords will call upon Her Majesty's Government to review that scientific evidence upon which diagnosis and treatment of ME are based.

“And you petitioners will ever pray etc'.

The Minister of State for Health ( Baroness Jay) did not respond to the petition; she suggested that those with ME take their grievances directly to the Royal Colleges.

The petition was rejected in that the Presidents of the Royal Colleges refused (in writing) to withdraw the joint Report CR54.

By contrast, in 1995-96, the US government voted \$11.8 million to CFS research.

## 2. A private meeting with the Chief Medical Officer. Sir Kenneth Calman

At the instigation of one or two people closely involved with ME, the CMO agreed to meet The Countess of Mar, Dr Betty Dowsett ( honorary consultant microbiologist with a lifetime's experience of ME) and independent ME researcher Mrs Doris Jones MSc; this meeting took place at the Department of Health on 11<sup>th</sup> March 1998. Its' aim was to present to the CMO and to the Minister of State for Health (Baroness Jay of Paddington) some of the published evidence on the organic basis of ME.

Although previously scheduled to be present, Baroness Jay failed to attend.

This meeting had nothing to do with the meeting with Department of Health officials in February 1998, attended by consultant immunologist Dr Anthony Pinching and members of the UK ME Association, although the combined effects clearly supported each other.

The CMO and an official from the Department of Health were presented with 73 major published references to the organic basis of ME / CFS (including a copy of "The Clinical and Scientific Basis of Myalgic Encephalomyelitis edited by Byron Hyde of Ottawa), together with evidence of recent difficulties in obtaining appropriate benefit and support for patients with ME / CFS.

Evidence was supplied on the general problems found in ME; on the historical reviews; on the epidemiology (non-psychiatric) of ME and on the clinical aspects; on virological and environmental factors; on neuroendocrmnological disturbances; on nuclear medicine findings; on muscle and exercise findings; on cardiovascular aspects; on immunological findings; on neuropsychiatric findings, particularly those ignored in CR54; on treatment and rehabilitation; on children and adolescents with ME and on visual disturbances in ME. An outline was given of the potential costs to the nation of the illness.

A detailed section dealt with case-histories of actual patients and the many problems which beset them.

A further section was entitled "Chronicity - Severity - Deaths", with long-term follow-up details.

Sir Kenneth Calman made the following remarks:

- A) He expressed great surprise that a report from the Royal Colleges should have made such an impact on the way doctors treat patients: he said that as a rule, such reports were either ignored or not taken seriously.
- B) He said that the purpose of CR54 was not to advise doctors on diagnosis and treatment, but to ascertain whether the disease existed or not, and that this had been established. In that context, the *causes* were of little consequence.

- C) The Countess of Mar then pointed out that in this instance, general practitioners were being guided by CR54 recommendations, not only for patients with ME / CFS but also for Gulf War syndrome veterans and organophosphate victims. The CMO acknowledged her concerns.
- D) The CMO asked that a copy of everything presented to him that day be sent to Professor George Alberti at The Royal College of Physicians (who had succeeded Professor Sir Leslie Turnberg as President of the Royal College of Physicians), promising that he would take up the issues himself with the Royal Colleges.
- E) The CMO requested the Countess of Mar to take up the benefits issue with Dr Mansel Aylward, Chief Medical Adviser, Department of Social Security.
- F) The CMO said that Lord Sainsbury (*who is believed to be a personal friend of Simon Wessely*) had generously donated £4 million for research into CFS.
- G) The CMO concluded by saying that ways should be found to make life easier for those afflicted by ME / CFS.

Both Sir Kenneth and the official from the D0H appeared to understand that there were big problems for ME / CFS patients.

### 3 A Meeting in the Grand Committee Room of The House of Commons

This was another patient initiative in protest at CR54; it was organised by Tania Harrison, a severely affected young person with ME and consisted of a packed audience of the seriously ill and their carers, together with 52 Members of Parliament.

#### 4. The setting up by the Chief Medical Officer of a new working group

On 16<sup>th</sup> July 1998 to mark the occasion of his retirement, in a widely-publicised press release, Sir Kenneth Calman announced that the Department of Health was to set up a new Working Group on ME / CFS, and that it should involve patients and carers. It was to be funded by the Linbury Trust (which is the Trust of the Sainsbury Supermarket family).

Whilst welcoming this news, many of the better-informed in the ME community had grave reservations about the fact that the Government appeared to have handed over financial control of the new Working Party to the Linbury Trust.

In July 1998 the Linbury Trust produced a booklet entitled “A Research Portfolio

on Chronic Fatigue” (*note: not chronic fatigue syndrome*) it was published by The Royal Society of Medicine and was edited by Robin Fox for the Linbury Trust.

Sixty-three per cent of the Linbury contributors are psychiatrists who might be said to belong to the “Wessely” school.

Seventy per cent of the reported work supported by the Linbury Trust has a psychiatric - psychological dimension.

Much of the work contained in the Linbury “portfolio” is based on the same poor epidemiology; the psychiatrists continue to confuse ME with chronic fatigue and with psychological illnesses such as depression.

Evidence which shows ME to be an organic illness is excluded or devalued.

The plight of the severely affected (and of children with ME) is ignored altogether.

On page 67 of the Linbury Trust “research portfolio” on chronic fatigue, there is an “Editorial Afterword”: it contains a diagram drawn by Dr Anthony Cleare (who co-authored with Wessely the paper which states *“There lies at the heart of CFS not a virus (or) immune disorder, but a distortion in the doctor-patient relationship”*: Anthony J Cleare. Simon C Wessely. *Update* 1996:61-69).

In summary, the “Editorial Afterword” affirms that patients with psychological defects are predisposed to develop ME / CFS owing to the mis-attribution of their symptoms to a *physical* cause. This prompts patients to avoid physical activity, which causes them to become deconditioned, which increases fatigue and psychological disturbance.

The message of the “research portfolio” into “CFS” is clear: cognitive behaviour therapy and drug therapy will control the patient’s mis-attributions.

Searching for causes is not only futile but may prevent recovery.

The first paper in the “research portfolio” is by Simon Wessely and is entitled *“Epidemiology in CFS”*; it has 18 references, of which no less than 10 (55%) are Wessely’s own papers. Ignoring all seminal papers which have charted the course of ME over the last 60 years, from sporadic cases to endemic clusters and as world-wide epidemics, Wessely recounts only his own work from 1988.

No attempt has been made in the Linbury Trust “research portfolio” to include the seriously and chronically disabled in any individual study.

Notwithstanding, in his “Editorial Afterword”, Robin Fox proclaims: *“we can state confidently that CFS is a symptom complex rather than a disease. . .it is not an inflammation of brain or a muscle disease. . .numerous psychological disturbances have*



*been identified”*

If taken to its logical conclusion, much of this “research” work re-inforces the inhuman child protection system, directly leading children diagnosed as having ME / CFS to be forced into psychiatric units against their parents’ wishes.  
(Acknowledgment to Dr B.Dowsett: “Chronic Fatigue” and The Linbury Trust Research Portfolio: August 1998).

It is not therefore surprising that alarm bells are ringing loudly about the fact that the CMOs new Working Group is in the hands of the Linbury Trust.

Alarm bells are also ringing loudly about the fact that Simon Wessely (now Professor of Epidemiological and Liaison Psychiatry at King’s College School of Medicine, London) is one of the members of the CMO’s Working Group, as are his close colleagues and collaborators Dr Anthony Cleare, (Senior Lecturer and

Linbury Trust Fellow, Department of Psychological Medicine, King’s College Hospital, London); Dr Trudie Chalder (a cognitive behaviour therapist at Kings College Hospital, London) and Dr Peter White (consultant psychiatrist, St Bartholomew’s Hospital, London), all of whose trenchant views on ME are documented only too well.

One illuminating disclosure is that the Chairman of the CMO’s Working Party (Professor Allen Hutchinson of the School of Health and Related Research at Sheffield University) has made it known that he will hear no criticism of Simon Wessely (*personal communication*).

Another is that the library of over 3,000 articles, editorials and letters etc relating to ME / CFS which will form the database of the Working Group has been donated by Simon Wessely.

5. The Publication of Research Paper 98/107 Chronic Fatigue Syndrome / ME I 1<sup>st</sup> December 1998. House of Commons Library, London. by Dr Alex Sleator

This 47-page document purports to discuss the “controversy surrounding Chronic Fatigue syndrome / ME”.

It is in the House of Commons Library and is for the use and enlightenment of Members of Parliament; it is standard practice for the House of Commons Library to publish documents on issues of current interest to MPs.

Whilst the first 18 pages give the impression that this is a fair assessment, it then becomes clear that it is little more than an endorsement of the joint Royal College’s Report CR54, with undue emphasis on the psychiatric - psychological bias of that Report.

The extent and degree of the justified criticisms of CR54 are grossly understated, which is misleading.

Quoted details on the Incapacity Handbook for the Medical Services doctors state there is no firm evidence that ME is different from CFS, nor that CFS is a physical disease. *(One of the issues raised by differentiating between ME and CFS is the difference in relation to cortisol levels, but this is not mentioned).*

The most telling details appear on page 39, where Baroness Hayman states “*The Department of Health has not commissioned any research in this area, and has no present plans to do so. We are, however, working with the Linbury Trust on issues related to the treatment and management of the problem*”.

Perhaps those who anticipate that the outcome of the CMO’s new Working Party on ME I CFS is a foregone conclusion may be justified in their negative expectations: it seems that Wessely’s influential involvement with industry (both Wellcome — who fund the Medical Research Council — and the Sainsbury’s Linbury Trust) determines who gets the financial grants and which research is done on ME I CFS in the UK.

*(Chronological review of short selection of Wessely & associates’ papers continued from page 46)*

Neuropsychological deficits in chronic fatigue syndrome: artefact or reality?

EDITORIAL: Rona Moss-Morriss et al. Department of Psychiatry, Auckland University Medical School, New Zealand (JNNP 1996;60:474-477)

*Whilst not authored by Wessely or his close colleagues, this paper is based on Wessely & colleagues’ views and influence — see references.*

The stated aim of this review is to provide a comprehensive summary and discussion of the results from neuropsychological studies which have compared CFS patients with controls or normative data.

Areas mentioned include global intellectual functioning, receptive functions, mental activity rate, attentional activities, memory, cognition, psychological factors and cognitive deficits, and physical factors and cognitive deficits.

The authors state that “A consistent finding across studies is the discrepancy between objective performance and subjective reports of cognitive difficulty.... Subjective reports of impairment have been consistently related to higher levels of psychopathology, anxiety, depression, and somatic complaints”.

“In summary, depression, emotional distress, fatigue and somatic ratings have all shown some relations to impaired performance in chronic fatigue syndrome”.

“Consequently, there is almost no evidence to date that organic factors contribute to the neuropsychological impairment in chronic fatigue syndrome”.

“Somatic focus and overconcern about symptoms may play an important part in speed of information processing by competing for attentional resources”.

### 1997

Chronic Fatigue Syndrome: is ME nothing more than chronic fatigue...? Frances Lee.  
*Health & Fitness, January 1997, pp 8 1-82*

It is not only in the medical press that Wessely and colleagues promote their own views; this article serves as another vehicle for the psychiatrists.

“Myalgic encephalomyelitis (ME) is dead but chronic fatigue syndrome (CFS) lives on, according to a controversial new report”.

“Although ME has long been recognised as a physical disease by the World Health Organisation, psychiatrists in Britain have claimed it as their territory”.

“A research group from three major medical bodies, the Royal Colleges of Physicians, Psychiatrists and General Practitioners., decided that ME... is simply CFS and is best treated by exercise and phsyiotherapy”.

“According to Dr Robert Kendell, president of the Royal College of Psychiatrists, the name has been changed to CFS because ... ‘there’s no such evidence of any inflammation, therefore (the use of ME) is inappropriate’ “.

“Dr Simon Wessely . . . says ‘because of the research, we are a lot more positive and optimistic about the best forms of management and rehabilitation’”.

“The Royal Colleges insist., that the search for any other tangible cause is likely to lead up a blind alley”.

“The Colleges reject any link between CFS and muscle disorders. Any muscle changes, they say, are the result of inactivity”.

“..anxiety and depression are the strongest risk factors so far identified for CFS”.

In this article, Dr Kendell says “It is important that everybody — patients, their relatives and their doctors — should realise that the distinction between mental and physical is illusory” (*see letter from H.J.H.Berger on page 67 above*).

Five days that shook the world. Ann Boston. *Guardian*: 11th March, 1997, p 16 This is an article about the potential dangers of psychotherapy.

“‘People involved in psychotherapy should know that it has side effects and risks’ said Dr Simon Wessely at the Maudsley Hospital. ‘There’s evidence that some intensive courses do have rates of casualties’”. (*Cognitive behaviour therapy (which Wessely promotes for those with ME / CFS) is a form of psychotherapy, so it is notable that Wessely is aware that psychotherapy has side effects and risks, given that he and his close colleagues promote it in ME I CFS on the grounds that it is safe, effective and “acceptable to patients”*).

You have to be mad to work there. Jeremy Clarke. *Sunday Telegraph*, 1.6.97

Jeremy Clarke makes the point that in *One Flew Over the Cuckoo’s Nest*, author Ken Kesey makes the startling suggestion that some mental illnesses exist *only in the minds of psychiatrists — all of whom are acting on behalf of the state*.

The germ bug. Hilary Bower. *Independent on Sunday*, 8.6.97

Germs may be responsible for many of the illnesses blamed on genes and vices: this article states that “Diseases that were once thought to be caused by our way of life, or by something wrong with the body, are turning out to be due to germs”.

Various examples are given, including *Chlamydia pneumoniae*, which is now known to set the scene for a heart attack.

The article discusses stealth viruses (how some viruses hide in the cells as parasites, just marking time until something — such as stress — triggers them into higher activity). Dr John Fazackerly, senior lecturer in virology at the University of Edinburgh, explained about viral “deviousness”, ie. when the virus is not immediately obvious but when immune tolerance is broken, which results in auto-immune reaction. He made the point that if the virus goes away, one is left with *auto-immune disease* (and not an obvious viral infection).

*(This pathway has been postulated as possible in ME).*

Although not a virologist, Simon Wessely gives his opinion that “we are a long way from proving viral causes of mental illness”. He adds “Mood can alter immunity, so infection could in fact be a consequence of a disorder rather than a cause”.

Clinical improvement in chronic fatigue syndrome is not associated with lymphocyte subsets of function or activation

Peakman M; Deale A; Wessely S et al *C/in Immunol Immunopathol* 1997; 82:1:83-91

Immune function was assessed in 43 patients with CFS (using the Oxford criteria including patients with depression and anxiety), and in 20 healthy controls.

The authors found no correlation between any immune variable and measures of clinical status ( except a weak correlation between total CD4 T cells and fatigue).

The authors conclude “we have been unable to replicate previous findings of immune activation in CFS and unable to find any important associations between clinical status, treatment response, and immunological status”. (*Compare these findings by Wessely with the papers listed on page 36 above*)

Changes in growth hormone, insulin, insulin-like growth factors (IGFs) and IGFbinding protein-I in chronic fatigue syndrome

Allain TJ; Beam JA, Wessely S et al *Bio/ Psychiatry* 1997;41:5:567-5 73

The aim of this study was to determine whether patients with CFS have abnormalities of the growth hormone / IGF axis basally or following hypothalamic stimulation with insulin-induced hypoglycaemia.

The authors state “This study provides preliminary data abnormalities of the GH-IGF axis in CFS”.

However, they then conclude “It is not apparent whether these changes are... acquired secondary to behavioural aspects of CFS such as reduced physical activity”.

Cognitive behaviour therapy for chronic fatigue syndrome: a randomised controlled trial

Deale A; Chalder T; Marks I; Wessely S. *Am J Psychiat* 1997;154:3:408-14

CBT for CFS was compared with relaxation in a randomised controlled trial. Treatment was completed by 53 patients.

According to the authors, at final follow-up (six months), 70% of the CBT group who completed the course achieved good outcomes, compared with 19% of those in the relaxation group who completed treatment.

(Note that there are no details regarding any history of infection, and there are no details about the presence of (or the effects on) any symptoms other than “fatigue” and depression; since ME symptoms fluctuate, a percentage of patients should have improved regardless of treatment, however, the controls did not do so and some patients were worse than if they had received no intervention. Also, a 70% improvement rate is not impressive when one considers that other studies have shown that evening primrose oil and magnesium injections both showed improvement rates of 80%).

The prognosis of chronic fatigue and chronic fatigue syndrome

Joyce J, Hotopf M, Wessely S. *QJM* 1997;90:3:223-233

This claims to be a “review” of “all” the research on the prognosis of patients with CF and CFS.

*(Note it did not include the research which indicates that attributions do not influence outcome).*

Of note is the fact that the authors concede “As the definition becomes more stringent, the prognosis appears to worsen”.

The authors rely on the study by their close colleague Michael Sharpe (*Followup of patients presenting with fatigue to an infectious diseases clinic. Sharpe M et al. BMJ* 1992.305-147-152), which found that belonging to a self-help organisation is associated with a poor outcome.

The overall conclusion was that in both CF and CFS, the untreated prognosis is essentially poor, and that “consistently reported” risk factors for poor prognosis include “illness beliefs” and “faulty attributions”.

In a brilliantly argued response (which the editor of the QJM printed unamended and in full), Dr T.E. Hedrick from the USA (see pages 65 -67 above) made the following points: (*Chronic fatigue syndrome: TE Hedrick. Quarterly Journal of Medicine* 1997;90:723-725)

“As a psychologist and research methodologist, I am very concerned that the recent article by Joyce, Hotopf and Wessely contained misleading conclusions about the prognostic importance of psychological risk factors for persons with CFS.

“Physicians may be led to erroneously conclude that CFS patients can be treated either by changing an individual’s belief that he / she has a physical illness or by solely focusing on psychiatric problems.

“The research cited does not support these conclusions.

“By grouping studies according to age and the stringency of the illness, they showed that recovery rates varied enormously.

“Unfortunately, when the authors summarized studies on the prognostic importance of psychological risk / illness beliefs, they were much less careful.

“The drew conclusions across seven studies that were based on different populations (from simple fatigue of 30 days to chronic severe fatigue of decades), different diagnostic instruments and definitions of improvement, and different timing of measures (prior to illness, at intake, years after onset of illness, at final follow-up).

“They did not assess the adequacy of the analyses performed, or discuss plausible alternative explanations for the findings.

“In some cases, they even left out findings from the cited studies that were inconsistent with their own conclusions.

“They fail to mention that one of their cited studies concluded that the same prognostic indicators were *not valid for CFS vs chronic fatigue cases*.

[see: Outcome and prognosis of patients with chronic fatigue vs chronic fatigue syndrome. Bombadier CH and Buchwald D. *Arch Intern Med* 1995;155:2105-10].

“Joyce et al state that ‘Psychiatric disorder is consistently associated with a poor outcome. Another consistent feature is the patient’s belief in a physical cause of their symptoms which predicted poor outcome in every study in which it was measured’ (p 225).

“These statement are then used to discuss opportunities for clinical intervention as if it is legitimate to assume that the two factors actually caused poor outcomes.

“In fact, the studies cited by Joyce et al do *not* yield a consistent pattern between psychiatric disorder and poor prognosis.

“A diagnosis of somatization disorder (SD) may be so arbitrary as to be rendered meaningless in controversial illness such as CFS (*ref 7 to response*). “Also, in one study, an overwhelming majority of individuals categorized by the researchers as ‘recovered’ had rated themselves as only slightly more than halfway recovered.

“Studies and review articles on psychiatric factors and CFS need to be subject to the same standards of scientific inquiry as studies investigating organic factors, lest the theoretical stance of the authors turns out to be the most powerful predictor of results.

“Not only did the Joyce et al article fail to summarize the psychiatric literature accurately, it omitted discussion of the many avenues now being explored on the organic underpinnings of CFS”.

(Note that Simon Wessely contacted Dr Hedrick, and that he unequivocally blamed his peer-reviewers for not having spotted the points raised by Dr Hednck. Dr Hedrick told Wessely that he was hurting the very people he was supposed to be helping; that he should make it very clear that patients generally are not recovering; that his data did not support his conclusions; that he was over-stating his beliefs and that he was harming people and should back off and take a little more time. Wessely did his utmost to persuade Dr Hedrick to review his (then) forthcoming book on CFS, but she declined - personal communication).

#### Reading about: Chronic Fatigue Syndrome

Simon Wessely. *B J Psychiat* 1997;171:92-93

Wessely here reviews books on CFS, both professional and “The view from W.H.Smith”.

Unsurprisingly, Wessely promotes his own book “History of Clinical Psychiatry” (Lutz and Wessely, 1996) which contains two essays on neurasthenia and chronic fatigue.

He dismisses the Jenkins / Mowbray 1991 textbook (*The Post-viral Fatigue Syndrome: ed. Rachel Jenkins & James Mowbray, 1991: John Wiley & Sons, Chichester*) saying that “it marks the golden age of the viral hypothesis, and much is now outdated”.

He skips over other “professional” books, stating that in 1991, “the emphasis on virology (that was the year of the persistent virus) is now dated, but good essays start to emerge on ... psychiatry and management”.

He praises the CIBA Foundation book (*Chronic Fatigue Syndrome (CIBA Foundation Symposium) ed Bock GR and Wheelan J. 1993 John Wiley & Sons, Chichester*), claiming that “this time, the essays were of a uniformly high standard”. (see *Denigration by Design? for a critique of the paper by Anthony David*).

Wessely states “The Americans have never been particularly sold on the idea of a persistent viral cause for chronic fatigue (*this is true, but the Americans differentiate between chronic fatigue and chronic fatigue syndrome*) but instead are enthusiastic for the concept of an immunological deficit”.

He then mentions the book published by The American Psychiatric Association entitled “Chronic Fatigue and Related Immune Deficiency Syndromes”(1993) edited by Goodnik F and Klimas N., saying that the title “did not bode well (as it is) a deliberate echo of AIDS. Unfortunately (or perhaps fortunately) CFS is not an immune deficiency syndrome”.

“In contrast, what soon must be called the ‘Oxford School’ have taken a broader view, and extend the frame to include chronic fatigue within the spectrum of medically



unexplained syndromes”. He then promotes “The Treatment of Functional Somatic Symptoms” , edited by his close associates Richard Mayou, Christopher Bass and Michael Sharpe (OUP 1995).

Wessely then states “The most recent serious title also reflects the weakening of exclusively immunological or virological theories. Edited by two psychiatrists, Mark Demitrack and Susan Abbey, it concentrates on psychological and neurobiological aspects of the condition, and also provides much-needed practical reviews on sensible management”.

“I would be failing my co-authors if I did not mention the first non-edited book, written by myself, Matthew Hotopf and Michael Sharpe (Wessely et al 1997). We attempt a comprehensive review of chronic fatigue and its syndromes. Our royalty payments will tell us how successful we were”.

“But there is more. To understand (what is really happening), we have to go down to W.H.Smith’s. It is in the paperback self-help books that we find a completely different discourse.

“First, the confessional. Most are written by people drawing on their own experiences. This gives them the energy to get their message across, and the required credibility.

“Next, the polemic. The bitterness of being misunderstood, of being denied a label, or even worse, given the wrong one.

“One can empathise with the hurt of being told there is nothing wrong when you are suffering, unable to work, unable even to get out of bed.

“Rather more often, the sufferer is told there is something wrong, but the diagnosis is not to their liking.

“Let’s face it, when sufferers protest about being asked to see one of us, they are right. Modern psychiatry has little to offer those who do not hear voices.

*(As he is discussing books on ME, one doubts that Wessely was here referring to those with psychotic illness (who do “hear voices”), it is more likely that he is again mocking those with true ME who steadfastly refuse to “hear” what he and his colleagues are preaching, ie. that ME does not exist).*

“After that, all turn to treatment... the exact permutation varies but the basic menu remains unchanging (a long list of things to avoid — chemicals, toxins, certain foods).

“What we are seeing is the rise of modern illnesses. Nearly all include a guide to the current Zeitgeist, the immune system.

“What is at stake is not an attack on science, but on doctors. We are being told to get our

act together and convert the sufferer's experience of illness into the legitimacy of disease.

"We as psychiatrists are the prime obstacle to this endeavour.

Wessely describes Hillary Johnson's "Osler's Webb" (Crown Publishers Inc, New York 1996 but for which he does not bother to provide a reference) as "nasty". He states that this book "is a warning of the coming clash between our desire for decision-making on the basis of evidence and ... the opposite demands of consumers and lobbyists". He states that the book is "a Greek tragedy of a decent scientist who could not face the possibility that she might be mistaken".

Wessely then states "If you want the facts, turn to the recent report produced by the three Royal Colleges (1996). **It is brief evidence based (and) practical**" (emphasis added).

Chronic Fatigue Syndrome: a 20<sup>th</sup> century illness?

Wessely S. *Scand J Work Environ Health* 1997;23, S3: 17-34

"The chronic fatigue syndrome has become the fin du siecle illness, now getting similar attention to that of neurasthenia at the turn of the century.

"Myalgic encephalomyelitis was an early term introduced in the UK in 1957 (*for someone who professes to value "evidence based medicine", Wessely would do well to get his facts right*) but it had little or no public or professional prominence".

"Myalgic encephalomyelitis continues to be the usual label in the UK". (*If a label has lasted for over 40 years, surely this contradicts Wessely's claim that the term ME had little or no public or professional prominence*).

The "relevant research linking CFS with somatization" is reviewed in this article.

"Understanding the nature of somatization can still shed some light on the meaning of chronic fatigue at the end of the 20<sup>th</sup> century".

When a niggle becomes a pain

Ann Robinson. *Guardian: Health*:9. 9.97

One person's headache is another's imagined brain tumour. So what can we do to prevent worriers draining the NHS and help them to get on with their lives?

"Undiagnosable common symptoms that worry people is the biggest single drain on NHS resources.

"According to Dr Simon Wessely, reader in liaison psychiatry at The Maudsley Hospital in London.... it is vital that doctors acknowledge that symptoms can be worrying even if

there is no underlying medical cause.

“Professor Richard Mayou, of Oxford University Department of Psychiatry... believes that for those of us who are not reassured by our doctor, referral for cognitive behaviour therapy is increasingly being seen as the answer.

“Dr Wessely says ‘It’s such a shame that at a time when human beings have never been healthier, we feel sicker than ever’”.

The prevalence and morbidity of chronic fatigue and chronic fatigue syndrome: a prospective primary care study

Wessely S, Chalder T et al *Am J Public Health* 1997;87:9:1449-1455

The authors claim that this study examined the prevalence and public health impact of chronic fatigue and chronic fatigue syndrome in primary care patients in England.

Measures included chronic fatigue, psychological morbidity, depression, anxiety, somatic symptoms, symptoms of chronic fatigue syndrome (ie. *symptoms which the psychiatrists’ believe represented chronic fatigue syndrome*), functional impairment and psychiatric disorder.

The authors state that “functional impairment was profound and was associated with psychological disorder”; they conclude that both CF and CFS are common in primary care patients and represent a considerable public health burden.

Chronic fatigue syndrome. A practical guide to assessment and management

Sharpe M; Chalder T, Wessely S et al *Gen Hosp Psychiatry* 1997; 19:3:185-199

This is a review of management advice for CFS which focuses exclusively on the authors’ beliefs about one type of fatigued patient.

In the authors’ view, the patients who cause the greatest clinical difficulty are those with both severe symptoms and strong beliefs, ie “with a *belief* that he / she has a fatiguing illness such as CFS, chronic fatigue and immune deficiency syndrome (CFIDS) or myalgic encephalomyelitis (ME)”. (Note that “CFIDS” stands not for immune “deficiency” syndrome but for chronic fatigue and immune dysfunction syndrome, which is different).

The authors state “The majority of patients seen in specialist clinics typically believe that their symptoms are the result of an organic disease process, and resent any suggestion that they are psychological in origin or psychiatric in nature. Many doctors believe the converse”.

The authors state the need to explore the patient’s own understanding of the illness, as

this “forms the basis for education of the patient... . Beliefs are probable illness-maintaining factors and targets for therapeutic intervention”.

The authors state “Many patients receive financial benefits and payments which may be contingent on their remaining unwell. Gradual recovery may therefore pose a threat of financial loss”.

“Most sufferers are seeking confirmation of their own intuition that they are suffering from a particular condition, rather than reassurance that they are not”.

“The (patient) literature is replete with statements such as ‘CFS is a real illness - it is not psychiatric’ and ‘CFS is a genuine physical disorder and not a psychiatric problem’ “.

In the section entitled “Presenting Complaints”, these authors state that *listening* to the patient may “reveal the presence of symptoms other than fatigue, eg major depressive disorder”, but they make no mention of any of the well-documented neuroimmunological or neuroendocrine symptoms, for example, vertigo, relentless frequency of micturition, ataxia, orthostatic hypotension, untoward hyperimmune response to things which the patients *likes*, eg alcohol, hair loss etc.

The authors are categorical that “a large number of somatic symptoms suggests a greater likelihood of psychiatric disorder and a poorer outcome”.

The authors state “Abnormal physical signs should not be accepted as compatible with a diagnosis of CFS” (*In ME/CFS there is frequently a positive Romberg sign, for which these authors do not look or else ignore.*).

As in other articles, these authors stress the importance of challenging patients’ rigid ideas, and they stress the need to discourage maladaptive coping strategies.

They state that patients’ “beliefs” should be treated with “respect”, even when they are inaccurate. (*Patients who have attended Wesse/y’s CFS clinic report that they are aware he is patronising them*).

The authors promote their view that the research evidence of immunological abnormalities is of no clinical significance.

The authors also disapprove of the persistent viral infection model.

They state that “the assessment of possible co-morbid psychiatric disorder... is mandatory”.

They stress that “treatment” requires that the patients be told the difference between factors which may have predisposed them to become sick (listed as “personality”), factors which may have triggered the illness (listed as “infection, life events”) and factors which

perpetuate the illness (listed as inconsistent activity, “misunderstanding of the illness, and fear of making it worse”).

The authors state “Interventions are then aimed at overcoming these factors”.

“The only treatment strategies of proven efficacy are cognitive behavioural ones... We have developed a more intensive therapy (ie CBT). . .this form of therapy is acceptable to patients, safe, and more effective than either standard medical care or relaxation therapy. It has also been shown to be cost effective”.

“An important task of treatment is to return responsibility to the patient for management and rehabilitation without inducing a sense of guilt, blame or culpability for his / her predicament”.

“It is usually possible to persuade these patients to try antidepressants... . CFS patients are also markedly sensitive to side effects so doses need to begin as low as possible”.

“Disability systems and insurance agencies are sceptical about CFS. . .much of the self-help literature on both sides of the Atlantic concerns the iniquities of the various benefits systems”.

The authors conclude by claiming that there must be an on-going review of any ‘catastrophic’ mis-interpretation of symptoms, and that CFS provides an example for the “positive management of medically unexplained illness in general”.

*(Note: this article contains a number of factual errors).*

Self-help treatment of chronic fatigue in the community: a randomised controlled trial  
Chalder T, Wallace P and Wessely S. *Brit J Health Psychol* 1997;2:189-197

This study compared 70 patients with “chronic fatigue” with 80 no-treatment controls.

The intervention group were assessed and then given a self-help booklet containing advice about balancing rest and activity.

The drop-out rate was 16.6%

The authors claim that 71% of patients in the intervention group said they had read the booklet and of these, 84% said they found it helpful.

According to the authors, general practitioners should be encouraged to use self-help literature in the management of patients with chronic fatigue.

Puzzling patients: Annabel Ferriman on how doctors are learning to deal with unexplained symptoms

*Daily Telegraph Magazine: 25.10.97/Health*

This is yet another bouquet for cognitive behaviour therapy by several close associates of Wessely.

“You see your doctor, list your symptoms... it’s best if the diagnosis is in Latin... for some people, however, the symptoms do not go away... these people go to specialist after specialist... the patient is made to feel a fraud for having a collection of symptoms that do not fit neatly into a modern medical diagnosis.

“Some doctors are beginning to get to grips with this problem, which they say is huge. ‘These patients account for a quarter of general practitioner consultations, as many as half of outpatient clinic attendances, and many hospital admissions’ says Dr Michael Sharpe, senior lecturer in psychological medicine at the Royal Edinburgh Hospital.

“The professionals ... want to see a greater awareness of unexplained symptoms because ... it can result in over-investigation and serious over-treatment.

“In a recent editorial in the British Medical Journal, Dr Sharpe and Professor Richard Mayou, of Oxford University’s Department of Psychiatry (of *which Sharpe was a member until his appointment in Edinburgh*) outline what can and should be done for patients with unexplained symptoms.

‘The first step is acknowledging the patient’s problem’ they say. ‘The second is identifying the factors that perpetuate the illness, including... misinterpretation of bodily sensations (and) unhelpful coping behaviour’.

“The third step is to make a management plan that targets the most important of these factors For example, a patient with chronic fatigue may benefit from information to combat unfounded fears.

“... mood-altering drugs. can be helpful. For others, therapy can be useful.

“Cognitive behaviour therapy, in particular, helps patients to think about their symptoms in a different way...

“Many patients with medically unexplained symptoms (MUS) end up seeing infectious disease consultants, because GPs think that a virus is responsible. One such physician, Dr Tim Peto (*a signatory to the Oxford 1991 CFS criteria and a member of the joint Royal Colleges’ working party which produced the much criticised CR54 report on CFS*) has made a particular study of the problem.

“(Dr Peto says) ‘We now have newer methods for helping people to cope, and the beauty

of the cognitive techniques is that they work, whatever the cause of the disability'.  
*(Compare this with the double blind, placebo controlled studies which found that CBTs no more effective than a placebo, eg. Immunologic and psychologic therapy for patients with chronic fatigue syndrome: a double-blind, placebo-controlled study. Lloyd AR et al. Am J Med 1993;94:197-203).*

“In the long term, tackling this problem properly will save a huge amount of money for the health service’... Dr Sharpe says.

“What can patients do in this situation? ‘It may mean seeing a psychologist or psychiatrist, but patients should not be put off by that. Such professionals may be the most useful people’ (said Dr Sharpe).

#### Chronic fatigue syndrome and occupational health

A.Mountstephen and M.Sharpe *Occup Med* 1997;47:4:217-227

*Not authored by Wessely, but by his close co-author Michael Sharpe, who was a signatory to the Oxford 1991 criteria for CFS*

The authors claim to review the nature and definition of CFS, the principle aetiologic hypotheses and the evidence concerning prognosis. The authors state that the conclusions of their review are then applied to the disability discrimination field. They argue that much can be done to improve the outcome in CFS, and that the most urgent need is for improved education and rehabilitation, especially in regard to employment.

The authors state “This paper considers first the nature of CFS and current views on its causation”, but then they immediately ask “What is *fatigue*?”

The authors make full use of the opportunity to be dismissive about the term myalgic encephalomyelitis, stating that it “has been used... to define a supposedly specific disease associated with viral infection... Despite this, the existence of ME as a specific syndrome remains unestablished (despite the fact that it is listed in ICD 10) and no specific disease process has so far been identified. Use of the term is best avoided”.

“Psychiatrists on the other hand have tended to assume that patents complaining of fatigue suffer from a psychological disorder, usually depression. Where depression was not obvious, it was often considered to be ‘masked’ or ‘atypical’ “.

“At present, a sensible approach is to qualify a diagnosis of CFS by any coexisting psychiatric syndromes”.

“The label of CFS. avoids the ... . connotations of ‘pseudo-disease’ diagnoses such as... ME”.

“Patients’ *beliefs and behaviour* are often a prominent and important part of the clinical presentation... (which) is most commonly... .diagnosed in young and middle-aged females”.

“... .the role of chronic infection in perpetuating CF~S is doubtful the evidence for an association between immunologic abnormalities and CFS ... remains unclear”.

“Importantly, current evidence suggests that exercise is not harmful for people with CFS”.

“... ‘somatization’ is commonly invoked to explain why patients present with medically unexplained complaints such as fatigue. It implies that the symptoms of CFS are caused by emotional distress being expressed somatically...”.

“Both self-help books and the media have tended to emphasise ‘medical’ explanations for the symptoms of CFS at the expense of more psychiatric or psychological conceptualisations”.

“... CFS may serve as a culturally defined function of social communication, which allows a socially acceptable. ..expression of distress”.

“For the purpose of planning treatment, illness perpetuating factors are more important than predisposing or precipitating factors”.

“...psychiatric assessment is recommended in *every case*” (authors’ emphasis). “In most cases of chronic fatigue, few laboratory investigations are necessary”. “Important aspects to be included are the individual’s beliefs about their illness”.

Under “General strategies” of management, the authors state it is basic “to provide education about the nature of the syndrome to both the patient and their family... and to encourage a return to normal functioning by overcoming avoidance. This. .15 a prerequisite to any more specialised form of treatment”.

“To date, (no pharmacological treatments) have been shown to be of proven efficacy and several are potentially harmful Despite this.., there is some evidence to support the use of (antidepressants) even in the absence of definite depressive disorder”.

“Exercise therapy... should be considered for patients who are physically inactive”.

“Patients may be reluctant to consider the role of psychological factors making the application of psychotherapy potentially difficult, but not impossible... .the only psychological treatment supported by the evidence is cognitive behavioural therapy (which) is well-fitted to the task of helping patients to achieve a more helpful view of the illness and to adopt more effective coping strategies”. “A further concern arises where there is the possibility of exposure to agents in the working environment which may themselves give rise to symptoms which may resemble those of CFS. ..for this reason work which may involve potential significant exposure to substances such as heavy metals



or solvents is probably inadvisable for those with persisting CFS symptoms”.

Under “Referrals of existing employees to occupational physicians”, the authors state “referral to multiple ‘specialists’ should be avoided as they can entrench illness behaviour and make return to work less likely”.

“Clearly the sufferer’s beliefs..., will have a powerful effect upon any such programme (of occupational rehabilitation)”.

“..a process of education to address inaccurate and unhelpful attitudes and beliefs may be a necessary preliminary step”.

“Our. .survey of occupational physicians indicated that they sought to promote rehabilitation of employees with CFS by advising..., an early return to work”.

Under “Eligibility for benefits”, these authors state “..the occupational physician should be aware of the Department of Social security’s current view on sufferers’ entitlement to Incapacity and Disability benefits where the diagnosis is one of CFS, the All Work test is likely to be applied..., those who fail the All Work test would normally be referred to the Employment Service with a view to a planned programme of rehabilitation”.

“The advice of the OLA Advisory Board is that the case for CFS being a physical disease is unproven”.

“The DSS’s Handbook further advises adjudication officers that in CFS there is unlikely to be a need for assistance with attending to bodily functions or with mobility unless inactivity has been so severe and protracted that muscle atrophy has occurred”.

“At present, less than 1 % of successful claims for Severe Disablement Allowance have a diagnosis of CFS or ME”.

Under “CFS and the Disability Discrimination Act”, the authors state “It will be unfortunate if the Act leads to an undue focus on long term disability at the expense of efforts directed at rehabilitation and recovery”.

Under “A Plan for Action”, these authors state “An awareness of the therapeutic approaches available and the evidence for their effectiveness is an essential prerequisite (for the occupational physician)”.

#### Randomised controlled trial of graded exercise in patients with the chronic fatigue syndrome

Fulcher KY and White PD. *BMJ* 1997;314:1647-52

*Note that consultant psychiatrist Peter White was a signatory to the Oxford 1991 consensus criteria on CFS and was a member of the joint Royal Colleges’ working*

*group which produced the Report CR54.*

This study purports to test the efficacy of graded aerobic exercise programme in patients with CFS.

Patients met the Oxford criteria for CFS.

The authors claim that graded exercise was more effective than relaxation and stretching exercises.

Five patients declined to participate and a further five were too ill to attend as outpatients.

The authors state that “almost three quarters of patients followed up felt better” and in a similar sample, only 2% reported spontaneous resolution of fatigue at 18 months: the authors thus claim “hence it is unlikely that spontaneous improvement would have occurred without significant exercise in our series”.

The authors state “The only other treatment of the chronic fatigue syndrome to show promise is cognitive behaviour therapy” (citing papers by Sharpe and Wessely in support of this claim).

*The following replies were published:*

Graded exercise in chronic fatigue syndrome

Charles Shepherd, Ann Macintyre. *BMJ* 1997;315:947

In a response to the article by Fulcher & White on graded exercise in CFS (*Randomised controlled trial of graded exercise in patients with the chronic fatigue syndrome. Fulcher KY, White PD. BMJ* 1997;314:1647-1652), Shepherd and Macintyre of the UKME Association make the following points:

- (i) they remain firmly opposed to graded exercise for patients with CFS which encourage them to increase their levels of physical activity without making allowances for fluctuating levels of disablement
- (ii) they have concerns about the way in which psychiatrist Dr White's results have been over-simplified in the media
- (iii) their concern is whether the results are as impressive as they seem; it seems strange that patients in the exercise group who rated themselves as "better" showed no significant improvement in either peak oxygen consumption or muscle strength than did other patients
- (iv) Shepherd & Macintyre note that no information is provided by the authors about what percentage of patients had stopped claiming long term sickness benefit — perhaps the most objective assessment of improvement.
- (v) Severely affected patients were excluded from the study.
- (vi) Fulcher & White seem to dismiss any possibility that fatigue could involve underlying physiological or biochemical defects.

Including patients who rated themselves as a little better would have altered results

Alan J Franklin (*ibid*)

Dr Franklin (a paediatrician specialising in ME/ CFS) makes the point that it should be made clear that Fulcher & White were treating a small subgroup of patients who were well enough to attend an outpatient department, whereas to most doctors dealing regularly with CFS patients, such patients are a small proportion (perhaps a tenth) of the total.

Dr Franklin states "Unfortunately, some doctors have trivialised this illness; ridiculed patients and their supporters; and subjected a few of them, including children, to oppressive, perhaps even abusive, forms of treatment".

Patients were selected group

Mike Sadler. (*ibid*)

Mike Sadler, a consultant in public health medicine, writes:

"Those readers who delve no further than the abstract and key points may welcome this 'take home message'. Several flaws in the paper... make accurate interpretation of the findings difficult.

“Firstly, less than two fifths of those screened for the trial actually entered it.

“Many of those who did not enter it were excluded on the basis of current psychiatric disorder, even though the Oxford criteria used by the authors do not specifically exclude patients with anxiety or depression.

“Given that this is already a subgroup selected by their referral to a psychiatric outpatient department, to select out those with a current psychiatric disorder makes them an unusual group indeed.

“In short, for those considering the options for managing this condition, especially those who commission services, the message should be that we need more information before we can tell if graded exercise will help most patients with the chronic fatigue syndrome”.

Increased serotonin function in men with chronic fatigue syndrome M.Sharpe et al *BMJ* 1997;315:164-165

The authors state that recent neuroendocrine studies suggest that patients with CFS may have increased brain serotonin activity, and serotonin pathways have a role in mediating central fatigue.

The authors aimed to measure the increase in plasma prolactin after administration of the selective serotonin releasing agent D-fenfluramine in ten men rigorously assessed as having CFS, and in matched healthy controls.

The results “show a significant rise in prolactin responses to D-fenfluramine in men with narrowly defined CFS”.

“This finding supports some, but not all, previous neuroendocrine studies, and suggests that the CFS is associated with increased brain serotonin function”.

“Though depressive symptoms are common in CFS, patients with major depression have unchanged or lowered prolactin responses to D-fenfluramine, making it unlikely that CFS and depression share a common pathophysiology”.

Nothing daunted, however, Sharpe et al are minded to conclude:

“Increased prolactin release mediated by serotonin in the CFS might... be a secondary consequence of behavioural changes such as prolonged inactivity..”.

Treating medically unexplained physical symptoms

EDITORIAL. EDITOR'S CHOICE. Richard Mayou, Professor, Oxford University  
Department of Psychiatry and Michael Sharpe, Senior Lecturer, Edinburgh  
University Department of Psychiatry. *BMJ* 1997;3 15: 561-562  
(Sub-heading: Effective interventions are available).

"Chest pain, back pain, headache, muscular pains, bowel symptoms, breathlessness, dizziness, and fatigue often remain unexplained after medical assessment. Such cases may be referred to as functional syndromes of chronic fatigue, chronic pain, fibromyalgia and irritable bowel syndrome, or as somatoform (somatisation) disorders".

"In many cases, the symptoms ... cause considerable healthcare costs" (*quoting joint Royal Colleges' Report CR54*).

"Evidence for the superiority of new ways of thinking about and managing such patients is growing".

"Several recently published randomised trials show that new treatments are both acceptable to patients and more effective than conventional medical care".

"These new treatments, often referred to as cognitive behavioural therapies... take an approach... (that is) in keeping with the evidence that the perpetuation of unexplained somatic symptoms is best understood in terms of... psychological factors...".

"This integrative approach (includes)... identifying ... the principal factors that perpetuate illness, including .... misinterpretation of associated bodily sensations... unhelpful coping behaviour..."

"Implementation of this new approach will require changes in both medical practice and the organisation of services".

"Innovative service developments such as joint medical-psychiatric clinics and dedicated liaison psychiatry... services will provide for patients who require more intensive treatment".

"The small but conspicuous group of patients who present with recurrent and multiple physical symptoms will be given pro-active and co-ordinated care aimed at limiting unnecessary medical intervention".

"If these simple and inexpensive changes in practice and service provision could improve patient care, why have they not been implemented? One reason is the widespread lack of awareness that effective evidence-based treatments are available... . Perhaps the main obstacle to change is the remarkable persistence

of mind-body dualism overcoming this intellectual obstacle.., will require changes in doctors' professional training and a greater dialogue with colleagues in psychiatry..."

"There are welcome signs of change, as evidenced by the recent royal college reports".

#### The relationship between infection and fatigue

EDITORIAL: Peter D.White *Journal of Psychosomatic Research*  
1997;43:4:345-350

The author states that there is no consistent evidence that patients with CFS have a persistent viral infection.

He promotes his colleague Wessely (referring to "this carefully conducted study), stating that Wessely found no excess fatigue in those clinically diagnosed as having an infection six months earlier.

What causes postinfectious fatigue? The "obvious aetiological candidates are the cytokines... however, no consistent relationship between the CFS and cytokines has been found".

"The reduced HPA axis activity may be secondary to the behavioural changes in CFS".

"The link with stressful life events and CFS may be related to comorbid psychiatric disorder".

"Premorbid psychological distress, styles of coping, holding a physical attribution and personality may perpetuate fatigue".

"There is now increasing evidence that chronic fatigue syndromes... are not maintained by the infectious agent but by a patient's consequent adaptation. This adaptation may be mediated by... physical deconditioning... Added to this, personality, illness beliefs.., as well as the doctor's own beliefs, may influence the long term outcome".

*Note that this article relies on 34.8% of references by the author's colleagues who hold similar views to his own.*

#### GPs "to blame for problem patients"

John Illman. *The Observer*, 28.12.97, page 13

"The New Year could be a happy one for thousands of people labelled as 'heartsink patients' because of the sinking feeling they give doctors.

"These patients return to the surgery time and time again with baffling symptoms that defy the best of modern medicine.

“Such people — often dismissed as malingerers or hypochondriacs — are to be examined with their hospital doctors in a pioneering study that could turn conventional wisdom on its head.

“They now have influential new allies who believe there are ‘heartsink doctors’ as well as patients.

“The £190,000 study testing this controversial view is being carried out by two academics from King’s College, London, Dr Matthew Hotopf and Professor Simon Wessely, and Professor Martin Knapp, of London’s Institute of Psychiatry.

“Prof Wessely said ‘We believe doctors create heartsink patients. Some doctors refer patients to colleagues because they don’t know what else to do.

“The professor’s fears are shared by the Royal College of Physicians which is worried about the decline of the general physician amid ever-increasing specialisation, which can make it harder for doctors to see beyond their academic areas.

(Professor Wessely said) “‘Specialists can become very narrowed and blinkered. It’s as if they can’t see what lies beyond the endoscope’.

“The researchers will try to find out if patients have been treated by the appropriate department, what is really wrong, and how much account is taken of social problems.

“There was initial opposition to the research for fear that it would further stigmatise the patients. But Prof Wessely said ‘It’ll have the opposite effect. These patients have complex, unrecognised needs’.

“Typical examples include giddiness, fatigue, indigestion and abdominal pain.

“Disenchantment with orthodox medicine can make heartsink patients easy prey for the less reputable fringe therapies”. (See *the original Denigration by Design? for an account of Wessely’s involvement with Healthwatch, whose stated aim is to expose fringe therapies” and medical practitioners who do not subscribe to the Healthwatch ideals of drug-based medicine in all eventualities).*

#### Letter to John Illman of The Observer

Doris Jones MSC. 30.12.97 (*German born and acutely aware of the atrocities committed on Jews and ethnic minorities during the Nazi era, Mrs Jones and her mother escaped by a hair’s breadth transportation to Siberian labour camps at the end of World War II. By a quirk of fate, Simon Wessely is the son of parents who settled in the UK as refugees from Nazi-occupied Czechoslovakia, and it is Wessely who now plays a very active role in determining the fate of countless severely ill and disabled people in his parents’ country of refuge. Some people have described Wessely’s treatment of these very sick*

*people as persecution).*

“What happened during the dark ages of Nazi Germany along these lines was later recognised as ‘brain-washing’ people, and the perpetrators were held accountable after the war.

“Are we about to go full circle for a second time round?

“How much more useful, practical and realistic it would have been to ensure that all GPs and specialists are given adequate training in identifying health problems and symptoms due to exposure to toxic chemicals and pesticides, due to vaccine complications and adverse reactions to drugs, or even to their synergistic effects”.

1998

Talking about the ME generation

Simon Wessely. *New Statesman* 30 January 1998, pp32-33

Wessely states “Ten years ago I started an NHS clinic for patients suffering from what was then called ME... my senior colleagues told me not to waste my time on a non-existent condition.

“Much has changed. We have just published a book reviewing the history and current knowledge of the illness” (*there follows a promotion for his book*).

“Its publication by that most academic of publishing houses, Oxford University Press, is a further sign of the change in the response of the medical and scientific establishment.

“This was further brought home by the unequivocal conclusion of the recent report from three Royal Colleges, representing the conservative voice of the profession, that the illness exists”. (*Wessely makes no mention that he was so involved with that report, but implies that it was an independent report which supports his own views*).

“Even the name has changed... we now follow the American lead and use the more neutral phrase chronic fatigue syndrome (CFS).

“The change of name has helped professional acceptance of the condition. ME can still induce a rage reaction in consultants and editors... for myself, I retain the term ME in the clinic, but use CFS for research... doctors now call it CFS”.



*(Another example of Wessely's patronisation of patients, many of whom are doctors themselves,, and most of whom are better acquainted with the international research literature than Wessely seems to believe).*

“Ten years ago the illness was seen as a... mysterious virus that remained hidden in the body, with a preference for infecting active, middle class professionals.

“It was the time of HIV, so few could fail to grasp the significance of a mysterious virus that affected the immune system, which was how ME was then viewed.

“..exercise programmes have been shown to be safe.

“Ten years ago, our clinic was dominated by doctors, teachers and nurses... .our fundamental understanding about what lies behind CFS has. .changed. In our book we devote considerable space to studies of brain function in CFS. Overall, anyone reading our book is bound to be struck by the wealth of information that is now available about CFS”.

*(It is informative to reflect on the percentage for which Wessely et al are themselves directly responsible).*

“We end our book with a discussion of the social background to CFS, and why it seems to have this unique ability to generate passion and argument. The answer lies in how doctors, and society at large, decide who is really sick and who isn't.

“...CFS patients usually look well cancer patients have a firm unequivocal diagnosis. Their status as legitimately ill is unchallenged (but CFS patients) remain in an ambiguous position in their dealings with doctors, employers and the welfare state”.

*(For reasons, one need look no further than Wessely himself since 1987, he and his co-authors have done more than anyone else to hinder the understanding of “pure” ME by his dilution of the ME criteria and by the senseless refusal to consider the merits of any ME research which reaches conclusions different from his own beliefs. He may or may not see it as his personal mission to address and curtail the problem of escalating NHS and social security costs, but his persistent “persecution” of those with ME (as distinct from those with ubiquitous ‘chronic fatigue’, for whom antidepressants, CBT and graded exercise may be of great benefit) is unacceptable, and his revisionist tactics (ie. his efforts to re-write medical history by attempting to discredit those clinicians who have spent their entire professional life dedicated to the study of “pure” ME) defy credibility. It should not be forgotten, however, that neither the welfare state nor insurance companies / employers could be held liable to pay life-long benefit for an illness which does not officially exist (whereas according to Wessely, “CFS” is amenable to psychotherapy and thus is treatable; in reality, “true” ME has a very poor longterm prognosis, with consequent healthcare costs). It should also be noted that the psychiatrists’ endeavours to promote their own discipline to a more accepted and*

*influential status within mainstream medicine (which currently it does not have) may also be on Wessely's agenda.*

### Chronic fatigue irritation

Julia Napier. *New Statesman*, 27 February 1998

In response to Wessely's article, Julia Napier wrote

"I began Simon Wessely's... article on chronic fatigue syndrome with the vested interest of a victim of this tedious affliction, and ended it with the feeling of irritation bordering on rage.

"Wessely takes pains to quote a 'book that advertised itself as the' Official Handbook of the CFS network'... Why did he not quote from the genuinely official 'Report from the National Task Force on CFS, ME and PVFS'?"

"I was not surprised to find Wessely's name on the panel of the rather unhelpful report of the joint working group of the Royal Colleges of Physicians, Psychiatrists and General Practitioners, 1996, with its emphasis on graded exercise and its bias towards psychosomatic disorder.

"I was also disappointed that he made no mention of the recent publication in the *Journal of Interferon and Cytokine Research*. July 1997, of a defective enzyme in all CFS patients tested. The low molecular weight of 2-5A Dependent RNase L is the best news so far. It means that CFS appears to have a cause, and everyone can start working on a test and looking for a cure".

### BOOK REVIEW: Chronic fatigue and its syndromes

Wessely S, Hotopf M and Sharpe M. Oxford *University Press* 1998. H/B. 416pp. £65.00

(Review by Dr E.Goudsmit).

This is a comprehensive reference text on all aspects of fatigue.

It is not an entirely objective account; the authors' interest in inactivity and deconditioning as a major source of CFS is very clear, and the reviewer was reminded as early as page 55 that the authors are three male psychiatrists who basically do not believe what their CFS patients say.

There is certainly a lack of respect for the experiences of patients, and the reviewer saw no evidence in the book that the authors had realised that "fatigue" is totally inappropriate to describe the exhaustion and weakness experienced by people with CFS.

The reviewer also noted an underlying sense of hostility towards patients and patient groups.

The reviewer stated that the authors continue to perpetuate the myth that sufferers tend to be stupid, and that every patient responds to fatigue in the same maladaptive way.

Dr Goudsmit states “You won’t find many references to sensible individuals, coping with courage and humour, in this tome”.

“As far as the aetiology is concerned, these psychiatrists seem to have a tendency to blame the patient for much of their own disability. Hence the obsession with the idea that attributions and excessive inactivity are major determinants of ongoing fatigue.

“To those unfamiliar with the literature on CFS, the text must appear authoritative and reliable.., but is as unreliable as a party political broadcast. attitude, inactivity, illness beliefs, avoidance behaviour, misinformation and occupational issues get three crosses (signifying an important role in a grid of perpetuating factors).

“The text mixes the findings on chronic fatigue and chronic fatigue syndrome, which not only simplifies an extremely complex subject, but also introduces errors and ends up trivialising CFS.

Dr Goudsmit writes: “I found the book desperately depressing because it gives such a distorted picture of CFS, the lives of the majority who suffer from it, and the work of the doctors and researchers from other schools of thought.

“There isn’t a single study supporting the view that the majority of people with CFS take ‘excessive rest’ and the authors do not provide any references from research on ME or CFS to back up their claim... .So much for evidence-based medicine!

“The authors argue that all studies to date which have assessed the influence of physical attributions on outcome have shown them to be ‘indicative of a poor prognosis’ (page 370), yet there are studies done by the authors’ own colleagues (Lawrie et al) which show no such relationship.

“Should we not expect a more balanced and fair representation of the research?

“As in other writings from this school of thought, there are a number of factual inaccuracies. ..Professor Wessely has been notified of them and he knows them to be true.., it serves as an excellent illustration of the lack of attention to detail which has been criticised before”.

Dr Goudsmit ends her review thus:

“...nor can I recommend (this book) to my colleagues, unless they don’t mind reading unbalanced textbooks which mislead readers, foster an antagonistic attitude towards

patients and contribute to the stigmatisation of the latter in the process.

“Most importantly, this is not a book on the illness ME. ..as the authors say on page 137 ‘CFS is more . . .than just fatigue’. Unfortunately, the rest of the text failed to communicate just how much more”.

Medically unexplained neurological symptoms

EDITORIAL: Michael D.O’Brien. Physician for nervous diseases, Guy’s Hospital.  
*BMJ* 1998; 316:564-565

*This editorial relates to an article in the same issue of the BMJ — see below.*

“A psychological component exists in all illness... At the benign end of this range are patients who describe their symptoms in more florid terms than seem to be justified. At the malignant end is malingering and the Munchausen syndrome.

“Between these extremes are a range of patients who present with non-organic signs or symptoms. ..usually called hysterical conversion disorder.

“If patients present with apparent non-organic signs or symptoms and are later found to have an underlying disease which might account for some if not most of their original problems, this is perceived as a hysterical elaboration of the underlying deficit.

“Crimlisk et al have looked at... patients who presented with purely motor symptoms for which no cause was found. ..Only three out of 64 subjects followed for a mean of six years were subsequently diagnosed as having a neurological disorder... ..this serves . .to emphasis the authors’ conclusion that patients with medically unexplained motor symptoms and who have been properly evaluated clinically... are unlikely on follow up to show evidence of an underlying disease that might have accounted for the presenting features.

“Crimlisk et al conclude that repeated investigations for the same problem are unprofitable.

“At least two other series on conversion disorders have been reported from the National Hospital for Neurology and Neurosurgery, the most influential being that of Slater in 1962. ..he identified three groups of patient. About a third were thought to have a hysterical conversion syndrome as well as an organic diagnosis, and on follow up, the organic disease prevailed. About a third were initially thought to have pure hysteria, of whom eight later developed an organic disease, and about a third had a psychiatric diagnosis. Twelve deaths occurred, including four suicides.

“Slater concluded that the diagnosis of hysteria was a disguise for ignorance and a fertile source of clinical error.

“Nevertheless, assuming proper clinical evaluation and negative results on investigation,

the chances of a patient developing a neurological disease that might have accounted for the original complaint is very small.

“The diagnosis can be reviewed if any new features develop”.

*Note that there are many references to the fact that cases of ME can develop into multiple sclerosis (for example, (i) CFIDS Chronicle Spring 1989:3-4, which reported that virologist Dr Jay Levy, well known AIDS researcher at the University of California presented to the San Francisco Conference on CFIDS on April 15” 1989 evidence that “CFIDS may be linked to the ‘eventual development’ of multiple sclerosis. Levy confirmed that “some of our patients have eventually developed multiple sclerosis and we are reminded of the fact that several acute syndromes of viral illness may give rashes, chronic myalgias, and then, many years later, the same agent may be responsible for a long-time, debilitating illness”; (ii) Dr E.G. Dowsett, former President of the UK ME Association and a microbiologist who has studied “true” ME for over 30 years, believes that 13% of ME patients have clinically indistinguishable MS also; (iii) one of the former names for ME was “atypical multiple sclerosis”~ as well as “atypical poliomyelitis” (The Disease of a Thousand Names. David S.Bell MD,FAAP. Pollard Publications, Lyndonville, New York 1991).*

Sipter revisited: 6 year follow up study of patients with medically unexplained motor symptoms

Helen L Crimlisk, Helen Cope, Anthony David, Maria Ron et al  
BMJ 1998;315:582-586

*Note that psychiatrist Anthony David is a very close associate and frequent co-author of Wessely, and that he is well known for his dismissive stance on ME; he was a signatory to the Oxford 1991 consensus and was a member of the joint Royal College’s Report CR54 on CFS. He was also a member of the 1998 joint working party of the Royal College of Physicians and Royal College of Psychiatrists on the clinical aspects of long term low dose exposure to organophosphates (see later). He is a contributor to the Linbury Trust “research portfolio” on CFS.*

The objective of this study was to investigate psychiatric and neurological morbidity, diagnostic stability, and indicators of prognosis in patients previously identified as having medically unexplained motor symptoms. 73 patients were admitted consecutively to the study from 1989-1991. Good 6 year follow- up data were available for 64 of those subjects.

Unsurprisingly, these particular authors claim that there was a high incidence of affective, anxiety, somatisation and personality disorders.

The authors feel secure in their belief that there is “high diagnostic accuracy”.

The authors state that “Pending litigation as is often suggested anecdotally emerged as an indicator of poor prognosis”.

They urge that “Treating depression and anxiety aggressively... may reduce disability in some patients, while for those with several physical symptoms and personality disorder... cost-effective management strategies aimed at damage limitation may be more appropriate”.

The state “Referral bias may explain the high social class ...and chronicity of our cohort”.

The conclude “Unlike Slater’s study of 1965, a low incidence of physical... diagnoses which explained these patients’ symptoms or disability was found. However, a high level of psychiatric comorbidity existed... The stability of the diagnosis in patients with medically unexplained motor symptoms who have been investigated thoroughly is high”.

Putting the rest cure to rest — again

EDITORIAL: EDITOR’S CHOICE. Michael Sharpe Simon Wessely.  
*BMJ 1998;316:796*

Subtitled “Rest has no place in treating chronic fatigue”

*Once again, Wessely uses different terminologies as interchangeable, with predictable results.*

““Go home and rest” is still the advice given to many patients who complain of chronic fatigue.

“The refrain is echoed in self help books and magazines and adopted by many patients.

“Chronic fatigue syndromes are not new... by the turn of the century the same private health clinics that once provided (rest cures) were changing to more active treatments and to the newer psychotherapies.

“...rest, as a treatment for chronic fatigue, resurfaced recently in conjunction with the rise in popularity of the diagnosis of myalgic encephalomyelitis, now called chronic fatigue syndrome.

“Studies of the effects of prolonged inactivity in healthy volunteers confirmed that the adverse physiological effects are both profound and prolonged. Furthermore, they include many of the symptoms considered typical of chronic fatigue syndrome.

“The evidence indicates that patients with chronic fatigue syndrome can exercise under controlled conditions without risk of damage or relapse”.

*(There is here a promotion of the Fulcher & White study reviewed above on pages 94-96).*

“Rest is not denied but included in a way that is planned and ... not as a response to symptoms.

“The Victorians gradually turned their backs on the rest cure. We should too”.

*In this editorial, the impression is again given that CFS is a single entity with a single common pathway and that a single treatment is appropriate — and safe— for everyone with unexplained chronic fatigue.*

*It is also implied that the main problem underlying CFS is excessive inactivity.*

*There is only one study which supports the view that some people with CFS rest excessively: this is the Sharpe et al trial of cognitive behavioural therapy where modestly disabled patients spent three days a week in bed. There is no other published evidence which supports the notion of total rest and complete avoidance of activity throughout the illness.*

#### Blame Mummy for a bad tummy

*Daily Mail, 17 April 1998*

This item states “Children who complain of persistent stomach aches are more likely to have over-anxious mothers than a physical illness.

“Professor Simon Wessely of London’s Institute of Psychiatry has carried out a new study into the matter.

“Tummy aches are a normal part of childhood but in a small number of cases it is the failure of anxious mothers to respond appropriately that reinforces the child’s concern’ he said.

“The BMJ says his study of 73 children with persistent stomach aches found 71 were perfectly healthy”.

Forwarded on behalf of Professor Simon Wessely I King’s College Medical School and Director of the CFS Research Unit (Co Cure Med. “I run an ME Clinic” Simon Wessely, Guardian, 21.04.98)

*This was slightly amended and duly published in The Guardian on 21 April 1998, Section 2, pp 14-15 under the title:*

*No-name illness. ME or yuppie flu, has never been fully accepted as a real condition, says Simon Wessely.*

“I love studying people’s reactions when I tell them I run a clinic for patients suffering from ME - their responses tell you much about why this illness is both so difficult and so fascinating.

“If I am talking to general practitioners, the usual reaction is ..the medical equivalent of ‘you poor thing’.

“This is followed by an invitation to review one or more of the doctor’s more intractable patients.

“If I say the same thing at some academic gathering of professors and other high ups in the medical firmament, the reaction is different—’Good God, old fellow, can’t you think of something better to do — these people aren’t really ill you know’.

“But what happens when I make the same announcement at a London dinner party? First, someone around the table has a relative or friend with the condition and takes the opportunity of unburdening themselves of the difficulties their friend has had with employers, the medical profession and the various parts of the welfare state...

“Next, someone points out ‘but you are a psychiatrist aren’t you — why do you see ME patients?’

“Doctors rarely say that, instead being divided between those who agree psychiatrists should be seeing such patients, and those who think no-one should be.

“Should doctors see ME patients? Should we call it ME at all?

“This week we publish a book (*see pp 103-104 above: it was published on 2~ March 1998*) in which we attempt to answer all these questions except for the last

“We don’t know what causes it. We are rather better at saying what doesn’t cause it. We know now that, contrary to the views expressed some years ago, that it is not due to a virus that doesn’t go away... long term ill health is not due to viral persistence.

“I notice as I write this piece, I seem to be switching between ME and CFS. ME is the term that dominates the clinics and media... doctors talk and write about CFS. Many doctors still can’t bring themselves to utter the word ME.

“Both ME and CFS are new terms - you will struggle to find them in the medical journals much before 1980. (*This is substantially untrue: the term ME was in common usage in the medical literature from 1956*).

“On the way home from the dinner party my wife often says ‘Why did you tell them what



you do?”. I am not sure myself, but there is one thing I always wish I had got across... now doctors and patient groups alike emphasise the drawbacks of rest... the research community, of which I am proud to be a member, has now contributed a series of studies showing that more active rehabilitation programmes are not only safe, but also effective in reducing symptoms and disability”.

Is ME real or in the mind

Dr Thomas Stuttaford. *The Times*, 7 May 1998, p20

*This is yet another promotion for Wessely's book, full details of which are listed at the end of the article.*

“George Beard, the 19<sup>th</sup> century doctor, started his account of neurasthenia, published in 1869, with the words ‘fatigue is the Central Africa of medicine, an unexplored territory which few men enter’.

“Neurasthenia was the chronic fatigue syndrome - or ME — of its day.

“Dr Simon Wessely, Professor Matthew Hotopf... and Dr Michael Sharpe start their own book *Chronic Fatigue and its Syndromes* with Beard's observation.

“These three psychiatrists have made a special study of chronic fatigue syndrome (CFS), sometimes referred to as ME. They are in a favoured position to write about the condition, as their expertise is accepted by most people.

“The book ... examines the evidence which could support an organic cause and gives detailed advice on the best way for doctors to treat patients.

“The authors even give examples of phrases those in the medical profession use that are guaranteed to alienate the sufferer.

“Neurasthenia was originally a disease which, almost by definition, could only affect hard-working members of the officer class. Later, it sank in social prestige and became... an excuse of the “worthless poor” who had neither the ability nor desire to work.

“Everything changed in 1956, when an outbreak of ME attacked staff at the Royal Free Hospital in London. This re-opened the long-dead neurasthenia debate.

“*Times* readers will remember Professor Wessely's regular features in the paper. Professor Wessely and his colleagues have written their book in similar style, full of interest, witticisms and apposite phrases.

“Those with an interest in CFS in particular... will enjoy learning from their account of the inter-relationship between fatigue, anxiety, stress and depression.

“Everybody would benefit from understanding that psychological conditions may cause physical symptoms every bit as disabling and real as those which result from viruses, bacteria or environmental toxins”.

Clinics in Controversy: Chronic Fatigue Syndrome.

Anthony J. Cleare Simon C. Wessely *Update 20 May 1998:1016-1026*

“Three royal colleges endorsed unequivocally the existence of chronic fatigue syndrome (CFS) in 1996— in a multi-disciplinary, evidence-based report acknowledging the suffering that CFS can cause...

“It would be nice to think, therefore, that the controversy about CFS had begun to settle. Sadly, it is far from over.

“CFS, sometimes known as ME, continues to be the subject of dispute between doctors and patients, and even between editorial writers of the most distinguished journals. The royal college’s report was greeted with high praise by the *BMJ* — and in the same week was condemned by *The Lancet*.

“Persistent fatigue is seen commonly in general practice.

“Research concentrates on the syndrome of CFS.... There is as yet no evidence that this is a discrete disorder. It may be better understood as the extreme end of a spectrum that starts with ‘feeling tired all the time’.

“Many people suggest that the condition should be called ME, but doctors and the editors of the journals have taken a firm stand against this label.

“Some claim that there are differences between CFS and ME, the main one being that the former is a psychological condition, the latter physical.

“There is no evidence to support this division.

“...a controlled prospective study (*Wessely’s own 1995 study*) (found) that those who ended up with CFS were more likely to have suffered fatigue or psychological distress before they presented with the viral infection.

“Previous psychiatric disorder... increased the likelihood of chronic fatigue after severe viral infection.

“The GPs response may also be important. A sick note and unclear diagnosis are both associated with development of CFS.

“Rates of depression and anxiety are much higher in these patients than in those with physical disorders causing comparable disability, suggesting that this is not a secondary

phenomenon.

“... psychological factors may be important in perpetuating CFS, regardless of whether formal diagnostic criteria for psychological disorders are met.

“CFS patients seen in specialist clinics commonly show characteristic type A personality traits, such as perfectionism and over-achievement.

“Such observations may reflect the desire to be seen as psychologically robust; or these traits may be associated with obtaining referral to a specialist clinic.

“Preliminary evidence from our group and from the USA suggests that a very low dose of cortisol (hydrocortisone)... alleviates fatigue symptoms in a minority of non-depressed CFS patients. (Note that Professor Anthony Komaroff of the USA recorded that “The finding of slightly low circulating levels of cortisol in patients with CFS led investigators at the NIH to conduct a randomized trial of low dose replacement the raov. . . It did not find a clear benefit. Clinical Crossroads. Anthony L.Komaroff. JAMA 1997:278:14:1179-1185. See pp 19-21 above. Also, Demitrack et al from the USA concluded that the degree of adrenal suppression from low dose hydrocortisone in CFS precludes its use — see Low dose hydrocortisone for treatment of CFS: a randomised controlled trial. McKenzie R, Dale J and Demitrack M. JAMA 1998:280:(12):1061-6. See pp 35-36 above).

“Several studies have used neuro-imaging techniques to study cerebral blood flow in CFS. A number of abnormalities have been found, including lowered perfusion of the brain stem and frontal lobes, but some studies have suggested that alternative illnesses were diagnosable in those with abnormalities: the relationship with depression remains unclear. (Wessely quotes a 1996 JNNP paper by Helen Cope and Anthony David, which was dismissive about neuro-Imaging in CFS — see Denigration by Design? lAppendix VI)

“Until these findings have been replicated, the results must be treated with some caution. (The results have been replicated and were presented at the 1996 AACFS Conference by Dr M. Tavio from Aviano in Italy, who found decreased brain metabolism in CFS patients; he found the greatest impairment to be in the right medial frontal cortex and the brain stem. (PET: A Useful Tool for Differential Diagnosis. M. Tavio. CFIDS Chronicle 1997:10:1:75). The results have also been replicated (1998) by D.di Giuda and D.Racciatti et al, who found brainstem hypoperfusion in 83.9% of CFS patients studied, and concluded that their study confirmed previous reports of brain perfusion impairment in CFS, providing objective evidence of central nervous system dysfunction — see pp30-31 above).

“Several cognitive and behavioural factors may be important in maintaining fatigue and disability when fatigue becomes chronic: Inactivity..., several studies have shown that coping with symptoms by avoidance behaviour is associated with worse disability... . Inconsistent activity... .this stop-start pattern means sufferers are unable to build up a

sustained level of recovery... . Symptom focusing... many patients have come to rely on day -to -day monitoring of their own symptoms — ‘listening to their body’ — as the best method of determining activity levels. Symptoms are often interpreted as ‘warning signals’... Increased concern leads to heightened awareness, selective attention and ‘body watching’, which can then Intensify both the experience and the perceived frequency of symptoms, thereby confirming illness beliefs and reinforcing disability. Emotional consequences: depression and anxiety are strongly associated with fatigue, muscle pain, impaired memory and concentration, and reduced activity.

“... a series of prognostic studies makes gloomy reading. However, the findings may be misleading. The studies involved specialist centres, where patients were from high social classes, had long illness durations and often fixed illness beliefs. Patients with CFS in primary care do not share these characteristics, and may have a better outcome.

Again, these authors then urge the use of graded exercise, CBT and antidepressants as “effective” treatments for CFS.

*Note that Anthony Cleare is supported by The Linbury Trust.*

Reviewing the reviews: the example of chronic fatigue syndrome

Joyce J; Rabe-Hesketh 8; Wessely S. *JAMA* 1998;28: (3):264-266

The stated objective was to test the hypothesis that the selection of the literature in review articles is influenced by the authors’ discipline and country of residence.

Sources were articles published in English published between 1980 and March 1996.

These authors found that authors from laboratory-based disciplines preferentially cited laboratory references, while psychiatry-based disciplines preferentially cited psychiatric references.

Wessely et al concluded that “Citation of the literature is influenced by review authors’ discipline and nationality”.

Screening instruments for psychiatric morbidity in chronic fatigue syndrome Richard K Morriss Alison J Wearden *JRSM* 1998;91:365-368

Not by Wessely, but by one of his non-medical colleagues Alison Wearden, this is an interesting paper in that it purports to understand that whilst physicians need a screening instrument to detect psychiatric disorders in CFS, one of those instruments (the Medical Outcome Survey / MOS) mental health scale yielded too many false positives to be recommended as a psychiatric screening test in CFS.

Illness beliefs and treatment outcome in chronic fatigue syndrome Deale A; Chalder T;

Wessely S. *J Psychosom Res* 1998;45: (1 Spec No.):77-83

The authors claim that longitudinal studies have shown that physical illness attributions are associated with poor prognosis in CFS.

Speculation exists over whether such attributions influence treatment outcome.

This study purports to report the effect of illness beliefs on outcome in a randomised controlled trial of CBT versus relaxation.

Physical illness attributions were widespread, and did not change with treatment, and were not associated with poor outcome in either the CBT group or the control group.

The authors conclude that their findings suggest that physical illness attributions are less important in determining outcome than has been previously thought.

Nevertheless, the authors state that good outcome is associated with change in avoidance behaviour and related beliefs (rather than causal attributions).

Results are contradictory for patients meeting different diagnostic criteria Riccardo Baschetti. *BMJ* 1998;317:600

(Response to article "Putting the rest cure to rest — again" by Michael Sharpe & Simon Wessely: see pp 107-108 above)

Riccardo Baschetti from Padua, Italy, (well known for his views on the similarities between CFS and Addison's disease), made the following points:

"To support their view that exercise is useful in treating chronic fatigue, Sharpe and Wessely cite a study that showed the beneficial effects of graded exercise in patients fulfilling the Oxford criteria for the chronic fatigue syndrome.

"To show that psychotherapy is also important in treating chronic fatigue, Sharpe and Wessely cite two studies that found cognitive behaviour therapy to be effective in patients fulfilling the Oxford criteria.

"However, such therapy has been found to be ineffective for patients meeting other diagnostic criteria. (Baschetti cites the Lloyd et al paper in *Am J Med* 1993;94:197-203: *Immunologic and psychologic therapy for patients with CFS: a double blind, placebo-controlled trial*).

"Additionally, evidence has recently been reported that patients fulfilling the Oxford criteria have increased concentrations of cortisol, whereas hypocortisolaemia is a consistent finding in patients meeting the original criteria.

“In view of these striking discrepancies, it seems likely that the researchers who adopt the Oxford criteria and those who adopt the original criteria are actually investigating two quite different clinical entities.

“The CFS diagnosed on the basis of the original criteria is extremely similar to adrenal insufficiency: these illnesses share 20 features.

“However, the CFS diagnosed on the basis of the Oxford criteria is more similar to depression: in both conditions, there is decreased cortisol concentration.

“Of course, if two different medical conditions have the same name ... we can only expect the confusion, controversy and discrepant findings that have so far characterised research on CFS”.

Randomised, double-blind, placebo-controlled treatment trial of fluoxetine and graded exercise for chronic fatigue syndrome

Wearden AJ; Pearson DJ; Morriss JA et al *Brit J Psychiat* 1998;172:485-490

Patients with CFS (Oxford criteria), of whom 46% had current psychiatric disorders were randomly assigned to four groups:

- (i) n=33 —graded exercise plus fluoxetine 20mg
- (ii) n=34 —graded exercise plus drug placebo
- (iii) n=35 —exercise when able, rest when needed plus fluoxetine
- (iv) n=34 —exercise placebo (exercise when able, rest when needed) plus drug placebo.

The number of drop outs was high (n=40 / 29.5%).

Subjects were assessed at baseline and after 12 and 26 weeks.

The authors claim that graded exercise significantly improved functional work capacity but not fatigue, and that fluoxetine was associated with lower depression scores at week 12 but had no effect on fatigue.

Exercise did not improve depression.

The authors suggest that graded activity may provide patients with the reassurance that exercise at a controlled rate need not exacerbate fatigue. Commentary by Deal A; Chalder T and Wessely S

These commentators note the “modest” effects, which they attribute to behaviour change as a result of which there was a cognitive shift away from fear and avoidance.

Doctors' Diagnoses and Patients' Perceptions: Lessons from Chronic Fatigue Syndrome

EDITORIAL: Michael Sharpe. *Gen Hosp Psychiat* 1998;20:335-338

This seems to be yet another essay on psychiatric circularity, with which this same group of psychiatrists continually flood the medical literature.

It begins with the “neurasthenia as the Central Africa of medicine” theme, and Sharpe states “Much of what Beard wrote (*in 1880*) could well be applied to the more modern medical conditions chronic fatigue syndrome (CFS) and the overlapping fibromyalgia syndrome”.

Again, there is obfuscation of terminologies, with almost no consideration or inclusion for discussion of the cardinal features of true ME.

Sharpe pronounces that “there is controversy and conflict — controversy among physicians over the use of medical labels for medically unexplained illness and conflict between physicians and their patients over psychiatric diagnoses”.

“If we assume that no pathophysiological mechanism has so far been reliably identified and that all the medical diagnoses for chronic fatigue are essentially descriptive labels, what is our choice? Available “medical” diagnoses... include “biological” connotations such as chronic fatigue and immune dysfunction syndrome (CFIDS) For many patients, the more clearly “biomedical” the diagnosis is, the more likely they are to welcome it.

*(Sharpe here relies on a reference (8) which is based on a study of CFS in women, about which he writes “One such report appears in the previous issue of this journal”, but he is unable to supply the citation, which suggests he had seen a pre-publication copy).*

“...studies suggest that these patients want a medical diagnosis for a number of reasons. First, it allows them to negotiate reduced demands and increased care from family, friends and employer”.

*(Sharpe makes no mention of the many patients whose marriage has failed due to ME, nor to those who have lost their professional career (and consequent financial security) and are now unemployed because of ME, nor does he mention that one of the biggest difficulties faced by those with ME is gross social isolation and loneliness: he does not include for consideration the fact that many patients simply do not have any opportunity to “negotiate reduced demands or increased care” from anyone).*

“Without such a diagnosis, the patient is open to the social stigma of psychiatric illness.

“In short, (a biomedical label) admits them to a bona fide “sick role”.

“Second, it may open the way for practical help in terms of financial and other benefits

from government, employers and insurers.

“Why are many physicians reluctant to provide a medical diagnosis?

“Two main disadvantages are suggested. The first is that to make such a diagnosis, especially if it is suggested by the patient, threatens the physician because it reduces his or her power in the transaction... and may risk the censure of peers.

“The second ... is the physician’s fear that he / she may influence the patient’s perception of his symptoms. ...by increasing anxiety over the ramifications of symptoms and encouraging excessive avoidance and “illness behaviour”.

“Furthermore, there is evidence that patients with CFS who believe their condition is “purely medical” have a worse outcome.

*(Sharpe here relies on the much criticised paper “The prognosis of chronic fatigue and chronic fatigue syndrome: a systematic review” by Joyce J, Hotopf M and Wessely S / QJM 1997: 90(3):223-233; see pp81-83 above, which unequivocally reveals the psychiatrists’ circularity of promoting and relying on each others’ papers in supposedly independent support of their own work).*

“The alternative (to giving the patients a “biomedical” label) is to eschew the medical diagnosis of CFS and instead, seek a psychiatric diagnosis.

“The application of (this) may give the physician the satisfaction of having maintained “medical integrity” and applied a label of which most of his peers would approve.

“The problem is that many patients not only fail to accept this diagnosis but respond to it with frank hostility because a psychiatric diagnosis... may offer lower financial benefits.

“Many of us may feel that it is not helpful to give a patients a medical diagnosis of CFIDS or ME.

“There may be.. benefit in helping patients to change unhelpful beliefs... Cognitive behaviour therapy for patients with CFS have shown a substantial improvement..., that is associated with a change in beliefs about their illness.

*(Here Sharpe relies on yet more circular self-references).*

“For many patients, obtaining an acceptable diagnosis becomes their main preoccupation.

Sharpe concludes by urging greater collaboration between liaison psychiatrists and “our more biomedically oriented colleagues” about the virtues of psychotherapy.



Chronic fatigue syndrome

JB Wright DW Beverly *Arch Dis Child* 1998; 79:168-174

*Whilst not authored by those In the innermost circle of the “Wessely school”, this paper carries 33 references by those who subscribe to their views.*

“The media has shown some interest in children with chronic fatigue syndrome... it is thus prudent to consider what current research tells us, particularly when there Is an apparent disparity of views about the illness betwaen parents, support groups, and professionals.

“This review seeks to delineate our knowledge from published work as It currently stands”.

These authors then trawl through the “neurasthenia” perspective, and note that such people were described as “sofa cases”.

The authors are clearly In support of the joint Royal College’s report CR54.

The authors note that the CDC criteria have been “updated specifically, this involved dropping all the physical signs from the Inclusion criteria”.

“Some workers have rightly pointed out that the illness behaviours (sic) of children may be significantly influenced by parental expectations and responses.

“The finding that enteroviral RNA has been discovered In muscle biopsy material of some patients has riot been significant when case controlled designs have been used.

“The infective argument ... .Is difficult to sustain In the absence of.. persistent infection markers.

“Similarly, the finding that there is hypoperfusion of the brain in CFS does not exclude excessive rest and inactivity as a cause”.

“Findings have often (sic) not been replicated... some commentators have sought to explain the findings as arising from inactivity... .there is considerable evidence to support this view.

“Whatever establishes the onset of this Illness, It has been suggested that an interplay Of social, psychological and physical factors maintains and perpetuates it.

“It Is prudent to examine some of these maintaining factors.

“In children, such issues are influenced by family factors. These include over-protectiveness, over-involvement, a powerful commitment by parents either to the notion of the illness (for example, “ME”) as an untreatable physical disorder, or to a self-help group that rejects rehabilitative interventions.

“Some workers have suggested that ...the syndrome reveals more about the emotional needs of the parents than the child, and that a variant of Munchausen by proxy may be “ME by proxy”.

*(The reference relied upon for the above claim is a 1992 one by Professor Elena Garralda, professor of child and adolescent psychiatry at St Mary's Medical School, London, and a member of the working group who produced the joint Royal Colleges' Report CR54).*

“Clusters may be related to... the modelling of responses to illness within the family or in communities.

“Some workers have drawn parallels with (the) understanding of conversion disorders... a child may find himself or herself in a predicament that needs an illness to resolve it, and an ally (such as a parent) who helps to perpetuate the illness.

“Some workers report adolescents with high standards and an emphasis on achievement, or highly successful adolescents unable to sustain early excellence.

“Depression is associated with CFS in 60-80% of children. Many people with fatigue have psychiatric symptoms and illnesses those with depression are more likely to have somatic symptoms and somatisation is a feature that is reported in association with CFS in children.

“Some children and their families become locked into a belief system that encourages... adoption of the sick role and withdrawal from social activity and school.

“Many physicians appear to continue recommending long term rest. Rest (leads to) a misplaced confirmation of serious illness.

“All of these issues (*rest, adoption of the sick role, withdrawal*) together with associated dependence and despondency, help to perpetuate the illness.

“(Management) in CFS means a shift away from an exclusively physical understanding of the illness”.

These authors recommend “a new approach”, which does not allow the physical, psychological and social elements to be split and which they describe as “psychoeducational”, stressing that “it will be important to explain the vicious cycles involved”.

“A graded and gradual increase in exercise ... and rehabilitation is now encouraged by most experienced clinicians.

“As with adult studies, the intention is to... renegotiate beliefs that have resulted in detrimental coping behaviours.

“Lask (a paediatric psychiatrist at Great Ormond Street Hospital, London, who was involved in the tragic case of Ean Proctor and who did not accept the diagnosis of severe ME made by consultant neurologist Dr J Morgan Hughes: see *Denigration by Design*, page 65) and Dillon have made the point that often children who do not improve are those with parents who are unwilling or unable to accept or co-operate with treatment.

“Home tuition may interfere with a return to school.

“Some children are lost to follow up because of resistance from the children themselves or their families, and this may be as high as 40%. This may in part be related to the family or child’s belief that the illness is exclusively physical.

“It is true that the minority of children who need to be admitted to a paediatric ward may have a less favourable prognosis. In one series, approximately 30% of this group were shown to have symptoms resistant to treatment that persisted for years.

“Chronic fatigue syndrome ... carries significant resource implications for both the community and the health service”.

## 1999

### Book of the month. Chronic Fatigue and its Syndromes

Brain Hurwitz. *JRSM: January 1999:92:47-4 8*

(For Dr Goudsmit’s review of Wessely’s book, see pp 103-104 above)

“Equating fatigue (even by metaphor) with a state induced by stresses acting upon metals, imputes a species of human incapacity that can arise sociogenically —as a by-product of the effect of society upon vulnerable individuals.

“Such a notion prepares us conceptually for some of the themes that Wessely and his co-authors have woven throughout the book.

“The authors believe recognition of a syndrome characterized by ‘easy fatiguability’ can be traced back to the 19<sup>th</sup> century disease complex ‘neurasthenia’, a state of enfeeblement without organic lesion that became a *maladie à la mode* by the end of the 19<sup>th</sup> century.

“Wessely et al point to the possible mutation of neurasthenia into what we now recognize as myalgic encephalomyelitis (ME).

“Given the lack of a clear epidemic or contagious aspect to neurasthenia... and the incontrovertible epidemic nature of the initial phenomena denoted by ME in the 1950s, it requires almost an act of faith to believe that substitution of the new term for the old allows reference to a similar disease complex.

“How the transfer of the label ME, designating an epidemic condition, to one designating a sporadic condition actually took place remains obscure, though mis-labelling may have played a part.

“... the reader is left with a sense that historical continuities are emphasised at the expense of discontinuities, and that a lot more research in this area remains to be undertaken”.

### Ill-defined notions

Ziauddin Sardar. *New Statesman*, 5 February 1999

Subtitled: Diseases are not what they ware. nor are their svmptoms. Ziauddin Sardar examines the bitter controversies surrounding ME and Gulf War syndrome

“Once upon a time, if you were sick, you ware really sick. You had a collection of recognisable symptoms.

“Now if you are ill there may not be a “cause”.

“You may be suffering from something but you may not be ill at all — according to the medical establishment anyway.

“We... recognise now that the “cause” of some illnesses is better seen as a lifestyle than a pathogen.

“Diseases have taken on a postmodern dimension.

“There is a blurring of boundaries, confusion between real and illusionary, and a deadly game of wordplay.

“Sickness is no longer simply a personal matter; it has become social, political, beaurocratic.

“When is someone sick, really sick? Who decides? By what criteria and procedures?

“The only thing that is certain is that the patients himself / herself has little power and cannot answer any of these questions. You are ill only when someone says you are ill.

“Consider syndromes. Once this was a name for a collection of symptoms for which no clear cause had yet been found.

“Now it stands for a bunch or bunches of symptoms lacking even the security of certainty that they are actually there.

“Most notorious is “chronic fatigue syndrome” At the far extreme, it is known as “ME”.

“From its first recognition as a large-scale problem... .horror stories abound of people (some of them children) whom the medical and psychiatric experts considered to be just faking...

“Sceptics about the disease were converted only when it hit their nearest and dearest.

“Even though ME causes real pain, it still remains a “syndrome”.

“The same can be said of Gulf War syndrome... .again, there are lots of nasty symptoms: mild to moderate chronic fatigue, double vision, severe urinary and sexual problems, memory loss, joint and muscular pain — to start with.

“But even though 400 veterans have actually died and some 5,000 are suffering from illnesses related to Gulf War syndrome, the syndrome does not officially exist.

“All the actors involved in this drama have their own perspective... .the government with avoiding paying compensation at all costs. So one would expect the Ministry of Defence to deny the existence of Gulf War syndrome and it does, operating on the simple basis of “no bug, no doosh”.

“...this makes life very hard for sufferers. They not only have to survive their disease: they must also fight for elementary decency. And that is a long and bitter task in itself.

“But what of researchers? Why should they deny the existence of Gulf War syndrome?

“The struggle over recognition hinges on research.

“But this research is a totally different exercise...

“How do you investigate this mess of symptoms?

“Not with biochemistry, but with psychiatry.

“The new societal syndrome of syndromatic diseases requires a new speciality, a syndromologist.

“Fortunately, one is to hand. His name is Professor Simon Wessely, consultant psychiatrist at the School of Medicine, King’s College, London.

“Wessely has been arguing that ME is a largely self-induced ailment that can be cured by the exercise programme on offer at his clinic.

“Recently he published the results of “the most definitive study” of Gulf War syndrome in... .the *Lancet*... .It concluded — surprise, surprise — that there is no such thing as Gulf

Way syndrome.

“So Wessely, who occupies a key position in our socio-medical order, denies the existence of Gulf War syndrome, just as he denies the existence of ME.

“Clearly, he is a follower of Groucho Marx: “Whatever it is, I deny it”. “Not surprisingly, lots of people hate him.

“A colleague from the States has come to Wessely’s defence with suggestions that are more ludicrous than insulting, such as the possibility that the mere experience of fear of chemical attack has brought on these permanent and debilitating symptoms.

“If Simon Wessely is our syndromologist-in-chief, who has chosen and vetted him for that post, and by what criteria and procedures?

“Where is the debate over the shaping of such research?

“When will we have the first officially sponsored study of such a problem which the sufferers do not have the occasion to call a whitewash?”.

Low dose hydrocortisone in chronic fatigue syndrome: a randomised crossover trial  
Cleare AJ; Wessely S et al. *Lancet*, 6 February 1999;353: (9151):455-458

(see p 112 above, also pp 35-36 above, to which article there were various letters of response, including the one by Baschetti below).

“Reports of mild hypocortisolaemia in CFS led us to postulate that low-dose hydrocortisone therapy may be an effective treatment.

Thirty two out of 218 screened patients met the authors’ criteria for CFS without co-morbid psychiatric disorder.

The authors conclude that the degree of disability was reduced with the hydrocortisone treatment (5 or 10 mg daily for one month) but not with placebo.

The authors believe that treatment for a longer time and follow up studies are needed to find out whether this effect could be clinically useful.

Low dose hydrocortisone for chronic fatigue syndrome  
Baschetti R. *JA MA* 1999;281(20): 1887

This letter makes the point that hydrocortisone should not be used as a prolonged method of treatment in CFS.

Tiredness is a price worth paying. Should doctors be so sceptical about the symptoms of low blood pressure?

Christine Doyle. *Daily Telegraph*, 16 February 1999:20

In this article about the symptoms of low blood pressure (listed as tiredness, weakness, anxiety, fainting and dizziness, feeling mildly depressed, low vitality), the differences in approach to low blood pressure by continental (especially German) and UK doctors is highlighted.

The article states:

“However, a few British doctors have, in recent years, put ‘Continental’ ideas to the test — with some surprising results.

“Following one survey, Professor Simon Wessely, consultant psychiatrist at King’s College Hospital in London, says he was “shocked” to find a distinct association between persistent fatigue and low (blood) pressure.

“There was also an association with faintness, but we did not find any link with headaches, palpitations or low mood”.

“Michael Marmot, professor of epidemiology and public health at University College Hospital, London... replicated, with his colleagues, the Wessely study in a survey of more than 10,000 male and female civil servants. As well as tiredness, they reported “There seems to be a strong relation between low systolic blood pressure and minor psychological dysfunction”.

“Neither researcher could offer any physiological explanation.

“Dr Wessely sticks firmly to the accepted British view. “I think we have all concluded that tiredness is a price worth paying for not having high blood pressure” “.

Mothering to death

Roy Meadow. *Arch Dis Child* 1999;80:359-362

Although not a member of the Wessely “inner circle”, Professor Sir Roy Meadow from the Department of Paediatrics and Child Health at St James’ University Hospital, Leeds, lists the first four of his references as his own self-references, of which three are on Munchausen syndrome by proxy; the fifth reference upon which this paper relies is one on ‘school phobia’ by Professor Sir Leslie Tumberg, (*who as President of the Royal College of Physicians, refused to consider withdrawing the flawed and much criticised joint Royal Colleges’ report CR54*).

The abstract of this paper states:

“Three families are described in which the healthy only child was... put to bed and treated as if ill, dependent and incapable..., the children died as disabled adults. In each case, the mothers evaded medical, educational and social services. The origins of their behaviour are examined, and the links with.... perceived and fictitious illness are discussed”.

“Classical and romantic literature is scattered with references to spinsters who spend their lives in bed feigning illness and being pampered by those around them.

“However, a bed-ridden life can be imposed on children, and... the psychological and physical consequences of being kept in bed and regarded as ill may ensure lifelong perpetuation of this lifestyle.

“The three families were notified to me by colleagues who were aware of my interest in unusual forms of child abuse.

The author describes three tragic cases where the child was without doubt “over-mothered”, but he then widens the issues:

“Usually when mothers invent or cause illnesses for their children they rely upon doctors and the health services as their accomplices.

“There are similarities with... cases of undetected Munchausen syndrome by proxy abuse... in which older children have come to regard themselves as ill, and to assume abnormal illness behaviour themselves as adults.

“Waller and Eisenberg adopted the term “masquerade syndrome” to describe children whose medical problems masquerade their difficulty in leaving home to go to school and pointed out that... it is often the result of the mother’s behaviour than the child’s.

“Care orders last only until the child reaches the age of 18 years.

“One would hope that if any such cases are occurring today, action would be taken by the appropriate agencies, if necessary using their statutory powers under the Children Act.

“But even today it is clear that there are major difficulties for both education and social services when the mother invokes illness as the reason for her child’s failure to attend school.

“...few doubt that some children who have the label myalgic encephalomyelitis (ME) would return to school and full activity much quicker if they were not being reminded regularly of their symptoms and their illness by the parents. Dealing with such cases requires persistence and resourcefulness by school authorities, health services and social services”.



Vitamin B status in patients with chronic fatigue syndrome

LC Heap, TJ Peters, S Wessely *JRSM* 1999;92:183-185

This paper claims to have assessed the functional status for the B vitamins pyridoxine, riboflavin and thiamin in 12 vitamin-untreated CFS patients and in 18 matched healthy controls.

For all three erythrocyte vitamin-dependent enzymes (thiamin-dependent transketolase, riboflavin-dependent glutathione reductase and pyridoxine-dependent aspartate aminotransferase), basal activity and activated enzyme activities were lower in the CFS patients than in controls.

The differences were most striking for pyridoxine.

The authors claim that this indicates a functional deficiency of the B vitamins, particularly pyridoxine, and claim that the most striking deficiency (that of pyridoxine), if present in the central nervous system, might account for the depressive features of CFS.

Wessely et al claim that such deficiencies are unlikely to reflect low dietary intake or malabsorption, since CFS patients are typically well-nourished.

The authors concede that “It is possible that subnormal vitamin activities at a cellular level are responsible for the observed findings.

The authors however then relate their findings to those of Baldewicz et al, who describe evidence of pyridoxine deficiency related to a measure of psychological stress in recently-bereaved homosexual men. (*Plasma pyridoxine deficiency is related to increased psychological distress in recently bereaved homosexual men. Baldewicz T et al. Psychosom Med* 1998;60:297-308).

The authors suggest that more detailed studies of functional vitamin status in relation to clinical features of CFS (particularly central nervous signs such as depression and memory impairment) are clearly indicated.

Wessely et al conclude that “clearly, many patients with CFS are currently taking vitamin and other supplements with little evidence of benefit”.

(*Note that the final conclusion fails to follow from the data supplied*).

Chronic fatigue syndrome — mapping the interior

EDITORIAL. Matthew Hotopf and Simon Wessely. *Psychol Med* 1999;29:255-258

In this Editorial, the authors discuss other articles on CFS in the same issue of

Psychological Medicine, and attempt to underline the complexity of CFS, starting with yet another trawl through Beard's "Central. Africa of Medicine".

Although they claim to focus on CFS, they again discuss several studies on people who do not have CFS.

As ever, the authors strongly promote graded exercise and cognitive behaviour therapy, and as ever, Wessely relies heavily on self-references and on those of his closest supportive colleagues.

They conclude that "The relative *role* of immune changes, viral infections, HPA axis underactivity, behavioural changes and attributional style may best be explored using prospective cohort studies of conditions which are known to be associated with later fatigue states. Such conditions might include stressful life events, viral infections or post-operative states".

You don't bring me flowers any more...

Dr Rai Persaud finds psychiatric patients are being short-changed by their visitors.

*Evening Standard (London) 4 May 1999, pp28-29*

An article which discusses the value of people taking gifts to their friends and relative who are in hospital, which is said to provide psychological support, but which consultant psychiatrist Dr Andrew Wiener from King's College Hospital, London found was being denied to psychiatric patients, who received significantly fewer gifts and even cards.

"Dr Simon Wessely, another author of the study (shortly to be published), argues that if you are thought responsible for your difficulties you will receive less commiseration from your friends and family, and so fewer visits from them or presents".

BBC Radio 4: Woman's Hour

Interviewer: Jenni Murray. *13 May 1999*

This item on *Woman's Hour* involved three people: Professor Simon Wessely, Dr Anne Macintyre representing the UK ME Association, and Helen Raymus, who is 17 and has had ME since she was 15.

In essence, it was a discussion about Wessely's treatment and an accolade from his patient about the efficacy of that treatment (ie. cognitive behaviour therapy).

Dr Macintyre said:

"I don't think it is appropriate to keep this illness entirely to the mind or family dysfunction or emotional problems.

“The other problem I find with Simon’s treatment ,which is known in jargon as CBT and is used for many illnesses, is that if people believe that CBT is the only treatment for this illness, there are dangers in some cases that if children don’t respond, and the families are perceived to be interfering with the treatment, there have been unfortunate cases of care proceedings being taken to take children away from their family, so that CBT psychiatric treatment is imposed on a child against their will. This is very worrying and it shouldn’t be happening”.

Simon Wessely replied:

“I agree it is very worrying. It has not happened to us. Under the guise of ME one sees bad things happening that we have to deal with, but we have never encountered that”.

*(See pp 4-5 above).*

Functional somatic syndromes: one or many?

S Wessely C Nimnuan M Sharpe *Lancet*, 1999: 354:936-939

*(This paper was briefly mentioned on p3 above)*

*As is customary with these authors, they rely heavily on self-references and on the supportive references of others in their own circle.*

“Patients seek help from doctors for symptoms... Diseases are objective observable abnormalities in the body. Difficulties arise when the doctor can find no objective changes to explain the patient’s subjective experience.

“The symptoms are then referred to as medically unexplained or functional.

“Many different functional syndromes have been described. In fact, each medical specialty seems to have at least one: for rheumatologists, prominent muscle pain and tenderness is fibromyalgia; for gastroenterologists, abdominal pain with altered bowel habit is irritable bowel syndrome; and for infectious disease specialists, chronic fatigue and myalgia is a postviral or chronic fatigue syndrome”.

*(The authors fail to note that for some psychiatrists, any disease which they do not adequately understand they categorise as somatisation).*

“We postulate that the existence of specific somatic syndromes is largely an artefact of medical specialisation.

“That is to say that the differentiation of specific functional syndromes reflects the tendency of specialists to focus on only those symptoms pertinent to their specialty, rather than any real differences between patients”.

*(The irony of this statement from Wessely and Sharpe is notable; see p114 above: Reviewing the reviews: the example of chronic fatigue syndrome JAMA (1998), in which Wessely found that psychiatry-based disciplines preferentially cited psychiatric references. Seemingly, it is quite acceptable for psychiatrists to focus on symptoms in their own discipline, but it is not acceptable in other medical disciplines).*

To explore their hypothesis, these authors claim to have reviewed the research literature with regard to three questions: (1) do the published diagnostic *criteria* for each of the specific functional syndromes overlap in their constituent symptoms? (2) Do patients identified as having one functional somatic syndrome also meet symptom criteria for others? (3) Are there similarities across syndromes in the non-symptoms characteristics of sex, co-existing emotional disorder, proposed aetiology, prognosis and response to treatment?

“Various names have been given to medically unexplained symptoms. These include somatisation, somatoform disorders, medically unexplained symptoms, and functional somatic symptoms. In this review, we use the term functional somatic symptoms.

“We define a functional somatic symptoms as one that, after appropriate medical assessment, cannot be explained in terms of a conventionally defined medical disease.

The authors then list “functional somatic syndromes” by specialty:

Gastroenterology	irritable bowel syndrome; non-ulcer dyspepsia
Gynaecology	premenstrual syndrome; chronic pelvic pain
Rheumatology	fibromyalgia
Cardiology	atypical or non-cardiac chest pain
Respiratory medicine	hyperventilation syndrome
Infectious diseases	chronic (postviral) fatigue syndrome
Neurology	tension headache
Dentistry	temperomandibular joint dysfunction; atypical facial pain
Ear, Nose and Throat	globus syndrome ( <i>ie. globus hystericus</i> )
Allergy	multiple chemical sensitivity

“Functional somatic syndromes pose a major challenge to medicine. Those symptoms ... are associated with... unnecessary expenditure of medical resources.

“Chronic fatigue syndrome is associated with worse disability than conditions such as heart failure.

“... three quarters of patients had symptoms more than 10 years after presentation.

“Thus, functional somatic complaints constitute a large... and costly health-care issue... that urgently requires... improved management.

“Does the current classification of such complaints into distinct functional somatic syndromes aid or hinder this process?

“Each medical specialty has defined its own syndrome or syndromes in terms of symptoms that relate to their organ of interest.

“In addition, other more controversial syndromes such as multiple chemical sensitivity and repetitive strain injury have been proposed but less widely accepted.

“...many of these syndromes are dignified by their own formal case definition and body of research that focuses solely on those patients identified as having the syndrome.

“We question this orthodoxy and ask whether these syndromes represent specific diagnostic entities, or are rather more like the elephant to the blind man  
— simply different parts of a larger animal?

The authors do not provide supportive data (they state “data available from authors”) but claim there is substantial overlap of symptoms and of case definitions of specific functional somatic syndromes.

“Almost all functional somatic symptoms are more common in women than in men. Clinical studies of patients with CFS, IBS, TMJP, globus syndrome and tension headache have all shown that such symptoms predominate among women”.

*(These authors make no mention of the known predominance of autoimmune disease in women, nor do they mention the established reasons for it, for example, the interaction of the hypothalamic-gonadal axis with the immune system<sup>1</sup>).*

The authors believe that irrespective of whether the diagnosis is CFS, FM, MCS or IBS, there is always a substantially increased rate of emotional distress.

*(The authors do not discuss the established neuroendocrine abnormalities which could account for the emotional lability which is such a cardinal feature of ME).*

In their own summary, the authors state “The hypothesis that patients with different functional somatic syndromes also share non-symptom characteristics is therefore largely supported, although available data are inadequate to answer this question definitively”.

They claim that there is a similarity in the treatments recommended for patients with

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<sup>1</sup> Collagen Disease: the enemy within. Lahita RG. *Int J Fertil Womens Med* 1998;43:5:229-234

various functional somatic syndromes and that there is “much evidence” of similarity in response to that treatment, stating that “low dose hydrocortisone therapy is helpful in the management of chronic fatigue syndrome” (*quoting Wessely’s own paper listed on page 125 above*).

The authors concede that “. . .whether or not these treatments truly are specific to certain syndromes (which goes against our hypothesis) ... remains unclear”, but then, in their customary fashion of forming a conclusion before they have generated their supportive data, the authors state “At present, the hypothesis that all functional somatic syndromes respond to the same therapies seems to be partly supported”.

*(These authors make this claim even though clearly they have no confirmatory data about all the syndromes which they are endeavouring to subsume into a single functional somatic syndrome”).*

“The main implication for classification is that the current practice of regarding patients as having clinically significant differences is questionable.

“Such patients may have..., variants of a general functional somatic syndrome.

The authors ask “Do we have a more meaningful way to subclassify patients?” and then postulate four approaches for consideration:

- (i) “The first approach is based on apparent clustering on the case definitions. For example, CFS, FM and IBS might form one cluster, and non-cardiac chest pain and hyperventilation another.
- (ii) “The second approach is based on epidemiological data... . based on a mathematical... analysis of the functional somatic symptoms.
- (iii) “The third approach is to use one of the existing psychiatric classifications that subclassify most functional somatic syndromes into depressive, anxiety and somatoform syndromes. This approach has some value in so far as it encourages the identification of psychological and somatic symptoms. We suggest, however, that whatever system is chosen, a classification based purely on symptoms is of limited value and offers little clinically useful information about the patients.

- (iv) “The fourth alternative to the diagnostic suggestions outlined above is a multi-axial approach. ..the relevant axes should include number of symptoms and their duration, associated mood disturbance (and) the patients’ attributions for the symptoms”.

The authors then discuss treatment, making a somewhat curious point:

“Most research on treatment selects patients on the basis of whether they meet criteria for a specific functional syndrome. This practice has limited the number of patients entered into trials and added a spurious complexity to our understanding of treatment.

“If we accept that functional somatic syndromes are considered together, we open the way for more general strategies ...for their management”.

*(This is perhaps the most significant sentence in the whole article, especially when viewed in the context of the Council of Europe 1996 Strasbourg Convention on Biomedicine. Only three European Union (EU) countries abstained from signing the preliminary draft on IV’ November 1996: Germany (ostensibly on moral grounds because of the atrocities committed there during World War II) and Belgium and Poland (probably on religious grounds, as both countries are almost entirely Catholic, and the Convention provides for research on embryos). Britain was a signatory to the preliminary draft, as were 35 other EU member states.*

*This Convention had no public airing beforehand and has been little reported since. In essence, the Convention confers certain rights on member states who sign the final document. The finalised Convention was signed by 20 EU countries on ~4” April 1997 — the UK did ~ sign on 4”” April 1997 (the anticipated date) due to the general election; ratification was to be dealt with by the incoming Labour government.*

*Of potential significance is the fact that the conferred rights include provision for drug and other medical trials on human beings which, in certain circumstances, could be carried out without the individual’s consent, ie. it paves the way for sweeping relaxation of informed consent to medical treatment. This would apply particularly to two groups of people: (i) those who are deemed to be mentally ill and (ii) those for whom no other known treatment is effective.*

*Being designed principally to facilitate progress in biomedicine, there appear to be many possibilities for misuse or abuse ie. ways in which the “safeguards” can be manipulated to suit researchers.*

*If the “Wessely” group of psychiatrists are ultimately successful in getting ME removed from its current neurological classification in ICD 10, and if they succeed in getting all conditions with “medically unexplained symptoms” such as ME! CFS, multiple chemical sensitivity (MCS), Gulf War syndrome (GWS), fibromyalgia syndrome (FM), irritable bowel syndrome (IBS), premenstrual tension syndrome (PMT) and tension headache re-classified as psychiatric “functional somatic syndromes”, it cannot be known whether*

*some ME / CFS / FM / IBS / GWS patients could be at risk within the framework of this Convention.*

*In the light of the heavy emphasis on psychiatric problems in ME! CFS patients by this particular group of psychiatrists — as expressed in the joint Royal Colleges' 1996 report CR54 — this possibility cannot be discounted.*

*Simultaneously to the European Strasbourg Convention, the American government decided that in future, individuals can be enrolled in medical research programmes without their consent: new Food and Drug Administration (FDA) rules now allow the use of experimental treatment in certain situations, which are similar to those set out in the Strasbourg Convention.*

*Despite the safeguards stipulated with the Convention, the provision within it (together with the changes by the FDA) appear to annul fundamental human rights which were laid down in the Code of Medical Ethics drawn up after World War II: this Code stated that no-one should ever be forced to participate in a trial again. Voluntary consent became the cornerstone of medical researchers' principles. The Strasbourg Convention and the new FDA rules imply that such consent will not always be needed.*

*Besides far-reaching implications for lawyers, researchers and ethicists, the most worrying aspect of the Convention document is that it seems to give medicine an open-ended ticket to do what it likes. Under the guise of individual "protection", the Convention says that in certain situations, "general interests" will take priority over those of the individual. There is even provision for organ removal from a living person without consent.*

*At present, many cases of vaccine damage remain unsettled, as do countless other pesticide and chemical injury cases. Under the Convention's rules, there will be virtually no chance to prove negligence or misdemeanor in cases involving those categorised as "mentally" ill.*

*At least one doctor (Dr Peggy North, Secretary of the European Doctors' Union) is critical of the lack of debate so far; she is particularly critical of article 17, which allows research to be carried out (subject to certain conditions) on people without their consent: she insists that "The basic rule should be that you cannot do research on someone without their consent — see European bioethics convention signed. Rory Watson. BMJ 1997:314:1066.*

*(See also (i) Sanctioning the light to lie: Doris Jones. What Doctors Don't Tell You: September 1997: page 12; (ii) FDA no longer requires consent for medical research: The Mouse Monitor, January 1997, page 27; (iii') European nations sign ban on human cloning: Giles Tremlett. The Times: 5 April 1997; (iv) Conseil de l'Europe Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention of Human Rights and Biomedicine. DIR/JUR (96) 14. Directorate of Legal*



*Affairs. Strasbourg, November 1996).*

*With particular reference to the implementation in the UK of forced psychiatric intervention in a worrying number of ME cases, at 3.16pm on 5<sup>th</sup> November 1998, the Countess of Mar rose in the House of Lords to ask Her Majesty's Government:*

*"What is the position of adults or parents of children who refuse treatment for themselves or their children recommended by their general practitioner or consultant when there is no imminent risk to life".*

*The Parliamentary Under-Secretary of State, Department of Health (Baroness Hayman) replied:*

*"My Lords, it is a general principle of law and medical practice that any adult person with the mental capacity to make a valid decision has the right to choose whether or not to accept medical treatment"*

*The Countess of Mar then asked:*

*"Is (the noble Baroness) aware that there is a growing list of children diagnosed as suffering from ME who are being placed by social services on the at risk register? Is she aware (of) the fact that some of the children are being forced into psychiatric hospitals for treatment which many practitioners agree is not the right treatment for ME?"*

*"In the light of the decision by the High Court Queen's Bench Division on 1~ October 1998 that referrals by community physicians to social services are illegal; that the use of Section 47 of the Children Act in these cases is also unlawful; and that parents should have the right to choose treatment for their children, will the Minister now instruct social services and all those physicians dealing with these children in the current state of the law and enable parents once more to exercise their right to consent?"*

*Baroness Hayman replied:*

*"I am aware that there has been controversy surrounding the treatment of certain children and young adults suffering from ME / chronic fatigue syndrome. This is an area where treatment is a matter of controversy".*

*The Earl Baldwin of Bewdley asked:*

*"Does the Minister agree that ME / chronic fatigue syndrome is not a psychiatric condition as such but is more usually multi-factorial, and that psychiatric symptoms can have physical causes. . . ?"*

*Baroness Hayman replied:*

*“Certainly the issues referred to by the noble Earl are of deep concern to patients and to carers of those suffering very distressing conditions. It is important that their views are well understood”*

*(See Hansard: Lords: Medical Treatment: Right of Refusal: 5 November 1998: 368 - 369).*

*It seems probable that the very existence of the Strasbourg Convention will strengthen the position of psychiatrists such as Wessely in the pursuit of his aim to amalgamate into one “functional somatic syndrome” several complex medical conditions for which the exact aetiology remains elusive; his article in the Lancet would seem to bode ill for unsuspecting members of the public.*

In their conclusion to the Lancet article, Wessely et al state:

“Functional somatic symptoms and syndromes are a major health issue. “They are common, and may be... costly.

“Most of the current literature pertains to specific syndromes defined by medical subspecialties. We have put forward the hypothesis that the acceptance of distinct syndromes as defined in the medical literature should be challenged.

“We contend that the patients so defined actually have much in common. A review of the published evidence (*not appended: instead, the authors advise that anyone interested must contact them for the required citations*) largely supports our suggestion.

“This hypothesis is open to further testing, and we are currently attempting to do just that in a study across medical specialties.

“We contend that the patients so defined actually have much in common. A review of the published evidence (*not appended: instead, the authors advise that anyone interested must contact them for the required citations*) largely supports our suggestion.

“This hypothesis is open to further testing, and we are currently attempting to do just that in a study across medical specialties.

“We propose an end to the belief that each “different” syndrome requires its own particular sub specialist.

“Our thesis is not new. A previous generation of physicians noted overlaps between what were then deemed “psychosomatic syndromes”, and also recognised the... sequence of different symptoms in the same patient.

“Unfortunately, none of these... theories were accompanied by empirical support, and consequently all have disappeared from our current thinking on the subject.

“We argue that their reinstatement is overdue”.

*This is a disturbing submission by Wessely et al for the reasons mentioned above.*

*Clearly, Wessely's aim is to remove from medical nosology as many as possible of the existing syndromes which he and his colleagues seem to despise, and to subsume them all within the umbrella of somatisation disorder, thereby ensuring for many medical conditions a psychiatric ascription (and thereby a reduction in state benefits payable to all such claimants, because psychiatric illness automatically carries a lower financial level of state benefit) even though those medical conditions in all probability will turn out to have an entirely organic pathoaetiology.*

*Psychiatrists have a long track record in medical mis-attribution: the literature is replete with examples of psychiatrists having claimed ( with absolute certainty) “unexplained” symptoms as psychiatric. One would hope that psychiatrists would be a little more cautious and circumspect, and that they would have learned by experience, but this is clearly not the case.*

*For example, all the following were at one time designated as “psychiatric”*

*1. Diabetes mellitus: DM was formerly held to be a manifestation of psychosomatic illness<sup>2 3 4</sup>. Indeed, DM was said to represent “the last strand of*

<sup>2</sup> Correlation between Emotions and Carbohydrate Metabolism in Two Cases of Diabetes Mellitus Meyer, Albrecht et al *Psychosom Med* 1945:7:335-341

<sup>3</sup> Present trends in the Evaluation of Psychic Factors in Diabetes Mellitus. Daniels, GE. *Psychosom Med* 1939:1:4:527-553

<sup>4</sup> Emotional and Instinctual Factors in Diabetes Mellitus: when infantile wishes conflict with frustrated demands. Daniels, GE. *Am J Psychiat* 1936:93:711-724

*the neurosis” caused by such sexual repression that “even the usual form of conversion hysteria was not acceptable for the patient”. Psychiatric misdiagnosis was not uncommon as recently as 1987<sup>5</sup>, when DM was misdiagnosed as hysterical hyperventilation.*

2. *Epilepsy: in the 19<sup>th</sup> century medical opinion was that epilepsy was caused by disappointment in love: it was not until 1928 that the true organic cause was established.*

3. *Multiple sclerosis: in 1873, Charcot maintained that MS was due to hysteria; this lingered amongst some doctors for many years: from 1947, and particularly during the 1950s and 1960s, many investigators of MS concerned themselves with the systematic study of the psychological and psychiatric aspects of MS<sup>6</sup>. It was not until 1978 that “a large body of evidence suggests that MS is an autoimmune disease that in some way may be related to a viral infection”<sup>7</sup>. With*

*the advent of nuclear medicine's imaging techniques, demonstration of demyelination plaques in the central nervous system finally despatched the long-held psychiatric label.*

4. Graves' Disease (exophthalmic thyrotoxicosis): *Wessely is following a strong tradition at King's College Hospital in claiming a psychiatric diagnosis for unexplained medical symptoms; in 1897, Graves' disease was said to be an "emotional" disorder and was described as a neurosis of the centres of emotion" in King's College Hospital Reports of that year.*<sup>8</sup>
5. Pernicious anaemia: *this used to be attributed to too much hostility, described as "evidence of a hostile feminine identification and pseudomascuine defenses (sic) are frequently noted"*<sup>9</sup>
6. Myasthenia gravis: *this is not infrequently diagnosed as a psychiatric disorder, especially in the early stages*<sup>10</sup>

<sup>5</sup> Misdiagnosis of Diabetic Ketoacidosis as Hyperventilation Syndrome. *Treasure PAR et al BMJ 1987;294:630*

<sup>6</sup> The Etiologic Significance of Emotional Factors in Onset and Exacerbations of Multiple Sclerosis (Personality Structure). *Philippopoulos GS et al. Psychosom Med 1958;20:6:458-474*

<sup>7</sup> Immunoregulation in Multiple Sclerosis. *Weiner HL & Hauser SL. In: Immunology of Nervous System Infections: Progress in Brain Research Ed: PO Behan, V ter Meulen & F Clifford Rose. Elsevier Science Publications, 1983:339-343*

<sup>8</sup> Graves Disease: An Emotional Disorder. *Crewfunl R. King's Coll Hosp Rep 1897;3:45 ~ Weiner H et al Psychosom Med 1957;19:1*

<sup>9</sup> *Weiner H et al. Psychosom Med 1957;19:1*

7. Parkinson's disease: *(named after Parkinson J, who in 1817 wrote an article entitled "An Essay on the Shaking Palsy", Sherwood, Neely & Jones, London). Right from 1817, some doctors insisted that psychological factors played a causative role; those who believed this offered several different explanations: Jackson, Free & Pike<sup>11</sup> asserted that it was caused by "psychological trauma or loss"; Jelliffe,<sup>12</sup> a leading psychoanalyst of his day, claimed that the motor symptoms that characterise Parkinson's disease were "physical manifestations of a defense against unresolved hostility, a result of suppression". In 1942 Shaskan, Yarnell and Alper<sup>13</sup> believed that people with histories of an insecure childhood and with poor adjustment to previous stresses were predisposed to Parkinson's disease. In 1948, Booth<sup>14</sup> described Parkinsonism as an "illness of the ambitious, moralistic man"; after analysing 60 cases, Booth concluded that the disease was the "result of a conflict between an aggressive drive toward action and an equally strong internal pressure to inhibit action. This conflict manifests in tremor" The cause of Parkinson's was then ascribed to "conflict resulting from the wish to masturbate". Prior to 1957, little was known about the biochemical processes which underlie the behavioural aspects of Parkinson's disease; once these biochemical processes were discovered, psychosomatic interpretations abruptly disappeared. It is now known that the symptoms of Parkinson's disease result from a dysfunction of a group of*

*nerve cells in the brain stem (the substantia nigra) and that these cells are involved in the production and storage of the neurotransmitter dopamine, and that in Parkinson's disease, there is a deficiency of dopamine in the corpus striatum, with a consequent disruption of the appropriate chemical message. The discovery of the role of neurotransmitters marked the point at which psychological studies of Parkinson's disease came to be dominated by a biomedical rather than a psychosocial orientation.*

8. *Gastric ulcers: in 1950<sup>15</sup> gastric ulcers were deemed to be caused by unconscious conflicts.*
9. *Migraine: in 1973<sup>16</sup> and in 1984<sup>17</sup> also was deemed to be caused by*

<sup>10</sup> Myasthenia Gravis: the problem of psychiatnc' misdiagnosis. *GA Nicholson et al Med J Aust* 1986;144:632-638

<sup>11</sup> The Psychic Manifestations in Paralysis Agitans. *Jackson JA, Free GBM and Pike HV. Archives of Neurology & Psychiatry* 1923;10:680-684.

<sup>12</sup> The Parkinsonian Body Posture: some considerations on unconscious hostility. *Jeliffe SE Psychoanalytic Review* 1940;27:467-479

<sup>13</sup> Physical, Psychiatnc and Psychometric Studies for Post-Encephalitic Parkinsonism. *Shaskan D, Vameil H & Alper IC Journal of Nervous and Mental Disease.* 1942;96:652-662

<sup>14</sup> Psychodynamics in Parkinsonism. *Booth G. Psychosom Med* 1948;10: 1-14

<sup>15</sup> *Alexander F. PSYChOSomatIC Medicine* 1950: Norton, New York

<sup>16</sup> *Grinker EE. Psychosomatic Concepts.* 1973: Amnson, New York

<sup>17</sup> *Appraisal and Coping. Lazarus RS & Folkman S. 1984: Springer, New York*

*unconscious conflicts.*

*Other medical conditions which used to be claimed as psychiatric include the following:<sup>18</sup>*

*Dupuytren's contracture*

*psoriasis*

*gout*

*glaucoma*

*keratitis*

*asthma*

*hay fever*

*ulcerative colitis*

*dysmenorrhoea*

*constipation*

*diarrhoea*

*arthritis*

*angina*

*hypertension*

*kidney disease*

*circulatory problems*

*impotence*

*eczema*

*Thus it can be seen that wrongful attribution of an organic pathology to a psychosomatic or psychiatric one by psychiatrists is far from uncommon.*

*Myalgic encephalomyelitis is still at the stage where it is receiving the customary*

*medical treatment.*

*Assumptions about the psychological origins of a disease or syndrome should not be made in the absence of identifiable pathology for their plausibility.*

*Rarely have psychosomatic diagnoses been based on positive findings; it is merely that the absence of knowledge of the relevant biological processes provides the ground in which easy psychiatric explanations can flourish.*

*Returning to Wessely's paper in the Lancet it is a striking feature of these particular authors that they so relentlessly fail to consider all the relevant and available published evidence.*

*They make sweeping claims: for example, they claim that all the symptoms to which they refer could more appropriately be uniformly classified as a "functional somatic syndrome" and that this should then fall into the realms of psychiatry, yet they have ignored or distorted research evidence which makes such a suggestion unscientific.*

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<sup>18</sup> Association for Research in Nervous & Mental Disorders (1952): *In: Case Histories in Psychosomatic Medicine*. Miles HHW, Cobb S & Shands HC (eds): 1959: 9: WW Noiton & Co Inc. New York

*Illustrations of the evidence which is not discussed by Wessely et al include the following:*

*In Fibromyalgia (of which there have been accurate accounts in the medical literature since the 1880s) there is a hypersensitivity response throughout the body which can result in symptoms such as headaches, irritable bowel, irritable bladder, sleep disorder, fatigue and memory problems; current research suggests that this hypersensitivity may be the result of neural transmitter imbalance in the central nervous system.*

*There is well-documented evidence that substance P is increased in fibromyalgia,<sup>19 20</sup> which increases pain perception; the sympathetic nervous system (which controls muscle tone) can become disturbed, leading to muscle ischaemia (oxygen depletion), resulting in greater substance P release and increased sensitivity.*

*In fibromyalgia there are low levels of somatomedin C (whereas somatomedin C levels are higher in ME! CFS); somatomedin C is an important mediator of growth hormone, which in turn is necessary for normal muscle homeostasis.<sup>21 22</sup>*

*Hypogammaglobulinaemia has been found in fibromyalgia, and 70% of FM patients have antibodies to 5- hydroxytyptamine (5-HT - serotonin), gangliosides and phospholipids, very suggestive of autoimmune disease.<sup>23</sup>*

*Patients with fibromyalgia have abnormal stimulated thyoptin and prolactin responses.<sup>24</sup>*

*They also have a reduction in 24 hour urine free-cortisol excretion, increased trough plasma cortisol levels with loss of diurnal fluctuation, and an exaggerated corticotrophin (but blunted cortisol) response to exogenous corticotropin releasing hormone.<sup>25</sup>*

<sup>19</sup> Chronic fatigue syndrome differs from fibromyalgia.

No evidence for elevated substance P levels in patients with CFS. *Evengard B et al Pain 1998;78:2:153-155*

<sup>20</sup> Advances in fibromyalgia: possible role for central neurochemicals. *Russell IJ. Am J Med Sc 1998;315(6):377-384*

<sup>21</sup> Fibromyalgia and Chronic Fatigue Syndrome: Similarities and Differences. *Dedra Buchwald. Rheum Dis N Am 1996;22:2:219-243*

<sup>22</sup> Somatomedin C. (Insulin-like Growth Factor I) in patients with CFS. *Adrienne L Bennett et al J Psychiat res 1997;31:1:91-96*

<sup>23</sup> High incidence of antibodies to 5-HT, Gangliosides and Phospholipids in patients with CFS & FMS & their relatives: Evidence for a clinical entity of both disorders. *R Klein PA Berg Eur J Med Res 1995/6:1:21-26*

<sup>24</sup> Neuroendocrine findings in primary fibromyalgia (soft tissue chronic pain syndrome) and in other rheumatic conditions. *Ferracioli G et al J Rheumatol 1990;17:869*

<sup>25</sup> Altered reactivity of the HPA axis in the primary fibromyalgia syndrome. *Griep EN et al J Rheumatol 1993;20:469*

*There is evidence that 20-47% of patients with FM and/or ME / CFS also have environmental chemical intolerance (CI) with multiple chemical sensitivities (MCS),<sup>26</sup> in that chemical and biologic stimuli can initiate and elicit sensitisation, which in turn gives rise to activation of the sensitised limbic system, and mesolimbic pathways then facilitate dysregulation of autonomic, endocrine and immune system functions. Research has demonstrated an increase in the expression of activation markers, supporting the theory of an underlying immune dysregulation.<sup>27</sup> There is also evidence that the overlapping symptomatology of CFS and multiple chemical hypersensitivity (MCS) might be explained by a defect in the antiviral pathway 2-5A: since interferon- induced proteins 2-5A synthetase and protein kinase RNA (RKR) have been implicated in the viral induction of ME / CFS, a study which was designed to utilise 2-5A and PRK activity for differentiation between CFS induced by either viruses or chemicals has found that 2-5A and PKR are not only biomarkers for viral induction of CFS, but are also biomarkers for chemical inducers of CFS.<sup>28</sup>*

*Fibromyalgia patients show higher values of IgG deposits in the dermis and vessel walls and show a higher reactivity for collagen III; they also have a higher number of mast cells.<sup>29</sup>*

*Fibromyalgia patients demonstrate pathological electronystagmography in 45% of cases<sup>30</sup>, confirming the vertigo and dizziness which was reported by 72% of patients.*

*Patients with fibromyalgia show overnight falls in SaO<sub>2</sub>, suggesting hypoxia.<sup>31</sup>*

*The association of allergy and fibromyalgia has been documented since 1977.<sup>32 33</sup>*

*There is an association between fibromyalgia and systemic lupus erythematosus*

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<sup>26</sup> Illness from low levels of environmental chemicals: relevance to CFS and FM. Bell IR *et al* *Am J Med* 1998;105(3A) 74S-82S

<sup>27</sup> Fibromyalgia and chronic fatigue syndrome: similarities and differences. Dedra Buchwald. *Rheum Dis Clin N Am* 1996;22:2:2190243

<sup>28</sup> Interferon-induced proteins are elevated in blood samples of patients with chemically or virally induced chronic fatigue syndrome. Vojdani A; Lapp C. *Immunopharmacol Immunotoxicol* 1999;21:2:175-202

<sup>29</sup> Dermal IgG deposits and increase of mast cells in patients with FM. Enestrom S *et al* *Scand J Rheumatol* 1997;26:4:308-313

<sup>30</sup> Otolaryngologic and audiologic findings in FM. Rosenhall U *et al*. *Scand J Rehab Med* 1996;28:4:225-232

<sup>31</sup> Fibromyalgia syndrome: overnight falls in arterial oxygen saturation. Alvarez Lario B *et al* *Am J Med* 1996;101:1:54-60

<sup>32</sup> Does allergy play a role in fibrositis? Koenig WC *et al* *Arch Phys Med Rehab* 1977;58:2:80-83

<sup>33</sup> The lymphocyte phenotype in patients with primary fibromyalgia. Samborski W *et al* *Ups J Med Sci* 1996;101:3:251-256



(SLE / lupus).<sup>34 35</sup>

*Wessely et al make no mention about the well-known association of ME with the post-polio syndrome (PPS),<sup>36</sup> in which Richard Bruno describes the similarities and correlations between ME and PPS dating from 1934, stating “More recent support for a relationship between Poliovirus and ME came in 1989, when a dangerously rising titre to Type III Poliovirus was documented. . . ‘ Bruno has shown that clinically dominant “central fatigue” arises from neuronal damage in the mid-brain, especially affecting the reticular activating system (RAS), the function of which is to alert the cerebral cortex to ascending sensory information and to maintain wakefulness and attention. It is notable that Bruno et al differentiate between ME and CFS; in comparing post-polio fatigue with CFS, they note that “85% of patients with CFS demonstrated an excess of irregular slow wave activity on EEG similar to that seen following ME and polio”. In discussing the neuroanatomic studies, Bruno notes the relationship between hyperintense signal (HS), impaired attention, and fatigue: in particular, he notes that periventricular and deep white (but not grey) matter HS have been imaged in between 40 and 100% of CFS patients and that these HS suggest either enlarged, fluid-filled spaces around arterioles or demyelination.*

*They make no mention of the documented ocular problems in ME / CFS<sup>37 38 39 40 41</sup>*

*The UK High Court has acknowledged fibromyalgia as a distinct nosological entity which can render the sufferer totally unable to follow gainful employment<sup>42</sup>,*

<sup>34</sup> Immunologic profile of patients with FM. *Smart PA et al Am J Med Phys rehab* 1997;76:3:231-234

<sup>35</sup> Clinical diagnosis found in patients with Raynaud's phenomenon: a multicentre study. *Grassi Wet al Rheumatol mt* 1998;18:1:17-20

<sup>36</sup> The Post-Polio Syndrome: Advances In the Pathogenesis and Treatment. *In: Proceedings of the First International Scientific Conference on the Post-Polio Syndrome: (Ed): Dalakas MC, Bartfleld H & Kudand LT. Ann New York Acad. Sci* 1995;753:1-409

<sup>37</sup> Eye Problems and CFIDS. *David J Browning. CFIDS Chronicle October* 1988:4-5

<sup>38</sup> Ocular Manifestations of Chronic Fatigue & Immune Dysfunction Syndrome. *Walter Potaznik et al Optomefry & Vision Science* 1992;69:10:811-814

<sup>39</sup> Survey of the Ocular Manifestations in CFIDS. *Walter Potaznik & Nell KozoL Clin Inf Dis* 1994;18: (Suppl 1)S87

<sup>40</sup> The ocular signs and symptoms of chronic fatigue syndrome. *BE Cafferty et al JAm Opt Assoc* 1994;65:187-191

<sup>41</sup> Neuro-ophthalmologic Manifestations of Chronic Fatigue Syndrome. *Alfredo A Sadun et al L&The Clinical and Scientific Basis of Myalgic Encephalomyelitis Chronic Fatigue Syndrome. Ed: BM Hyde. Nightingale Research Foundation, Ottawa, 1992*

<sup>42</sup> Unum versus Napier. Queen's Bench Division (Basingstolce) May 15 1996. *Lloyd's Law Reports* 1996;2:550-558

and the UK High Court has also recognised ME as a distinct and legitimate condition.<sup>43</sup>

For the last seven years, fibromyalgia has been formally classified by the World Health Organisation in the International Classification of Diseases as a Soft Tissue Disorder (Rheumatism)<sup>44</sup> and not as a “psychiatric” disorder; equally, ME is classified in ICD 10 as a neurological disorder<sup>45</sup> and the major 724 - page textbook<sup>46</sup> contains enough neurological evidence to convince any but the obdurate.

There are many similarities but also significant differences between FM and ME / CFS, and there is abundant evidence to refute Wessely’s proposal to reclassify both ME / CFS and FM as primary psychiatric disorders.

The literature abounds with warnings about the injudicious ascription of a psychiatric label to such conditions: it was recognised in 1956 that “The emotional overlay in the (ME) patients. . . is very apparent and very confusing. However, all physicians are agreed that the common anxiety neuroses of adult females cannot explain in entirety this syndrome”<sup>47</sup>; with regard to fibromyalgia, Don Goldenberg (one of the world’s leading experts in FM) advised “(fibromyalgia) overlaps with other poorly understood syndromes, such as CFS and irritable bowel, that have often been termed ‘functional’ as opposed to organic. Such distinctions are outdated and interfere with an appropriate understanding and treatment”<sup>48</sup>; with regard to both ME / CFS ~ fibromyalgia, it has been stated (in a review article about some of the problems surrounding the diagnosis of somatisation) that “there is increasing evidence that an amplification of bodily sensations in fibromyalgia is due to abnormalities of central processing and these abnormalities cast doubt on the concept of somatization”.<sup>49 50</sup>

<sup>43</sup> Page versus Smith. Queen’s Bench Division (London) 22 December 1992; Concurring Judgement by The Master of The Rolls, 12<sup>th</sup> March 1996 (3 All ER 272-280).

<sup>44</sup> International Classification of Diseases (ICD) 10: M79.0

<sup>45</sup> International Classification of Diseases (ICD) 10: G.93.3

<sup>46</sup> The Clinical & Scientific Basis of Myalgic Encephalomyelitis Chronic Fatigue Syndrome. Ed: BM Hyde. The Nightingale Research Foundation. Ottawa 1992

<sup>47</sup> Letter dated 9 May 1956 from Dr James Bond, Florida State epidemiologist to the CDC: *Reflections on Epidemic Neurasthenia (Chronic Fatigue Syndrome)*. D.A. Henderson. In: *Clinical Infectious Diseases: an official publication of the Infectious Diseases Society of America*: pub. The University of Chicago Press. Volume 18: Supplement 1; January 1994 (entire 167 page supplement devoted to CFS)

<sup>48</sup> Introduction. Don L Goldenberg (Guest Editor): *Rheum Dis Clin N Am* 1996;22:2

<sup>49</sup> Rethinking somatization. McWhinney IR et al *Ann Int Med* 1997;126:747-750

<sup>50</sup> Fibromyalgia, chronic fatigue syndrome and myofascial pain. Robert Bennett. *Cur Opin Rheumatol* 1998 10:95-103

*Although the symptoms are indeed protean, on clinical grounds alone common sense dictates that observable signs (none of which is merely subjective) must be afforded due and proper consideration. Such objective findings (which are well-documented throughout the ME / FM literature) include the following:*

*hair loss; nystagmus; a positive Romberg sign; ataxia; frequency of micturition (including nocturnal micturition); recurrent severe mouth ulcers; paroxysmal orthostatic tachycardia; flattened and inverted T waves on 24 hour Holter monitoring; Raynaud's phenomenon; low NK cells; an increased CD4:*

*CD8 ratio which strongly correlates with symptom severity; findings that 89% of CFS patients have suboptimal levels of DHEA and DHEA-S<sup>51 52</sup>, baseline differences in cardiovascular profiles and in haemodynamics in ME / CFS patients<sup>53</sup> clearly visible fasciculation; evidence of defective ionophores at cell membrane level<sup>54 55 56</sup> and evidence which shows clearly visible and very swollen muscle cells, with hypertrophy of the mitochondria (which confirms that the muscle cells are disordered and dysfunctional).<sup>57</sup>*

***Without due consideration of all the available published evidence, Wessely and colleagues' claim to be practising "evidence-based medicine" is unsustainable.***

<sup>51</sup> A pilot study employing dehydroepiandrosterone (DHEA) in the treatment of CFS. Himmel PB et al *J Clin Rheumatol* 1999;5:2:56-59

<sup>52</sup> Differences in adrenal steroid profile in CFS, in depression and in health. Scott LV, Dinan TG et al *J Affective Dis.* 1999;54:1-2:129-137

<sup>53</sup> Cardiovascular responses during head-up tilt in CFS. LaManca JJ, Natelson BH et al. *Clinical Physiology* 1999;19:2:111-120

<sup>54</sup> Arguments for a role of abnormal ionophore function in CFS. Abhijit Chaudhuri, Peter O.Behan et al. *In: Chronic Fatigue Syndrome. (ed): Yehuda and Mostofsky: Plenum Press, New York 1997: presented at the 2<sup>nd</sup> International Conference held in 1995 at Bar-Ilan University, Ramat Gan, Israel (Falter Centre)*

<sup>55</sup> Chronic Fatigue Syndrome: A Disorder of Central Cholinergic Transmission. A. Chaudhuri, T.Majeed, T Dinan, P O Behan. *JCFS* 1997;3:1:3-16

<sup>56</sup> Chronic Fatigue Syndrome is an Acquired neurological Channelopathy. Abhijit Chaudhuri and Peter O.Behan. *Hum Psychopharmacol Clin Exp* 1999;14:7-17

<sup>57</sup> Slides of Withemina Behan of The University of Glasgow Department of Pathology

**Wessely and colleagues' involvement in related disorders**

**Gulf War Syndrome**

1997

Gulf war research oiven ao-ahead Susan Mayor.. BMJ 1 January 1997;314:95 (Sub-titled "The British government has finally decided to carry out a rigorous epidemiological investigation into Gulf war syndrome).

"Since the conflict in 1990 there have been reports of a wide range of complaints in veterans, including headaches, fatigue, sleep disorders, and musculoskeletal complaints, as well as congenital malformation in their offspring. There have also been suggestions about the possible role of organophosphorous insecticides and the combination of vaccines that military staff were given.

"'But this is all speculation' points out Simon Wessely, professor of epidemiological psychiatry at King's College School of Medicine, who is about to start a third research project into symptoms. 'All we do know is that some of the 51,000 people who went to the Gulf war from the United Kingdom have since become sick — that is not disputed'.

"An appreciable number of the veterans have psychiatric symptoms.

"But other problems, including skin disorders, respiratory conditions... and irritable bowel have also been found. The problem with these data is that they are from a self-selected group of people.

"A second hurdle facing the researchers is that the whole incident is shrouded in secrecy... . Following up Gulf war veterans is being hampered by poor record keeping during the war.

"'The new studies will not give us all the answers'... .concluded Professor Wessely".  
(*Had Wessely made up his mind about his outcome findings in advance?*).

**Is there a Gulf War Syndrome?**

Searching for Syndromes by Factor Analysis of Symptoms.

Robert W Haley et al. *JAMA* 15 January 1997;277:3:215-222

In sharp contrast to the anticipated stance taken by Wessely, Haley et al (from the Epidemiology Division of internal Medicine and the Department of

Neurology at the University of Texas) set out to search for syndromes in Persian Gulf War veterans based on factor analysis-derived syndromes.

They developed a single Case Definition from the veterans' symptoms; this definition (which the authors state resembled chronic fatigue syndrome) was developed for the US Department of Defense and was based on 52 unambiguous symptoms, including balance problems, slurred speech, dyspnoea, chemical sensitivities, arthralgia, low back pain, generalised motor and coordination problems, abdominal pain, swollen glands, fever, night sweats, problems with bladder control, together with a multiplicity of cognitive problems.

The degree of association was assessed with logistic regression analysis. Six identifiable syndromes were found, and some veterans were found to have more than one syndrome; these syndromes were classified as follows:

Syndrome I was termed "impaired cognition" syndrome.

Syndrome II was termed "confusion - ataxia" syndrome.

Syndrome III was termed "arthro-myo-neuropathy" syndrome.

Syndrome IV was termed "phobic - apraxia" syndrome, which included nausea, dizziness, faintness, chest discomfort, numbness of hands, arms and trunk.

Syndrome V was termed "fever-adenopathy" syndrome. Syndrome VI was termed "weakness - incontinence" syndrome.

All six groups of veterans with the six syndromes had the same clinically significant profile, differing only in severity.

All veterans scored between 0 and 3 on the malingering scale (which is below the level of 4.4 expected for subjects attempting to feign abnormalities).

These authors found the standard profile for somatoform disorder in only two subjects out of the 249 evaluated, and malingering in none.

The authors state that this profile did not reflect malingering or exaggeration of illness and that it did not represent other classical psychological illnesses.

Instead, it is typical of patterns found in general medical illnesses, reflecting sufferers' concerns over specific sensory, motor and cognitive deficits.

The authors note that further studies into GWS could be affected by selection bias.

Haley et al conclude that at least 25% of ill veterans in the reserve construction battalion whom they studied have symptoms which may reflect generalised neurologic injuries.

The authors suggest that most of the symptoms in the Gulf war veterans could be explained by varying combinations of damage to the brain or brain stem (eg. vestibular and cognitive dysfunction), the spinal cord and the peripheral nervous system (eg. parasthesias of the extremities, muscle pain and weakness, joint pains and urinary incontinence) and the autonomic nervous system (eg. diarrhoea), ie. dysfunction of the central, peripheral and autonomic components of the nervous system.

### Evaluation of Neurologic Function in Gulf War Veterans

A blinded case-control study.

Robert W Haley et al: *JAMA* 15 January 1997;277:3:223-230

The object of this further study by Haley et al was to determine whether Gulf War-related illnesses are associated with central or peripheral nervous system dysfunction.

Laboratory studies confirm that combinations of the cholinesterase-inhibiting chemicals to which many veterans were exposed in the war caused delayed, chronic neurotoxicity in humans.

Taken together, these findings support the hypothesis that chronic symptoms in many Gulf War veterans are due to chemical injury to the nervous system.

Six neurologists, who had not participated in the study and who were blinded to the subjects' status (ie. whether cases or controls), reviewed the clinical findings on each subject. Those six neurologists were unable to arrive at a diagnosis of any known syndrome in any subgroup of the veterans.

The results of this study demonstrate that after serving in the Gulf War, veterans consistently showed more objective abnormalities on tests of neurologic function than control veterans.

Haley et al make the point that objective tests that obviate bias (such as evoked potentials and electromyography) are essential.

### Gulf war illness

Anthony David, Susan Ferry, Simon Wessely. *BMJ* 25 January 1997; 314:239-240

Commenting on the above studies by Haley et al in the previous week's *JAMA*, David and Wessely run true to form. They write:

"Extrapolating directly from reports of physical symptoms to specific aetiologies is perilous — somatic symptoms are common and usually remain medically unexplained.

"The symptoms could be put down to the natural terror that such a perceived threat

(*exposure to chemicals*) would induce.

“The authors (*Hayley et al*) concluded that the tests provided evidence of generalised injury to the nervous system. Possible confounders, such as excess alcohol use, were not addressed.

“We should take care before generalising the results to British veterans. Reserve troops may be more vulnerable to various outcomes because of differing expectations... . compared with the United States, Britain made far less use of reservists.

“No single health problem has yet emerged as a focus for aetiological studies.

“...some veterans and their spouses have given birth to children affected by various congenital abnormalities... .this is not *prima facie* evidence for a link with Gulf service.

“Even when there is a consensus about the existence of any particular adverse outcome, linking it with particular exposures years after the event will be far from easy.. . contemporary records... may be difficult to obtain.

“In Britain, the Ministry of Defence... .deserves credit for its response to the individuals affected.

Diary: Matthew Norman. *The Guardian*, March 6, 1997, page 15

“We are intrigued to note that the Ministry of Defence has endorsed the Gulf War Syndrome research programme.... of Dr Simon Wessely.

“Dr Wessely’s last foray into the public eye came last year, when he was associated with the controversial report dismissing ME as having no physical basis. He has since been forced to change his mind on that one.

“Let us hope he makes no similar mistake about Gulf War Syndrome being a malingerer’s charter”.

#### Gulf fatigue

Reply from Simon Wessely to Matthew Norman’s Diary. *The Guardian*, 11 March 1997, page 14

“Matthew Norman ... states that I was one of the authors of the detailed report on chronic fatigue syndrome (CFS/ME) published by the three Royal Colleges last year.

“True enough, but I have not changed my mind about its conclusions and nor do I need to...

“Anyone who, like myself, has spent time with the veterans will know that suggesting that Gulf War syndrome is a “malingerer’s charter’ is absurd”.

Gulf veterans harassed over health claims

Ian Burrell. *Independent*, 13 March 1997

“The Defence Minister has been told that Gulf War veterans have been intimidated and followed home by plain clothes investigators.

“The veterans, campaigning over Gulf War syndrome believe they are being harassed as “subversives” by officials because of their attempts to find out what happened to them in the war.

“One of those who has been targeted is Angus Parker... who is now showing the symptoms of Gulf War syndrome... visited London to be assessed. As he left, he was followed into a nearby café by a man in a suit.

“The man... knew Mr Parker was going for a medical (and) asked the veteran whether he intended to make any more information public, and refused to identify himself.

“An argument ensued, and the investigator left. The ten days later, he reappeared, following Mr Parker outside his home in Newcastle upon Tyne.

“(The Defence Minister) has agreed to meet Mr Parker at Westminster today, when the matter will be discussed”.

Gulf war illness

Why it took so long to decide to investigate.

Peter Beale (Chief medical adviser, British Red Cross Society)

*BMJ* 5 April 1997:314:1041

“The Gulf conflict in 1990-1991 itself was short, casualties mercifully few, and the sickness rates were unremarkable.

“At that stage, little evidence existed of psychiatric illness.

“Some 18-24 months later, however, we became aware of a campaign by lawyers to recognise a specific Gulf illness.

“A preliminary paper in the summer of 1996 concluded ‘From our small database it would not appear that there is a unique cluster of symptoms which would suggest a new pattern of illness in veterans’.



“There was, however a higher than normal incidence of psychiatric..., disorder”.

US cash for study of Gulf victims

Jeremy Laurence. *Independent*. 4” June 1997

“The biggest study of the health of Britain’s armed forces, paid for with \$1 million from the Pentagon begins this week in an attempt to settle the question of whether Gulf war syndrome exists.

“The Pentagon-funded study is being led by two specialists in unexplained syndromes at King’s College Medical School, London.

“Professor Tony David, a neuropsychiatrist who is leading the study with Professor Simon Wessely, an expert in chronic fatigue syndrome, said the toughest task had been to design a questionnaire that servicemen and women would want to fill in.

“Professor David said: ‘We have complete academic freedom — that is written in stone’.

“An independent advisory committee found little evidence that exposure to chemical weapons was the cause of health problems and concluded that the stress of combat was probably to blame”.

Gulf War Illnesses are not all in the minds of veterans, says US report Cesar Chelata, Michael McCarthy. *Lancet* June 21, 1997:349:1817

“There is substantial evidence linking nerve gas and other chemical and biological weapons to an array of health problems experienced by Gulf War veterans. This is the main conclusion of a report released this week by the General Accounting Office, the investigative arm of the US Congress.

“This contradicts Pentagon findings and those of a special White House panel, that concluded Iraqi chemical and biological weapons were not responsible for veterans’ health problems and that symptoms were probably the result of wartime stress.

“The Presidential Advisory Committee on Gulf War Veterans’ Illnesses has responded with a harsh 10 page rebuttal, which charges . . .that the report is riddled with factual errors”.

Gulf War syndrome: is it due to a systemic shift in cytokine balance towards a Th2 profile?

Graham A W Rook Alimuddin Zumla *Lancet June 21, 1997:349:1831-1833*

“Patients with chronic fatigue syndrome have an increased frequency of allergic events, twice the usual rate of allergic skin reactions, low natural -killer cell activity, and low production of interferon gamma and interleukin-2. Mood swings and depression are common among such patients.

“These characteristics are compatible with a Th1 to Th2 switch in cytokine profile.

“Gulf War syndrome may represent a special case of chronic fatigue syndrome, in which the Th2-inducing stimuli can be identified because Gulf War veterans were given multiple Th2-inducing vaccinations.

“... a long-lasting systemic cytokine imbalance can occur., in the general population as a result of . . . Th2-inducing environmental stimuli and infections, which may account for the frequency of chronic fatigue syndrome.

“Potent immunogens can have systemic long-lasting non-specific effects on the nature of the immune response to unrelated antigens.

“Our hypothesis provides an explanation for the diversity of symptoms as seen in Gulf War syndrome and chronic fatigue syndrome.

“A systemic shift in the Th1 / Th2 balance towards Th2 will lead to an increase in diseases that are exacerbated by diminished Th1, diseases mediated by increased Th2, and mood disorders attributable to neuroendocrine changes.

“These effects can explain the diverse nature of Gulf War syndrome, because the signs of the syndrome will vary between individuals and will also depend on other genetic and environmental factors”.

#### Gulf War Syndrome: all in the mind's eye

Elaine Showalter *Independent, 2<sup>nd</sup> August 1997*

American Elaine Showalter seems to be a staunch Wessely advocate (see below in the section on Wessely's influence).

In this virtually full-page article, she promotes the Wessely view.

“The real gulf in this illness is the one between alleged causes and proven effects.

She quotes from a study published in 1996 by former Medical Assessment Programme (MAP) director Group Captain Bill Coker in the *Journal of the Royal Naval Medical Services*, which concludes “The non-specific, multi-system nature of many veterans' symptoms is compatible with many of the manifestations of psychological stress”, and

Showalter then triumphantly claims “The import of Group Captains Coker’s original study is therefore the opposite of what the veterans wanted to hear”.

She then proclaims that there is no evidence to implicate either nerve gases such as sarin, or the multiple vaccinations the troops received, and states that the evidence about pesticides (organophosphates) is just as weak.

She states “A huge problem with most Gulf War illness stories is that symptoms are self-reported”.

Showalter concludes “We have seen virtually identical patterns of delayed illness after every modern war, caused by the after-effects of anxiety and stress. Until we can create an environment of respect. ...for psychologically caused illnesses... . Gulf War syndrome will continue to spread”.

*(Note that Elaine Showalter is not a medical doctor nor a scientist, but a teacher of English in America; she is an acknowledged self-publicist).*

#### Stress did not cause Gulf war illnesses

Andrew Watterson. *Independent*, 5<sup>th</sup> August 1997

In response to the above article by Elaine Showalter, Professor Watterson pointed out that contrary to Showalter’s claims, there is plenty of evidence showing a range of organophosphates cause neurological damage.

“One ‘knee-jerk’ official response to any report of illnesses due to chemical exposures has... been that workers are “stressed” or hysterical, and that the problem is psychological and not physical; hence the cases cannot be the fault of employers or governments who regulate such chemicals.

(Stress) may well be an easy and neat excuse for those governments wanting to avoid explaining what did happen in the Gulf and why many people serving there reported symptoms consistent with chemical poisoning”.

#### Identification of Gulf War Syndrome: methodological issues and medical illnesses

Victor Gordon. *JAMA August 6, 199 7:278:6:383*

Dr Gordon, from the Veterans’ Affairs Medical Centre, Manchester, NH, USA, makes the point that

“Many veterans in my group developed high intolerance to chemicals existing in the surrounding environment (and) experienced the onset of new allergies, including life-threatening reactions to bee stings.

“... psychological stress frequently is invoked as the cause of... unexplained illnesses

(but) many veterans deny experiencing any psychological stress.

“I have difficulty accepting psychological stress as the common denominator of all the illness in Persian Gulf veterans receiving my medical care”.

### Gulf War! 1998

Is the Gulf War syndrome an immunologically mediated phenomenon?

EDITORIAL: Graham AW Rook; Alimuddin Zumla. *Hospital Medicine*  
*January 1998;59:1:10-11*

This is a paper explaining the basis of the authors' 1997 paper (*see page 153 above*); it describes the roles of T (helper) Th-1 lymphocytes (which release interleukin-2 (IL2) and interferon gamma: their function is the activation of macrophages and cytotoxic T cells that together constitute cell-mediated immunity (CMI) ) and Th-2 lymphocytes (which in contrast release IL-4 and other cytokines associated with antibody production).

The authors note that the seemingly heterogeneous cluster of symptoms found in Gulf War syndrome and also in chronic fatigue syndrome can in fact be attributed to a single underlying immunological imbalance, and that the key may be the balance of Th-1 to Th-2 lymphocytes.

There are similar findings in patients with on-going allergic reactions, which also occur in patients with on-going Th-1 -mediated immune reactions when that reaction is failing, as in late stage melanoma or tuberculosis.

The authors state that psychological and physical stressors induce increased cortisol levels, and T lymphocytes recruited in the presence of such cortisol levels tend to become Th2.

The maintain that such a shift of cytokine balance would, on recent evidence, cause prolonged effects which would still be demonstrable months or years later.

Rook and Zumla conclude that “A subset of Gulf war veterans may be suffering from a syndrome brought on by a massive and persistent Th1 -> Th-2 shift. This is manifested in individuals with the appropriate genetic and immunological background as increased allergic symptoms”.

The authors believe that in other subgroups, this is shown as a mild (Th-1 mediated) defect in CMI.

These effects result in a variety of manifestations, the most common of which is the prolongation of the time required to eliminate persistent viruses.

The authors state that the mood changes which are often reported can be accounted for by secondary effects on the HPA axis, which is very sensitive to changes in the balance and rhythm of cytokine production, and to cytokine-induced changes in the metabolism of glucocorticoids.

Gulf War Syndrome again linked to CFIDS  
*CFIDS Chronicle January/February 1998:30*

This news item records that at a meeting of Veterans' Affairs Gulf War Expert Scientific Advisory Committee on 18<sup>th</sup> November 1997, Dr Reeves of the CDC (one of the authors of the current CFS criteria) presented data linking CFS with GWS:

"CFS illustrates an ill-defined condition which is virtually identical to the sort of illness that several research groups have identified as affecting large numbers of Persian Gulf War veterans"

Dr Reeves also announced that the National Center for Health Statistics (NCHS) is considering creating an ICD-9 code for CFS (code to be 780.71).

Gulf War / 1999

No such thing as Gulf War Syndrome, says official report  
 Jo Revell. *Evening Standard, Friday 15 January 1999*

"There is no such condition as Gulf War Syndrome, the authors of the most comprehensive study ever carried out into illness among the veterans stated today.

"It is impossible to point to a single factor which has caused it, according to researchers at King's College School of Medicine., in London.

"Although Gulf War veterans suffered a two-to-three-fold increase in symptoms, there was no one factor that increased the likelihood of illness.

"Professor Simon Wessely of King's College said 'Modern warfare is extremely hazardous physically and psychologically. There is no single cause, and attempts to look for (one) are not going to succeed, I believe'.

"The new study contradicts one from the Centres for Diseases Control (CDC) in Georgia, which was hailed last September as a 'breakthrough' by Armed Forces Minister Douglas Henderson".

Agony of the Gulf Veterans

Mark Reynolds. *ibid*

“For the many British veterans of the conflict in the Middel East, the news that experts at King’s College have concluded that Gulf War syndrome does not exist comes as a bitter blow.

“Shaun Rusling... Chairman of the National Gulf Veterans and Families Association. said he is certain that its only. a question of time before the

Government will have to acknowledge that Gulf War Syndrome is a real phenomenon.

““Since the end of the conflict, 400 veterans have now died... there have been suicides, chemically-induced cancers and ischaemic heart disorders. These are mainly physical illnesses in previously extremely fit men’.

“Shaun believes the new report is ‘a complete sham’, and a continuing effort by the Ministry of Defence to cover up the existence of Gulf War Syndrome. The study was funded by the US Ministry of Defence.

““Basically in compiling this report they have only sent questionnaires to veterans who are not suffering.

““I’ve not received one epidemiological study to fill in, and the forms were not sent to any Gulf War veterans who are actually ill’.

““It really is a complete sham””.

Bridging the gulf war syndrome

Stephen E Straus (*Wessely’s ever-supportive colleague from the US*).

*Lancet January 16, 1999:353:162-163*

“Over 50,000 British, Canadian and American troops returned from battle as changed men.

“Specialised research units were commissioned and the best medical minds were enlisted to study these men.

“Some reports claimed that the fear of injury and exposure to poison gas had emotionally crippled these young men.

“The year was 1918.

“...reports of ill veterans (of the Gulf War) precipitated rancorous debates as to the nature

of the “Gulf War Syndrome” and whether it was being responsibly addressed. Several scholarly committees... advised targeted research funds... Two papers in this issue of *The Lancet* are products of that research enterprise.

“The primary paper, by Catherine Unwin and colleagues (*Simon Wessely and Anthony David*) is one of the most definitive epidemiological studies of Gulf War veterans conducted to date. (*cf what Straus said in support of the joint Royal Colleges’ report CR54 on CFS: see page 50 above*).

“The dominant finding was that the Gulf War veterans were roughly twice as likely as members of the other military cohorts to report chronic fatigue, irritability, headache and other symptoms, which were remarkable similar to those reported after the Great War. The Gulf War veterans also showed higher levels of psychological distress.

“... in the aggregate (symptoms) did not lead to higher levels of divorce or unemployment.

“Unwin and colleagues’ report, however, does show that the increased risk of developing chronic illnesses with... psychological features extended to all branches of the military. Moreover, the risk of illness correlated significantly with risk of potentially harmful exposures.

“Among these factors, vaccination..., correlated highly with illness. The investigators speculate that these vaccines..., had unanticipated effects. For instance, knowing that one is being prepared for biological warfare is frightening”.

Straus note that the accompanying paper by Ismail et al (ie. *Simon Wessely and Anthony David*) used factor analysis to reveal categories of symptoms that best define and contribute most to the severity of an illness; Straus compares the Ismail study with one by Fukuda et al in 1998 and claims that both studies found that a unique Gulf War syndrome could not be found.

“The cumulative studies now confirm that there is no unique Gulf War syndrome.

“... the Gulf War seems to differ from others only in a quantitative sense and in the intensity of the public debate about it.

“There were highly prevalent exposures that, together with the fear of injury and death... made service in the Gulf more hazardous than the mere ‘body count’ would suggest. Perhaps it was that very lack of mutilation and death in that war that permitted the true... emotional costs of battle to be revealed.

“Military scientists ... need to undertake prospective studies to define the preexisting attributes of an individual.. .that correlate most to the risk of long psychological illnesses”.

Health of UK servicemen who served in Persian Gulf War

Catherine Unwin, Nick Blatchley, William Coker, Susan Ferry, Matthew Hotopf, Lisa Hull, Khatida Ismail, Ian Palmer, Anthony David, Simon Wessely.

*Lancet* 16 January 1999: 353: 169-178

*Catherine Unwin co-ordinated the study; William Coker and Ian Palmer are grant holders and provided military advice and liaison; Lisa Hull traced veterans; Khalida Ismail did the follow up study; Susan Ferry was the initial study coordinator; Matthew Hotopf gave epidemiological advice and was involved in the writing of the paper. Anthony David and Simon Wessely were the principal investigators and planned, designed and supervised this study, as well as drafting the paper.*

This study claims to have compared the health of Gulf War veterans, servicemen deployed in Bosnia and servicemen who served in the Gulf but were not deployed there.

Significantly, the authors acknowledge that “Adjustment for possible confounders and psychological disorders lessened the association for symptoms in the Gulf War cohort”.

Also significantly, the authors state “We present logistic regression results for only the 15 most reported symptoms and complaints”.

*(Does this not dilute the validity of this study: for example, severe neurological dysfunction was not in the authors’ selection of the 15 “most reported symptoms”, all of which are non-specific and (with the exception of night sweats) feature prominently in the criteria for psychiatric illness: they are listed as:*

*feeling unrefreshed after sleep; irritability or outbursts of anger; headaches; fatigue; sleeping difficulties; fatigue; joint stiffness; loss of concentration; flatulence; pain without swelling in several joints; feeling distant; avoiding doing things or situations; chest pain, tingling in fingers or arms; night sweats.*

*Perhaps it needs to be recalled that the veterans maintain that no survey forms for this study were sent to any of the severely ill veterans: see page 158 above.*

*Indeed, the authors themselves acknowledge (on page 176) that We have not reported the frequency of disorders such as asthma, neuropathy, (or) chronic fatigue syndrome . . . which require a clinical interview and examination. We did not do physical examinations (as) Gulf War veterans seem to have no increased rates of defined physical disorders that might explain increased symptom reporting”).*

The authors state that they reported associations with exposures (including petrochemical, smoke from oil-wells, pesticides, paints or solvents, dismembered bodies etc) only for self-reported physical health, the COG syndrome, and post-traumatic stress reactions, and that they found an association with the *belief* of exposure to a chemical attack.



The authors state that multiple vaccinations were associated with poorer health after control for deployment, and that veterans who recalled experiencing side-effects to the vaccinations were more likely to have current symptoms.

The authors conclude that UK veterans of the Gulf war have” a decreased perception of well-being than servicemen who were not deployed in the Gulf War, despite... no excess of objective outcomes, such as birth defects, cancers or death”.

“Disability was not severe, and there is no evidence of an increased rate of adverse outcomes such as unemployment or marital breakdown.

“Nevertheless, we believe that our data constitute firm evidence that service in the Gulf War has affected the health of servicemen.

“...psychological mechanisms should be taken into account that are consistent with our data, for example, symptoms experienced acutely after vaccination could generate health anxiety and (could) prime recipients to detect similar generalised symptoms occurring later.

“We prefer to broaden the definition of stress.., the mechanisms linking (the exposures which occurred in the Gulf) to ill health might not be specific. One pathway could involve perceived risk and later ill health. We suspect that the threat of chemical attack was one such exposure recall bias in which servicemen with more symptoms recall more exposures may be a further general link.

“A fuller understanding of why service in the Persian Gulf War was associated with a definite decline in general well-being will come from assessment of the effects of... perceived exposure to physical and psychological adversity...”.

#### Is there a Gulf War syndrome?

Khalida Ismail, Brian Eveitt, Nick Blatchley, Catherine Unwin, Anthony David Simon Wessely. *Lancet January 16, 1999:353:179-182*

The stated aim of this study was to investigate whether the pattern of symptom reporting by Gulf War veterans differed from that of active servicemen who had not fought in the Gulf War or who had fought in other conflicts.

The authors claim that in their first paper (*see above*), they used the empirical approach with epidemiological evidence, but an alternative approach is an analytical one by factor analysis.

They identified three factors: factor 1 was mood / cognition (headaches, irritability, sleep difficulties, feeling jumpy, unrefreshing sleep, fatigue, feeling distant or cut off from others, forgetfulness, loss of concentration, avoiding doing things or situations); factor 2 was respiratory symptoms (inability to breathe deeply, fast breathing, shortness of breath at rest, wheezing) and factor 3 was peripheral nervous system (tingling in fingers or arms,

tingling in legs or arms, numbness or tingling in fingers or toes).

“Whether these three factors we analysed represent conventionally defined psychiatric disorders such as depression, anxiety, posttraumatic stress disorder, chronic fatigue syndrome, (or) a variety of these... cannot be inferred from our data.

“The three factors will require validation against criterion measures for recognised psychiatric... disorders.

“Although illness reporting was more common among men who served in the Gulf War, our evidence did not support the existence of a unique Gulf War syndrome”.

#### Gulf war syndrome

EDITORIAL: Frances M Murphy. (Department of Veterans Affairs, Washington DC) *BMJ*. 30 January 1999;318: 274-2 75

This editorial supports the views of Stephen Straus and basically accepts the Wessely et al findings that there is no such thing as Gulf War syndrome:

A well-focused, co-ordinated UK Gulf health research programme, overseen by the Medical Research Council... has been developed (which) failed to identify a unique illness among Gulf War veterans.

“A growing consensus is emerging from the clinical and epidemiological evidence that there is no Gulf War syndrome.

“There is now a growing awareness in military medicine that in future wars combat, casualties often will not have visible wounds”.

#### Call for inquiry on Gulf War illness

Letter signed by Colonel TH English. (*Controller Welfare, Royal British Legion*); the Countess of Mar et al. *limes*: 18 February 1999:23

“Negative publicity following the publication in January of the initial findings of two medical studies that have discounted the existence of Gulf War syndrome is causing alarm among veterans and serious concern for The Royal British Legion and the Gulf War parliamentary group.

“The Legion is still waiting for a response from the Prime Minister to the demand for a public inquiry into Gulf War illnesses, and the need for one is ever more urgent in the light of the results of the medical studies announced by Professor Simon Wessely....

“...we share the veterans’ grave concerns that publicity about the absence of a syndrome

could obscure the full extent and seriousness of their ill-health.

“The time for decisive action is now. For many it is too late”.

Genetic link in Gulf War syndrome

Cherry Norton. *Independent* 18 June 1999.

“Research published this week from the UT Southwestern Medical Center in Dallas reveals that some veterans of the Gulf War may have suffered from certain chemical exposures while others did not because of variations in a gene known to produce an enzyme which destroys the damaging chemicals.

“Now the Dallas researchers believe they have established why one person became ill while the person next to him didn’t.

“‘This is one of the major puzzles that made many people think the symptoms were just due to stress’ said Dr Robert Hayley, head of epidemiology at the centre and co-author of the study.

“‘Now we know that there appears to be a genetic reason why some people got sick and others didn’t, and this genetic difference links the illness to damage from certain chemicals’.

“The researchers have found that people with a gene that causes them to produce high amounts of a particular enzyme did not get sick after exposure to certain chemicals... while others who produce low amounts of the same enzyme did get sick.

“The gene controls the production of an enzyme called PON-Q, which eats up pesticide chemicals such as organophosphates, and makes them harmless.

“In some people the gene produces high levels of PON-Q which allows the body to fight off these poisonous toxins, but in others, the levels produced are too low.

“Professor Simon Wessely, consultant psychiatrist at King’s College Medical School and author of the British research questioning the existence of a Gulf War syndrome said...

‘We and other groups are also looking at this particular gene because it is known to produce enzymes which eat up organophosphates and make them harmless. We did not find a unique illness called Gulf War syndrome. If there is a genetic basis it will only apply to certain people in certain conditions’ he said.

“‘Genes may provide a couple of pieces of the jigsaw but they will not provide the full picture. These are preliminary findings and we need to know whether this can be replicated by other groups’”.

Gulf health research — past, present and future

Nicola J Stimpson Hollie V Thomas. *JRSM September 1999;92:476-477*

This is a brief report on a meeting held at the Royal Society of Medicine to hear of new findings and debate the direction of future Gulf health research.

Professor Simon Wessely highlighted the value of historical enquiry into war syndromes in general.

“A primary concern... is to ascertain whether the illnesses are related to a general exposure to war or to the specific exposures with the Persian Gulf.

“Captain Greg Gray of the Naval Health Research Center, San Diego... doubted whether any single wartime exposure was responsible for the increase in symptoms, which was more likely to be due to the aggregate stressors of war”.

*As the Lancet Editorial pointed out after the publication of the joint Royal Colleges' report CR54 on CFS I ME: 'Psychiatry has won the day for now' (see page 62 above): such is the extent of Wessely's power and influence that, in the UK at least, it seems to be winning the day with Gulf War syndrome also.*

**The organophosphate Issue**

Although ostensibly not personally involved in the report of the joint working party of the Royal Colleges of Physicians and Psychiatrists Organophosphate sheep dip: clinical aspects of long-term low-dose exposure (November 1998 / CR67), Wessely's influence shines through, and it is the case that a large number of the 85 references are his or those of his close colleagues.

It is also the case that Wessely's regular collaborator Professor Anthony David was a member of this working party, as was Emeritus Professor P.K.Thomas.

*(This is the same P.K. Thomas who, with Wessely, published a chapter on ME in a major textbook of clinical neurology, stating “A number of patients diagnosed as having.. .myalgic encephalomyelitis were examined. In many of them, the usual findings of simulated weakness were present ME may have resulted from altered medical perception. . .efforts are often made to over-interpret laboratory findings.... Over-spousal of new illness.. .can be harmful.. .it may legitimise maladaptive behaviour”<sup>58</sup>*

It is a matter of note that the 1996 findings of Professor Peter Behan linking ME / CFS to chronic low dose organophosphate (OP) exposure<sup>59</sup> were excluded from the report's references, given that Behan found CFS to be clinically identical to chronic low-dose OP

exposure and that such OP exposure “in some way prepared the patients for the later development of CFS” and that the abnormalities found in both CFS and OP poisoning “is compatible with a decreased responsiveness of CNS type II glucocorticoid receptors, (confirming) the, hypothesis of brain steroid receptor resistance in patients with the delayed response to OPs and in CFS”.

Before publication of this joint Royal Colleges’ report on OPs, the Countess of Mar made two important contributions:

<sup>58</sup> The chronic fatigue syndrome — myalgic encephalomyelitis or postviral fatigue. *Wessely S, Thomas PK In: C.Kennwd (ed): Recent Advances in Clinical Neurology No 6. Churchill Livingstone 1990: 85-13.2*

<sup>59</sup> Chronic Fatigue Syndrome as a Delayed Reaction to Chronic Low-dose Organophosphate Exposure. *Peter O.Behan. J Nutrition & Environmental Medicine 1996:6341-350*

- (i) on 24<sup>th</sup> June 1997 she rose in the House of Lords<sup>60</sup> ask Her Majesty’s Government how members of the advisory committees concerned with the licensing and use of OPs are selected for appointment and whether HMG is satisfied that the advice received is, in every respect, impartial.

Lady Mar pointed out she was not certain that the Government’s advisory committees were at all “independent” of the industry which they were set up to regulate and that in many cases, members of advisory committees will have come from the chemical companies and will return to the industry.

Lady Mar further pointed out that the scientific community is very close knit, with specialist members all knowing each other and all being dependent upon one another for support, guidance, praise and recognition.

In her speech, Lady Mar said “My Lords, those who believe their health has been damaged by OPs and others who are working with them have the distinct impression that the establishment is demonstrating a distinct unwillingness to accept the evidence of hundreds of published scientific papers and thousands of individuals who are ill after using OP pesticides.

“Members of advisory committees... will be involved with colleagues who are dependent upon chemical company research funds for the continuation of their departments... Is it unreasonable to suggest that... these people may be influenced by the pressure put upon them by their need to ensure the viability of their faculties?

“Once a licence has been granted for a product, it is contrary to human nature to expect that either the licensing authorities or the manufacturers will willingly admit that they have failed to detect effects which subsequently come to light, for to do so is likely to result in huge compensation claims.

“...there is also an inherent bias in that human nature decrees that arbiters tend to

favour their own judgment and resist the opposite view.

“OP victims are tired of, and distressed by, a medical profession which tells them that they should see a psychologist... simply because the medical profession is confounded by the multitude of symptoms with which their patients present, and there is no easy explanation in the medical literature and no clear lead from the Department of Health”.

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<sup>60</sup> Hansard. House of Lords. Organophosphates. 24 June 1997:1555 . 1568

- (ii) on 30<sup>th</sup> June 1997, Lady Mar presented her evidence in person to the joint Royal Colleges’ working party on OPs, in which she said as follows:

“... the failure of most ... medical practitioners, whether they be GPs or consultants, to recognise that their patients may have an illness which cannot be attributed to an accepted cause, has been the driving force behind my requests to the Government, repeated regularly in the House, in correspondence and at meetings, that specialist centres be established to diagnose and treat patients suffering from chemical exposure.

“What we need to understand is that in the last 40 years there has been an enormous increase in the number of chemicals to which human beings are exposed. They may not show toxicity on their own, but they would appear to do so in combination.

“Many of these chemicals are licensed products and have been presumed by the public to be safe.

“On 11 July 1996 I tabled a question asking to which specialists those who believed they had been exposed to OPs were referred.

“Baroness Cumberledge... advised me that she had sent the Chief Medical Officer to see the Presidents of the Royal Colleges of Physicians and Psychiatrists and that they had agreed to set up a working party to look into diagnosis and treatment.

“With the greatest respect to members here, the Working Party as presently constituted and its terms of reference are not in accord with the objectives behind my request.

“The first Term of Reference is ‘To advise on clinical management of patients with symptoms which may be attributable to chronic OP exposure’. If this is to be an objective, then surely there should be practising physicians... with experience of seeing patients in this category on the Working Party. How many members have this clinical experience?

“In her reply to me, Baroness Cumberledge assured me that you would see anyone I wished you to see.

“I understand that you have declined to see at least two of the people I have

recommended.

“If you are not prepared to see those who have a record of success with treating patients... and none of you has the relevant expertise, how are you going to advise on the clinical management of patients?”

“The second Term of Reference: to review any new clinical evidence and to bring it to the attention of the Medical and Scientific Panel of the VPC (*Veterinary Products Committee*) is an irrelevance. The Panel is, or should be, under its own terms of reference, well aware of all new evidence. The presence of three members of the Medical and Scientific Panel on this Working Party would also make the need to advise the Panel unnecessary.

“In addition to this, I believe that this is a Department of Health matter.

“I raised the question with a Minister of Health and the reason was because both GPs and consultants were failing OP sufferers.

“Why then are not your Terms to advise the Department of Health or the Chief Medical Officer?”

“What you seem to be totally unable to understand is that this Working Party, as presently constituted, does not have the trust of those it was set up to serve— the patients.

“They have learned to question decisions, and experience has taught them that the doctor is not always right.

“I have already voiced my doubts about the need for members of the Medical and Scientific Panel to be on the Working Party, and I cannot see that a Professor of Morbid Anatomy, who has made public his antipathy to the problems suffered by sheep farmers and others exposed to OPs can give a balanced judgement.

“What additional contribution will two members whose speciality is epidemiology in the field of psychiatry be able to make?”

“We know that OPs affect proteins in the brain. Would it not have been advisable to have a specialist in this field, or are you already of the opinion that our symptoms are caused by socio-economic problems?”

“Why, too, do you need two neurologists and two psychiatrists when it is known that OPs affect the heart, lungs, and immune system, for example? There must be specialists in those fields who would be able to offer their services.

“I know that what I have had to say is likely to make some of you feel the hairs bristle, for you are “experts”.

“What I am saying is that you are not the *only* experts.

“It would have made a great deal of difference to your credibility as a deliberative body had you selected individuals with the appropriate expertise and without any prior association with the matter in hand.

“It is my understanding that you deliberately did not select the two consultants who have probably seen more patients exposed to OPs than anyone else in the UK because they would have “preformed opinions” and you wanted to avoid bias.

“This I could accept if you had not selected others who are known to have opinions on the subject and who also might be said to have reasons to obstruct a quick resolution of the suffering being endured by so many.

“There are two ways forward. The Working Party could be reconstituted so that its membership has no connection with... the bodies who advise Government... and who have no links with the manufacturers of OPs.

“The deliberations could then be seen to be both independent and impartial.

“They would be expected to hear evidence from all those who have developed expertise in these fields, whether or not their faces fit in the establishment... it is his or her clinical management you are considering.

“I have long experience and, far from being cloistered in the Palace of Westminster, I do have many personal contacts and I receive letters from all parts of the UK

“I would ask you not to underestimate the intelligence or the power of the sufferers and their relatives. I never cease to be amazed by the vigour and basic common sense they apply to their researches.

“I ask you, on their behalf, to give serious consideration to what I have said today and to act to erase the impression of a lack of balance, if not bias, in your dealings”.

HEALTH: Are we having allergic reactions to our greenhouses? Dr Richard Horton.  
*Observer Life*, 3 August 1997:41

Picking up on the Countess of Mar’s approach, Richard Horton (editor of *The Lancet*) made some salient observations:

“OPs are currently the focus of intense scrutiny by a committee created at the behest of the chief medical officer Sir Kenneth Calman at the department of Health.

“This working party is organised by the Royal Colleges of Physicians and Psychiatrists and its remit is to focus on ‘new clinical evidence’, management of ‘patients with



symptoms which may be attributable to chronic OP exposure' and the prospects for any future research.

"All together there are ten members, including six professors.

"A committee with such a distinguished provenance would seem immune from criticism. Far from it. Not one of its members has direct experience of looking after patients exposed to OPs.

"Even more odd is why a working party exists at all.

"Only recently the Government allocated £500,000 to two research teams in Edinburgh and Glasgow to study the effects of OPs on the community as well as in individual cases.

"The committee's conclusions therefore are bound to be based on wholly incomplete evidence.

"There is another, even more troubling matter. It is common in the UK for important investigations to be held in secret.

"We have seen such closed deliberations become the hallmark of science in the public domain, whether we are discussing Creutzfeld-Jakob disease or chronic fatigue syndrome.

"In America, such proceedings are entirely different. Sensitive investigations that have vast implications for those who are ill are held in both open and closed sessions. Journalists are present.

"Pompous and complacent scientists are *seen* to be pompous and complacent. The committee becomes accountable to the public in a very public way".

REPORT: Organophosphate sheep dip. Clinical Aspects of Long-term Low-dose Exposure. Report of a joint working party of the Royal College of Physicians and Royal College of Psychiatrists. November 1998 / CR67

*The Report makes it plain that the selection of the members of the working party, its activities and the production of the Report took place under the auspices of the Royal Colleges.*

This 53-page report carries unmistakable shades of CR54 on CFS / ME, but it does have to concede that "Existing NHS clinical services do not, in the main, provide satisfactory management for those with symptoms associated with OP sheep dip exposure" (paragraph 5.12).

As anticipated, however, the authors attempt to diminish the severity of the physical

symptoms. For example: “Abnormalities identified in some - but not all - studies include subtle cognitive impairment (eg. impaired attention and reaction times), greater psychiatric morbidity and minor sensory changes”).

Under Analysis of clinical symptoms, the Report states “Other possible explanations for the symptoms are naturally-occurring illnesses, for example, severe anxiety or depression, which have been intuitively attributed by the sufferers to OP exposure” (page 2).

Unsurprisingly, the authors do not fail to suggest that in the working party’s opinion, previous studies of the effects of OPs “suffer from a number of methodological weaknesses such as small numbers (*one of Wessely’s own 1989 studies used only 47 CFS<sup>61</sup> patients; another used only 32 CFS patients<sup>62</sup>; another used only 12 CFS patients<sup>63</sup> in another study<sup>64</sup>, only 10 patients were used; and in another study<sup>65</sup> only 9 patients were used; in Sharpe’s study<sup>66</sup> only ten men were used, yet no-where does this group criticise their own colleagues’ use of “small numbers” as “methodological weakness” and they draw conclusions from their own small studies which they themselves promote as ‘evidence-based’*) poor response rates (*their own response and drop-out rates are significant*) selection bias (*their own studies acknowledge their own selection bias — see page 114 above*) and inappropriate or questionable control subjects, all of which could affect the outcome of the study” (Summary, page 1). (*It is notable that these authors are eager to cite limitations which they claim as detractors from others’ work when they do not acknowledge exactly the same limitations as detractors in their own work*).

<sup>61</sup> Fatigue syndromes: a comparison of chronic ‘postviral’ fatigue with neuromuscular and affective disorders. S.Wessely R.POWeU. *JNNP* 1989;52:940-948

<sup>62</sup> Low dose hydrocortisone in chronic fatigue syndrome - a randomised cross-over trial. Anthony Cleare, Simon Wessely et al. *Lancet February 6, 1999;353:455-458*

<sup>63</sup> Vitamin B status in patients with chronic fatigue syndrome. LC Heap, TJ Peters, S Wessely. *JRSM* 1999;92:183-185

<sup>64</sup> Salivary cortisol profiles in chronic fatigue syndrome. Wood B, Wessely S et al. *Newcastle Journal of Medicine* 1998;373:1-4

<sup>65</sup> Neuroendocrine responses to d-Fenfluramine and Insulin-Induced Hypoglycaemia in Chronic Fatigue Syndrome. Jenny Beam, Simon Wessely et al. *Biol Psychiatry* 1995;37:245-252

<sup>66</sup> Increased brain serotonin function in men with chronic fatigue syndrome. M.Sharpe et al *BMJ* 1997;315:1644-1645

### The Report's Recommendations

In the section on Diagnosis, the Report once again urges against “over-investigation”: “The temptation to over-investigate should be resisted, since it may increase the sufferers anxiety, and may bias the consultation towards a narrow physical orientation” (page 30, paragraph 6.8).

In the section on Management, the inevitable conclusions from this group are to be found:

“Although some sufferers were helped by treatment strategies offered by NHS practitioners or by those in the private sector... there is currently no objective evidence-based Justification for their use” (page 2)

“The clinical symptom pattern... has some common elements, but these are diagnostically non-specific” (page 32).

“Multiple referrals from specialist to specialist create their own problems for patients, and may increase anxiety or incur considerable expense” (page 2).

“The management plan does not need to presuppose a particular aetiology” (page 33).

“We can... extrapolate . . . from the management of other poorly understood medical syndromes such as Irritable bowel syndrome, tension headache, fibromyalgia and chronic fatigue syndrome.. treatment plans must be... agreed between patients and therapist” (page 33).

The section on Treatment is entirely predictable:

“....cognitive behaviour therapy has proved relatively effective in such conditions” (page 3).

The authors urge the use of “....antidepressants as well as cognitive behavioural techniques to counteract beliefs and subsequent behaviours which may develop (and which may serve to perpetuate it)” (page )•

“For an OP related illness... an initial trigger... activates a vicious circle of fatigue, sensory symptoms and disability which then become self-maintaining. A combination of variables influence both development and maintenance, including.., illness beliefs and fears about the meaning of symptoms... “(page 34).

“For chronic unexplained medical conditions, one useful set of techniques known as cognitive behavioural approaches offer an excellent basis for management... it is based upon the model of the condition which distinguishes between precipitating and perpetuating factors” (page 35).

“Antidepressants have proven effective in a wide range of somatic disorders” (page 35).

“in practice, treatment entails ... identifying and modifying illness beliefs, fears and anxieties that may prolong disability” (page 36).

“Favourable outcome with cognitive behaviour therapy has been reported in several recent treatment studies of patients with medically unexplained symptoms” (page 37).

“Such treatments... represent a considerable step forward in the rehabilitation of patients with chronic fatigue syndrome” (page 37).

“It is... important to ensure that family members or carers are aware of the rationale and the aims of treatment, otherwise they may inadvertently be reinforcing unhelpful coping strategies” (page 37).

In the section entitled “Strength of attribution”, the authors state:

“Where a person believes in a particular cause for their state with passionate conviction, it may be difficult if not impossible to open a dialogue... attributions which are clear-cut and focus on purely physical explanations occasionally fall into this category” (page 39).

“Previous experience from studies of individuals with concerns about allergies... suggests that avoidance ( of the situation or substance believed to be harmful) is a potent source of secondary disability and prolonged ill-health” (page 39).

‘An individual reluctant to come into contact with OPs should be made aware of the ubiquity of OPs in the environment and the impossibility of being totally free of OPs. . . A degree of re-exposure is therefore inevitable” (page 39).

“...the patient can be invited to entertain the possibility that whatever caused the initial illness may be quite different from factors which perpetuate it. Hence fear of recurrence of symptoms, feelings of hopelessness and lack of control, anticipatory anxiety, conditioned responses etc may all be possible explanations for supposed ‘hypersensitivity’ or ‘recurrence on re-exposure’” (page 39). In the Summary of this section, the authors state:

“In the present state of knowledge, an open-minded... approach to management is recommended. This can follow principles used in a range of other poorly understood medical disorders; cognitive behaviour therapy has proved relatively effective in such conditions (and) aims to counteract beliefs and subsequent behaviour which may develop in the aftermath of an acute illness and serve to perpetuate it” (page 40).

In the section Research, the authors recommend:

“...an open treatment trial of a cognitive behavioural approach” and “a randomised controlled trial of antidepressants” (page 44).

At the end of the Report there is a three line paragraph (9.5) which barely mentions the well-known problems of anaesthesia for those with OP exposure:

“Anecdotal evidence for adverse reactions to anaesthetic agents in OP-exposed individuals needs to be verified or refuted. A formal review of exposed people needs to be undertaken...”.

*(This might possibly amount to a charge of scientific misconduct, given that in 1987 Her Majesty's Stationary Office (HMSO) published a Guidance Note MS 17 from the Health and Safety Executive (Medical Series 17) entitled Biological monitoring of workers exposed to organophosphorus pesticides this was originally published in 1981 and was revised in 1986, with a second revision in 1987. It unambiguously states:*

*“acute and subacute exposure to OP pesticides can produce harmful effects in man, and repeated exposure at lower doses may cause insidious cumulative toxicity.*

*“Repeated absorption of small doses, as may occur from contaminated clothing, has cumulative effects resulting in progressive inhibition of nervous tissue cholinesterase.*

*“Symptoms of poisoning include... central nervous system effects (1) depression of the respiratory centre....*

*“There is a series of genetically determined variants of plasma cholinesterase and these may be associated with **increased sensitivity to the muscle relaxant succinyl choline, used by anaesthetists**”.*

*Also in 1987 and again published by HMSO, by command of the Defence Council, the UK Ministry of Defence produced its Medical Manual of Defence Against Chemical Agents (JSP 132). In section 10 (Combined Injuries). paragraph 1002 states:*

*“The dangers presented by this form of combined injury are from the nerve agent itself, from the interaction of respiratory depression... **and from the reduced cholinesterase activity upon the drugs used in anaesthesia** Reduced cholinesterase activity will affect the use of relaxant drugs used during anaesthesia. On basic principles the action of anticholinesterases, including to a lesser extent pyridostigmine pre-treatment, may be expected to potentiate the action of depolarizing relaxants such as succinyl choline, but to oppose the action of non-depolarizing relaxants of the current type”.*

*Further, the Newsletter of The Royal College of Anaesthetists No 25, December 1995 (Supplement) carried on page 9 an item entitled ORGANOPHOSPHATE COMPOUNDS AND ANAESTHESIA in which the editor (John Norman) specifically drew this important issue to the attention of candidates for the Part II examination for the Fellowship and the (then) forthcoming Primary examination; he also pointed out to anaesthetists that Dr M. J. Chapman of the Department of Anaesthetics at Derriford Hospital, Plymouth, has an interest in the topic.*

*Dr Chapman's name does not appear in the list of those who were invited by the joint working party to give evidence.*

*Neither the HSE document nor the MOD document is listed in the references to the joint Royal Colleges' Report on OPs.*

In her response to this report, the Countess of Mar described it as "a very unpleasant suared pill" (see below).

Response by The Countess of Mar to the Joint Royal Colleges' report on OPs Hansard / Lords / 19 December 1998; 1011-1024

The Countess of Mar rose to ask Her Majesty's Government what is their response to the report of the Royal Colleges of Physicians and Psychiatrists-on organophosphate sheep dips.

Lady Mar made the following points:

"The working party comprised 11 members. One of them, Sir Cohn Berry, chairman of the Advisory Committee on Pesticides responsible for licensing OP products and a member of numerous other scientific advisory committess, has publicly stated that those who attribute symptoms to exposure to toxic chemicals have a

'desire for attention, the comfort of being able to abdicate responsibility for one's failings by ascribing them to an illness, the luxury of receiving therapy, the excitement added to a humdrum life by weird beliefs about one's past, the propagation of stories produced by hysterics by the niass media, the attempts by therapists to push their clients into revealing multiple personalities, non-existent sexual abuse and even alien abduction in the mistaken belief that such revelations may effect a cure'.

"That statement immediatejy aligns Sir Cohn with another two members of-the working party, both psychiatrists; namely, Professor Anthony David, who works with Professor Wessejy at King's College Hospital, the promoter of this profound assessment of sufferers of complaints such as ME, multiple chemical sensitivity, fibromyalgia and even Gulf War illnesses, and Professor Hawton.

“Dr Bateman is chairman of the Medical and Scientific Panel of the Veterinary Products Committee. His past record appears to indicate that he -has an interest in preventing the admission that OP products have harmful effects on human health.

“Professor Thomas is also a member of the Veterinary Products Committee.

“To have five working party members whose credentials are perceived to include a bias that OPs are safe does not fill one with confidence.

“Who was responsible for setting the terms of reference?

“I made my concerns known to their chairman Professor Newsom-Davies, to the Registrar of the Royal College of Physicians, Professor London and to the Minister for Public Health. I was assured that the members would make an unbiased assessment. I now see that my initial suspicions were correct. This report is a very unpleasant squared pill.

“We are told that... ‘specific symptoms... should be managed vigorously in the usual way: for example, antidepressants as well as cognitive behavioural techniques to counteract subsequent behaviours which may develop in the aftermath of an acute illness and serve to perpetuate it’.

“This is straight from what is becoming known as the “Wessely School”. “The same recommendations were made in the now notorious Royal Colleges’ report on ME and chronic fatigue syndrome.

“Sections 4.5 and 4.10 link symptoms of OP exposure with affective disorders.

“In section 4.9 the group blithely reject the concept of multiple chemical sensitivity on the grounds that most authorities reject its validity for lack of evidence. Since 1987, many US government and state agencies make provision for people who suffer from MCS.

“I also wonder whether the recommendation that the temptation to over-investigate should be resisted on the basis that many of these patients are not found to have abnormalities could be because the right tests are not being conducted in the first place.

“Why should the doctor and patient accept the limitations of scientific knowledge? Who is to say their searches are likely to be futile?

“I simply ask whether we would have been able to cure TB, eradicate smallpox, prevent the infectious diseases of childhood or establish the link between asbestos and lung disease if the medical practitioners of the time had accepted the limitations of scientific knowledge.

“After all the evidence the working party heard and read, where is its natural curiosity?

“It repeatedly mentions that there is a lack of causality, yet it makes no recommendations for causal research. Is this because. .. it does not wish to know?”

“The passage on the treatment of specific symptoms deals only with the affective disorders... There is the inference that the pain., weakness and incontinence described by sufferers are ‘all in the mind’ and can be cured by cognitive behavioural therapy.

“This section has clearly been written by the psychiatrists as there were no clinicians practising in other specialties on the working party. It is also almost a straight lift from the Royal Colleges’ report on ME / CFS.

“In paragraph 7.7 and in the last sentence of paragraph 7.8 we come to the nub of the problem. It is the far-reaching implications for the pesticide industry, for the Armed Forces, the Ministry of Agriculture, Fisheries and Food and the Department of Health, together with the financial and occupational implications which are the working party’s prime cause for concern.

“Antidepressants and cognitive behavioural therapy will have to satisfy the patients.

“The status quo must not be disturbed.

“In the next paragraph (the report) has the audacity to recommend an open-minded, eclectic and pragmatic approach to clinical management, yet it has all too clearly demonstrated how closed its members’ own minds are”.

The Earl of Clanwilliam made the following point:

“Having listened to the noble Countess and her reference to a sugared pill, I can only say that I hope the committee feels duly chastised by her severe, excoriating criticisms of its work”.

Lord Clement Jones observed:

“The remit of the report was extremely limited. Its conclusions were limited, not to say unhelpful.

“The Ministry of Agriculture has known about problems with organophosphates since 1951 when the Zuckerman Committee, under Lord Zuckerman, recommended that urgent research be carried out to replace organophosphates.

“Toxicologists and physicians, and the World Health Organisation, were warning of the consequences of lack of protective clothing as far back as 1957-58. MAFF, needless to say, did not heed any of that at the time and continued not to do so until recently.

“It amounts to a complete failure of risk assessment for those chemicals. “Blame must also be laid at the door of manufacturers.



“In the view of these Benches, the report of the OP group was far too cautious.

“We take very seriously the advice given by Dr Goran Jamal to a briefing of MPs earlier this year. He is a consultant neurophysiologist. He said:

‘I can say with absolutely no hesitation that these products are unsafe’.

“He has pointed to at least 12 studies which show chronic low level damage caused by organophosphates.

“In the field of further research, one of the most worrying aspects... is the omission of any official work on the effect on children. The official OP report did not address, in particular, the question of genetic damage being caused by exposure of mothers to OPs or damage caused by contact with parental clothing.

“There are also implications for children’s headlice treatments using melathion” (*sic*).

Earl Howe made the following points:

“What I found disappointing, indeed shocking, was the not very veiled criticism of the methodology of the epidemiological work which has so far been published. It seemed to me that paragraph 2.26 of the report is about as damning an indictment as there can be in civilised language.

“There is even a suggestion that the interpretation of the results from some of the population-based studies is open to question and that in certain quarters a bias may exist against publishing negative findings.

“The report suggests that anxiety, depression and general frustration are often sufficient in themselves to trigger the symptoms which the patient associates with OPs and — apparently — may also account for reported cases of chemical hypersensitivity”.

Responding for the Government, Baroness Hayman said:

“The report recommends adopting a strategy of supportive treatments because, it says, the principles of rehabilitation following substantial illnesses are similar.

“For the present time, however, I believe that the Royal Colleges’ report offers an opportunity to increase awareness among the medical profession that these patients have genuine needs, and to improve the general level of care that is offered to them”.

Study shows 'OP link' with chronic ill health

Dr Charles Shepherd. *Perspectives - Journal of the ME Association: Autumn 1999: 72: Medical matters (1)*

*(This refers to the study mentioned by the editor of The Lancet — see pp 169-170 above. The UK Ministry of Agriculture, Food and Fisheries, together with the Health and Safety Executive, granted £500,000 to The Institute of Occupational Health (IOM) in Edinburgh to look for signs and symptoms of nerve damage in 612 agricultural workers who had been exposed to OPs. For the Royal Colleges of Physician and Psychiatrists to undertake their own assessment before the findings of this major study were announced is remarkable).*

*Unsurprisingly, the IOM results are very different from the report of the Royal Colleges of Physicians and Psychiatrists.*

“Further evidence of the link between prolonged, low-dose exposure to OP sheep dips and various forms of chronic ill health, including chronic fatigue, appear in a new report from the Institutue of Occupational Medicine in Edinburgh.

“Dr Adele Pilkington, co-ordinator of the study stated that ‘There was quite a strong relationship between exposure to the concentrated form of OP and health effects in terms of both symptoms and clinical signs’.

“Of partcular interest was the fact that a number of those who had been using the OPs developed evidence of a toxic neuropathy (OP-induced damage to parts of the peripheral nervous system which carry sensory information back to the brain).

“Neuropsychological testing of the OP group also revealed increased levels of anxiety and depression.

“...the case for some form of compensation for those affected by OPs grows stronger.

“Professor Liam Donaldson, Chief Medical Officer at the Department of Health, has written to all public health departments to alert them to the contents of the IOM report”.

*(The IOM report costs £132 in several volumes, and is available from 0131 -667-513 1).*

*It will be interesting to see how the “Wessely School” attempts to demolish the findings of the IOM report concerning organophosphates.*

### **Illustrations of Wessely's influence**

*(This was addressed in detail in the original "Denigration by Design?").*

Apart from mutually supportive and similar articles by other members of the "Wessely School" mentioned above, Wessely's influence seems to be determined by the "Topsy" effect: it just grows and grows.

His promotion of graded exercise and cognitive behavioural therapy as catch-all solutions are undoubtedly attractive to a cash-strapped health service, and also seem to appeal to a certain calibre of physician.

For example, an editorial in the *Journal of Psychosomatic Medicine*<sup>67</sup> by Henningsen and Priebe asserts that disorders such as ME / CFS, where the patients "persist" in attributing the complaints to a physical cause, are described as being "not part of the official classification of diseases".

This is misleading and is simply inaccurate (ME -- the term which preceded CFS -- **is** listed as a neurological disorder in the World Health Organisation ICD 10 at G 93.3), yet the journal's referees seem to have been so brain-washed by the pervasive "Wessely School" influence that even basic facts are not challenged but are accepted as valid.

Henningsen and Priebe (like Wessely) focus on chronic *fatigue*, and state that patients are currently fighting for "legitimacy" through self-help groups, the media, the Internet, and through politics as well as the law.

These authors state that this "fierce" campaign increasingly bypasses both medicine as a science and the medical institutions.

The authors suggest two reasons for the current "campaign". The first is the wish to avoid the stigma of mental illness. The second is the need to avoid the "illegitimate" part of the complaint, ie.. the underlying meaning, which the authors claim is 'not wishing to do something'.

They also link the condition to the failure to achieve personal or professional goals, but claim that since using "tiredness" as an excuse is not acceptable to the patients, this has to be disguised in order to reach their goal of "legitimate incapacity".

These authors claim that proponents of disorders like CFS are by-passing "evidence-based" medicine completely.

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<sup>67</sup> Modern disorders of vitality: the struggle for legitimate incapacity. *Henningsen, P and Priebe, S. J Psychosom Med 1999;46:3:209-214*

The authors' assertion that proponents of CFS are by-passing evidence-based medicine is not consistent with the facts.. In the UK, patients groups have helped to organise and fund postgraduate seminars at hospitals and medical schools, and patients have succeeded in being permitted to sit on the Chief Medical Officer's Working Group on CFS; in recent years, only the joint Royal Colleges' Working Party on ME/CFS (where Wessely was prime mover) has refused to consult with patients.

These authors refer to "fatigue", which always obfuscates scientific discussion of the facts and (as does Wessely) they ignore all the evidence which implicates an organic aetiology. They also ignore medical history, which clearly documents that ME occurred in epidemics: the literature on this goes back to the 1930s, but these authors do not discuss how personal feeling of failure might occur in epidemics.

(Wessely's ploy is to ignore completely the neurological symptoms seen in ME, and then to "re-educate" his readers into accepting his various views (a) that ME is not the same as CFS because he says there are no neurological signs in CFS and (b) CFS is the more apposite term for what was formerly called ME).

This article appears to be based almost entirely on ignorance, dis-information and personal prejudice.

It will almost certainly add to the unjustified stigmatisation of patients with ME / CFS.

By ignoring all the published research which contradicts their own view, these authors undermine-the already precarious) reputation of psychiatry as a medical specialty which claims to be based on science.

It does not serve the interests of good science for a journal such as the Journal of Psychosomatic Research to publish editorials which contain misleading information and for which there is no scientific evidence.

This article was not an opinion piece; it was presented as an editorial. Why was it accepted by the editors?

Given that the message of the article is that there is nothing wrong with these people about whom they are writing, and that the patients are merely using illness as an excuse, how do the editors believe such articles might improve the patients' situation?

Do they believe that by reducing the disorder to "fatigue" and a lack of vitality, physicians would have a greater understanding of their patients' distress?

One thing is certain: the editors of the Journal of Psychosomatic Medicine cannot plead ignorance about CFS / ME. One of the British editors co-authored a paper on CFS (Professor Weinman) and the other (Professor Creed) was a member of the joint Royal Colleges' Working Party on CFS / ME which produced the 1996 report CR54.

It is no longer acceptable to write defamatory articles about people with AIDS, but it appears to be perfectly permissible to insult patients with ME / CFS.. To do so will not lead to criticism from colleagues, let alone to disciplinary action.

Why is there no desire to present balanced and accurate information about CFS / ME in the medical press which is controlled by UK psychiatrists? In this case, these authors imply that CFS specialists are just as misguided as their patients (p.214) and that their research should therefore be ignored.

One would perhaps expect that psychiatrists above all medical disciplines would be sensitive to the psychological damage which this might reasonably be expected to do to sick and vulnerable patients, but the evidence speaks for itself.

This astonishing lack of respect for the rules of science is largely limited to British journals and authors, most particularly to those of the “Wessely School”.

Since accounts such as this one by Henningsen and Priebe distort reality, clinicians are encouraged not to understand their patients’ experiences, and so the myth that there is nothing wrong with these patients is perpetuated again and again, with the result that patients are endlessly discredited and are stigmatised as inferior, manipulative, lacking in sense, a nuisance, “heartsink” patients and even deviant ie. they use ME / CFS as an excuse to engage in court cases for personal gain.

Indeed, one psychiatrist published an article which is entitled “Chronic Litigation Syndrome,”<sup>68</sup> which has the subheading: “By equating psychological and physical damage, courts help create a nation of writ-happy inadequates”. This 1996 article (by consultant psychiatrist Anthony Daniels but written under one of his pseudonyms of Theodore Dalrymple) stated “If one were actually trying to create a population of litigious, querulous, self-absorbed people without the slightest resilience or self-reliance, one could not do better than to make (the dictum that psychiatric damage should be assessed no differently from physical damage) widely known”. Naturally, one noted the date on which the article was published, but given the nature of Daniel’s other published outpourings about ME sufferers (see *the original Denigration by Design?* pp 3,4,5, 27), this can be safely disregarded.

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<sup>68</sup> Chronic Litigation Syndrome. Theodore Dalrymple. Daily Telegraph April 1 1996

Another example of Wessely’s influence can be found in an article by Barsky and Bows in the *Annals of Internal Medicine* entitled Functional Somatic Syndromes<sup>69</sup>. This review suggests that CFS has much in common with functional somatic disorders, defined here as syndromes “characterized more by symptoms, suffering and disability than by consistently demonstrable tissue abnormality”.

The authors convey their view that “benign symptoms and self-limited conditions” are amplified and re-attributed to external factors such as viruses, and that this phenomenon

is reinforced by media publicity, sympathetic physicians and litigation.

(Notably, deflecting patients' attribution of symptoms to viruses (which he regards as mis-attribution) is a long-running theme of Wessely's, for example, in one chapter<sup>70</sup> he wrote:

"It is of interest that the 'germ theory' of non-specific illness is gaining popularity..., at the expense of a decline in the acceptance of personal responsibility for illness... such attribution conveys certain benefits, irrespective of accuracy... in other words, there is avoidance of guilt and blame".

In another article<sup>71</sup> Wessely wrote:

"Sufferers from mysterious conditions... no longer consider themselves to be oppressed by spirits and demons but by mystery gases, toxins and viruses".

In a lecture he gave in 1994 entitled "Microbes, Mental Illness, the Media and ME: The Construction of Disease"<sup>72</sup> Wessely said "I am going to talk not about an illness but about an *idea* I will argue that ME is simply a *belief* that one has an illness called ME... what lies behind all this talk of viruses and immunity? The Royal Free Disease is itself part of the world of myth").

Clearly, Wessely's expressed views that any connection between viruses and ME / CFS is delusional have been adopted and promulgated by other psychiatrists, it is therefore these *psychiatrists* who are responsible for perpetuating 'the world of myth'.

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<sup>69</sup> Functional Somatic Syndromes. Barsky AJ and Bows JF. *Mn mt Med* 1999;130:1.1:910-921

<sup>70</sup> Chronic Fatigue and Myalgia Syndromes. Simon Wessely. In: *Psychological Disorders in General Medical Settings*. (~N.Sartorius et al Hogrefe & Huber, 1990

<sup>71</sup> The psychology of multiple allergy. Louise M Howard Simon Wessely. *BMJ* 1993;307:747-748

<sup>72</sup> Microbes, Mental Illness, the Media and ME: The Construction of Disease. Simon Wessely. *The 9<sup>th</sup> Eliot Slater Memorial Lecture, London, 12<sup>th</sup> May 1994*

Barsky and Borus state that chronicity is associated with secondary gains.

The arguments in this paper rely heavily on other people's opinions and they ignore or distort research evidence, a trend also evident in other articles by psychiatrists (eg. Henningsen and Priebe above).

One further example is a letter in *Psychosomatic Medicine* by Bohr<sup>73</sup> which implies that CFS is a somatisation disorder; this author expresses extreme views which are noteworthy because they illustrate the continuing hostility of some clinicians, as well as the misinformation and prejudice surrounding CFS.

A further illustration of Wessely's influence surfaced at an important medico-legal conference in London on 15<sup>th</sup> January 1999, when a consultant immunologist advised a Queen's Counsel by praising and quoting from Wessely's book Chronic Fatigue and its Syndromes (see pp 103-4 and 121-122 above); the immunologist advised the barrister that people who get ME are "over-achievers" who suffer from "negative thinking" and that people with ME get *angry* at their illness and it is this anger which perpetuates the cycle; he relied on Wessely's book to inform the QC that ME (quote) "is *devastating* for them because they cannot cope without success". The consultant immunologist spoke highly of the joint Royal Colleges' report CR54. he advised the QC that there had been "over-interpretation" of the Plaintiffs laboratory tests, and that ME is a *psychological* state, not viral or immunological.

The consultant advised the QC that he was "unable" to comment on the Plaintiffs ME-related (and laboratory proven) pancreatic exocrine insufficiency and that he doubted that pancreatitis was ever part of ME because it is not mentioned by Wessely in his book The Plaintiff advised that Wessely's book was not about ~ but about "fatigue", but was disregarded.

The QC took down details of Wessely's book and said he would get a copy; he declined to look at the medical reference papers provided by the Plaintiff which contradicted Wessely's view and advised the Legal Aid Board that there was no merit in the Plaintiff's case, and Legal Aid funding was withdrawn.<sup>74</sup>

Wessely's influence is regularly apparent in the media. It was in 1997 that a US feminist named Elaine Showalter burst onto the ME scene in typically dramatic and histrionic fashion by publishing a book called Hystories — Hysterical Epidemics and Modern Culture (Picador, London, £16.99), claiming~that people

<sup>73</sup> Socioeconomics and Illness in CFS. Bohr *T.Psychsom Med* 1999;61:256

<sup>74</sup> Further details available from present author

who think they have ME or Gulf War syndrome or OP poisoning are merely "hysterics".

Showalter, an assistant professor of English at Princeton University, New Jersey who claims to have spent the last eighteen summers studying women and psychiatry at the Wellcome Institute for the History of Medicine in London, seems to be very well acquainted with Wessely's ideas (it must be remembered that Wessely too has strong associations with Wellcome).

The furore surrounding Showalter ran in the media for the best part of a year, which was unsurprising as she attempts to dismiss serious neuroendocrinological illness (which, not being a doctor or a scientist, she clearly does not understand) as hysteria on very precarious "pseudo" evidence.

Indeed: the majority of her supportive “evidence” about CFS does not come from scientific texts at all. Out of the 54 references she cites, only 21 are from medical publications; these represent eight separate sources (mostly reviews) of which six were written by Simon Wessely or those who agree with him. Most of the rest of her “evidence” is taken from newspaper cuttings and glossy magazines.

Showalter claims that the “hysterical” disorders of modern times are spread by the media in that vulnerable personalities read about an illness and then unconsciously develop those complaints; once developed, the condition is perpetuated by sympathetic doctors, self-help groups and further publicity.

Among the “psychogenic syndromes of the 1990s” she discusses are: alien abduction, multiple personality disorder, satanic ritual abuse, CFS and Gulf War syndrome.

Her claim that CFS is a modern form of hysteria is primarily based on Wessely’s view that CFS patients are dismissive of psychogenic illness, and her own view that there are no consistent neurological, endocrinological or cardiovascular abnormalities and that such patients have a large number of symptoms. She also claims support for her views by relying on the angry reaction of the audience who took part in the Esther Rantzen programme when former GP Dr Thomas Stuttaford claimed that depression was the cause of ME, apparently believing that their anger is proof of their prejudice against “mental” illness ~she does not consider the possibility that their anger might have been an indication that Stuttaford may have been wrong).

In her chapter on Gulf War syndrome, Showalter believes the real problem is “war neurosis”, the growing evidence implicating vaccinations is dismissed. Out of 38 references she cites, only one is from a medical publication (JAMA). The rest of her references came from newspapers and magazines.

This book reveals that, like Wessely, Showalter is happy with any bits of information which appear to support a psychological cause and (again like her Weilcome-supported model) she is happy just to ignore the rest of the available evidence.

This is not what one expects of scholars.

If nothing else, her book reveals that the analysis of modern medicine requires a scientific background and cannot be addressed by attention-seeking professors of English from the standpoint of an armchair psychiatrist.

Examples of the media interest (and consequent promulgation of Showalter’s damaging views) are as follows:

Diagnosis: Hysteria.

Laurie Abraham. *Mirabella* 1997:152-158



In this magazine interview, Showalter underscores her belief that thousands of sick, traumatised people do not have what they think they have and — “raising her thesis to the level of the almost sublimely offensive—that what they really have is in their heads”.

““Contemporary hysterical patients blame external sources — a virus... . chemical warfare... .satanic conspiracy... for psychological problems’.

Gulf War veterans who believe they have Gulf War syndrome are — according to Showalter “as deluded as people who believe they consort with aliens”.

Showalter claims that it is “muddled reportage” which is transforming Gulf War syndrome into a virulent epidemic, and is “shifting the debate from the symptoms to the cover-up”, and that it is the media which are pointing to toxic chemicals, specifically the nerve gas sarin.

According to Showalter, physicians who collude with hysterics out of kindness prevent them from getting the needed psychological help and strip sufferers of dignity.

“Hysterical epidemics undermine our respect for evidence and truth”, says Showalter in this interview.

It’s all in the mind, bud

John Carlin. *Independent on Sunday*, 27 April 1997

(Subtitled We’re living in an age of hysteria, says an American academic — and she’s aot the hate mail to prove it

This serves as another platform for Showalter and she performs superbly.

Her book is given the customary plug; in it, she argues that Gulf War syndrome and chronic fatigue syndrome are “bound together” with “recovered memory loss, satanic ritual abuse, multiple personality disorder and alien abduction”.

“In it, Ms Showalter argues that America is in the grips of a ‘psychological plague’; a ‘pandemic’ of ‘epidemic proportions’.

“The decisive role of the mass media, Ms Showalter says, is to endow the symptoms with social legitimacy.

“Hysteria, an unconscious affliction that produces the appearance of disease, is more contagious than ever in the Nineties.

“America’s belligerent CFS lobby ... has gone to extraordinary lengths to twist the scientific evidence, according to Ms Showalter.. ‘I discovered.., that the CFS people were literally recruiting new victims’.

“Imaginary illnesses have struck with as much intensity in other parts of the world.

“Ms Showalter sneers... (at the idea that) the Pentagon is concealing the deaths of ... Gulf War veterans.

“Not that she lacks sympathy for sufferers like Troy Allbuck, a Gulf War veteran, and his wife Kelli. . . .According to Mrs Ailbuck her husband returned from the war with toxic semen that ‘causes sores — blisters which actually open and bleed’.

“Ms Showalter’s... conviction (is) that the Allbucks and thousands like them would stand a better chance of obtaining cures if they could accept that their symptoms would be healed more effectively by psychotherapy than by endless inconclusive medical tests which encourage paranoia while obfuscating science.

“Unwilling to accept the blow to their self-esteem, victims seek to dignify their condition by bestowing upon it a fictitious medical belief.

“The (hysterical) epidemics will end only when people confront their feelings of guilt, shame and helplessness in a sincere spirit, without looking ‘to invisible enemies, devils and alien invaders for the answer’”.

#### Try a Gulf War chemical cocktail yourself

Elizabeth Sigmund (OP Information Network). *Independent on Sunday*, 4 May 1997.

In her response to the above article, Mrs Sigmund makes the point that “We have evidence connecting the research being carried out by Simon Wessely and Anthony David with the Wellcome; both these men have a) suggested that GWS is psychosomatic... and b) have received large chunks of funding from the Pentagon”.

#### War of words

Professors Anthony David and Simon Wessely. *Independent on Sunday*, 11 May 1997

In their response to Elizabeth Sigmund, David and Wessely write “The possible adverse effects of service during the Gulf war is an area surrounded by myth and misinformation... we are funded by the US Department of Defence and we are honoured to receive its support”.

#### Truly, madly, hysterically

Suzanne Glass. *Guardian*. 29 April 1997

This interview allows Showalter to reveal that she has received death threats since the

publication of her book.

In answer to the interviewer's question if she has a medical degree, Showalter answers "No, but I've read vast quantities of medical literature..., and it's just so obvious to me that (Gulf War syndrome) is the same as the post-world war one shell shock".

"We owe our war veterans a serious debt" she says in her book, 'but continuing to deny the validity of war neurosis is not the way to pay it'.

"There is this vague conspiracy theory circulating about me, this ridiculous idea that some huge corporation has put billions behind me for its own ends'.

The article mentions that one of the items of hate-mail on the internet reads:

"Controversy can be turned into dollars regardless of the negative impact it has on its victims".

#### First casualty of the Gulf war

Elaine Showalter. *Guardian*, 17 May 1997

In this essay, Showalter appears to revel in being the receiver of so much hate-mail; the subtitle is "Undaunted, she now urges the British Government to be sceptical in its new study of what she sees as an "hysterical epidemic".

Showalter here re-hashes the view that all war results in "war neurosis" which she equates with what Israeli research called "existential helplessness".

Showalter writes that it remains to be seen whether "Britain can be more successful than the US in establishing confidence in a scientific investigation of Gulf War Syndrome, especially if that investigation, like all the American ones, finds no evidence for the drugs / vaccine scenario".

*(Not only is she factually incorrect in her claim, but also note that Showalter wrote this essay 20 months before Wessely and David's official report was published in the Lancet in January 1999 (see page 157 above), yet she seems to pre-empt exactly that report's findings).*

She continues "In this case, reason, science and history are all on the side of psychological rather than chemical for the syndrome".

"A century after Freud and 80 years after the Great War, psychologically caused illness is still stigmatised and mocked".

*(It seems to have escaped Showalter that by augmenting and supporting the stance taken by Wessely and David, she herself has contributed significantly to such stigmatisation and mockery).*

### Hysteria and Gulf War Syndrome

Jason Cowley. *Times*, 22 May 1997, p21

Subtitled: Elaine Showalter's questioning of conditions such as Gulf War syndrome and ME has proved so inflammatory that she faces death threats.

This article provides Showalter with yet more opportunity to reveal that she faces "almost daily calls for her murder"; that she now requires "constant protection", and that when she has taken part in a television show in which she "boldly dismisses Gulf War syndrome as a psychogenic sickness, an itinerant band of veterans are often lying in wait, sometimes dressed in uniform".

"Vague conspiracy theories suggesting that her research is funded by shadowy arms corporations with a vested interest in exposing Gulf War syndrome as nothing more than a psychosomatic illness refuse to go away.

"The histories of these syndromes are linked and overlapping. They all move towards suspicion, conspiracy theories, witch-hunts and mass panics.

"As the panic reaches epidemic proportions,' she writes, 'hysteria seeks out scapegoats and enemies — from unsympathetic doctors, abusive fathers, and devil-worshipping sadists, curious extra-terrestrials and evil governments'.

"With the obvious exception of Gulf War syndrome, 90% of hysterical syndrome patients are women this has something to do with the multiple roles women are struggling to fill, wrestling with frustrations and anxieties that they are unable to articulate.

"Showalter feels (*as indeed does Wessely, because he has published articles which state this*) the victims of syndromes are encouraged to blame external sources for psychic problems... she suggests they learn about diseases from the media, unconsciously develop the symptoms, and then attract media attention in an endless cycle.

"Dr Charles Shepherd, medical director of the British Myalgic Encephalomyelitis Association, has already accused her of crass irresponsibility.. 'I feel very angry about her' he says. 'Patients have had a raw deal for 15 years. Research confirming that chronic fatigue syndrome is not in the mind has come through in the past two years and this sort of madness is ammunition for the sceptic. One person a month commits suicide because they are not getting the support they need... I'm not surprised she has had death threats'.

"Showalter is saddened by these remarks, dismissing them as outrageous and irresponsible. 'It is shocking to me that a British doctor should say such incendiary things'.

"She insists that her book is balanced and moderate.

“‘The symptoms caused by war neurosis’ in short... are cultural phenomena.

“She remains confident that society has the knowledge to control ‘epidemic hysteria’”.

Trying to recognise the symptoms of dis-ease

Peter Ackroyd. Book review. *Times*, 22 May 1997 p 39

In this review of Showalter’s book, Peter Ackroyd writes: “Showalter tracks the course of those large movements of feeling which are otherwise known as “collective paranoia”.

“The central theme of this book lies in the self-evident fact that the late 20<sup>th</sup> century is still a ‘psycho-analytic age’, which is precisely why various hysterical symptoms become so popular and so contagious.

“Showalter enters more forbidding territory in her account of ‘chronic fatigue syndrome’ and ‘Gulf War syndrome’: there are so many interested, not to say partisan, groups concerned with these matters that it is impossible to speak sensibly without being accused of prejudice. But Showalter displays an admirable ability to dispel the cloudy theories.

“Showalter suggests that ‘chronic fatigue syndrome’, for example, is closely related to the epidemics of ‘neurasthenia’ of the 19<sup>th</sup> century.... the belief that there is a mysterious virus....which is creating the more recent condition is a textbook example of the hysteria created by the collusion of doctor and patient”.

Misery can make you ill

Anthony Daniels. *Sunday Telegraph*, 25 May 1997

Subtitled: Anthony Daniels agrees with an American feminist that many epidemics are all in the mind

Never one to miss an opportunity to express his contempt for suffering humanity, consultant psychiatrist Daniels writes in support of Elaine Showalter’s views:

“When people have no words for their distress, or when to express it openly would....destroy their carefully constructed self-image, they often develop symptoms for which no purely physical explanation exists.

“The conversion of unhappiness into illness used to be considered a response peculiar to women.

“...in this book, Elaine Showalter, a well-known feminist professor of English at Princeton attempts to show how modern epidemics of somatised unhappiness...come about.

“These epidemics include chronic fatigue and Gulf War syndromes, about both of which there has been an immense amount of inconclusive research.

“The mechanism by which such epidemics are propagated is essentially the same as that which has produced epidemics of ‘recovered’ memory syndrome, abduction by aliens from outer space and multiple personality disorders.

“It is a pleasure to acknowledge Professor Showalter’s common sense about such phenomena.

“Her thesis is that hysterical epidemics require three conditions to spread: first, a susceptible population, second, a group of doctors prepared to validate the syndrome as a genuine illness and third, a willingness on the part of the media to give the alleged illness publicity.

“Professor Showalter’s analysis is welcome...

“She insists that sufferers from the various syndromes are genuinely suffering, though not from what they think they are; she therefore tries, not entirely successfully, to avoid passing any adverse judgment upon them.

“...she does not speculate as to why suffering in an age of comparative physical ease should be so widespread. In fact, it is all part of the modern cult of victimhood.

“...apart from the normal human desire to blame others for our dissatisfactions or to profit from them, it is as if we cannot bear to admit that we are....by far the most fortunate people who have ever lived.

“Perhaps we need to invent sufferings for ourselves....our lives are apt to seem petty, insignificant and smug.

“Feminism is undoubtedly one of the wells from which those with a taste for victimhood have slaked their thirst.

“It has taught even highly privileged people that they are, in reality, very oppressed and unfortunate. It has therefore made them vulnerable to epidemics of an hysterical nature.

“Furthermore, the tendency of people to make their hysterical conditions the focus of their existence (in a way which people with more conventional physical illnesses try not to do) is very striking....The hysterical condition gives meaning where there was none before, and fellow-sufferers organise themselves as if for...a religious revival.

“Professor Showalter’s book is a serious contribution to her subject”.

Talking Point

Geoffrey Hollis. *Farmers Weekly*. 11 July 1997, p 81

Subtitled: OP dip sufferers are victims of mass hysteria. Don't be too quick to rubbish that statement, says Geoffrey Hollis

"Do you suffer from poisoning by sheep dip? Do you fear pesticides? If so, please read what follows carefully.

"I have recently finished a stimulating book by an American, Elaine Showalter, entitled *Hystories – Hysterical Epidemics and Modern Culture*.

"Ms Showalter strongly attacks several modern causes dear to lobbyists, labeling them as examples of mass hysteria. Her targets include Gulf war syndrome, ME, Satanic ritual abuse, and even alien abduction. She says that all these have common characteristics....the result is a wave of people who believe they have a physical problem when they really have a mental one.

"My interest stems from my time in charge of pesticides at the MAFF. All those symptoms were in evidence at one time or another during my tenure.

"There are still those who argue that pesticides are responsible for many illnesses in this country, even though there is no proof.

"What about the recent scare story that tents used in the Gulf War and sprayed with pesticides might even now be being used by – horror of horrors – Boy Scouts.

"A long-running hysteria surrounds OP sheep dips. All the symptoms as defined by Ms Showalter are to be seen. People suffer from mystery ailments which they feel can only have been caused by sheep dip. Doctors are willing to swear that this must be the case even without proof....And we have strong accusations that the government and its advisers are seeking to hide incriminating evidence.

"...I am persuaded by (Ms Showalter) that many are probably suffering from stress or other psychiatric problems which have nothing to do with sheep dips.

"May I suggest that any OP sufferer who is exploding with anger at this article should not write it off as rubbish but read her book (published by Picador at £16.99) and judge for themselves".

### Talking Point

Elizabeth Sigmund. *Farmers Weekly*, 25 July 1997

In this response to Geoffrey Hollis' article (*above*), Elizabeth Sigmund asks if he has read the book entitled *Clinical and Experimental Toxicology of OPs and Carbamates*, edited by Dr T.C.Marrs (chief scientific adviser on OPs to the Department of Health and a former senior scientist at Porton Down Chemical and Biological Defence Establishment –

not exactly an hysterical or anti-establishment figure) and Brian Ballantyne, which contains 59 scientific papers on the toxicity of OPs and carbamates, none of which claims that ill-health caused by exposure to OPs is imaginary, hysterical or neurotic illusion.

“To be fair to Elaine Showalter, she does not make such a ludicrous claim in her book. She never mentions exposure to agrochemicals.

“As Mr Hollis has declared his own vested interest....has he not got a powerful reason for wishing to deny the undoubted widespread suffering....caused by exposure to OPs?

“For a man with his history to publish such an ignorant and ill-informed article smacks of a degree of arrogance which would explain how the OP tragedy has been allowed to continue for so long.

“Perhaps Mr Hollis should read Dr Marrs’ book, and learn just how dangerous OPs really are, rather than pouring over a money-spinning work of science fiction written by an American lecturer in English Literature, who does not even mention OP poisoning”.

OPs – facts, not fiction, please

Countess of Mar. *Farmers Weekly*, 25 July 1997

In this letter of response to Geoffrey Hollis’ article, the Countess of Mar writes:

“Mr Hollis would do well to deal in facts rather than the fiction which much of the book by Elaine Showalter promotes as a scientific study.

“We can all be selective in our reading and both Mr Hollis and Ms Showalter demonstrate the extremes to which that selectivity can be taken by those who have an interest in obfuscating the facts.

“There is an increasing body of scientific evidence that chronic, low-level exposure to OPs has harmful effects upon human central, peripheral, autonomic nervous, immune and endocrine systems, as well as the major organs such as the heart, lungs, liver and brain.

“What is singularly evident is that all those concerned with the manufacture, licensing and distribution of these products have demonstrated a lack of responsibility in their duty to ensure that consumers, the general population and the environment are protected.

“It might pay Mr Hollis to recall that multiple sclerosis was known as the ‘idle man’s disease’ between the two world wars”.

*(There were more articles, but the above serve as illustrations. The Elaine Showalter phenomenon was not, however, willing to go away).*



I am Duvet woman: this bed is my mother, my lover, my wife

Elaine Showalter. *Independent on Sunday*, 25 January 1998

Subtitled: Why are 85 per cent of ME sufferers women? Cultural historian Elaine Showalter critiques a new anthology of their experiences

Whilst the women portrayed in this book are perhaps unfortunate to say the least, in her six column critique of the book (entitled *Knowing ME*, published at £8.99 by the Women's Press on 12 February 1998), Showalter again gives full vent to her bile about myalgic encephalomyelitis.

“85 per cent of patients around the world with ME are female and despite an enormous medical research programme (*Showalter provides no factual evidence of an “enormous” medical research programme*) no physiological or biochemical explanation of the illness has ever been confirmed.

“Caela March, a novelist who has had ME for nine years....has edited a collection of personal narratives by British women from a variety of backgrounds, many of them lesbian.....as the stories make clear, finding the ‘right’ name for their disorder, one that satisfies their need for legitimacy and that fits in with their...beliefs, is a turning point in ME women’s lives.

“Once they undergo conversion, ME women follow a way of life with its own rituals and networks.

“March and her contributors see this process as one of discovery...but medical historians like the University of Toronto’s Dr Edward Shorter view it as a spiral of suggestion.

“According to Shorter, ‘Patients are exposed to a diagnosis and assured by a sensation-hungry media that it represents the explanation of their problems.... This is a recipe for the disintegration of medical authority and a psycho-circus of suggestion’.

“When the symptoms hit, (ME women) give up school, leave their jobs, and enter a culture of illness and invalidism that often lasts for decades.

“They think ME is caused by organophosphates, viruses, chickenpox, electro-magnetic fields, anything but their feelings and conflicts.

“...programmatic resistance to psychological explanations, diagnoses or treatments is the single most characteristic trait of patients with chronic fatigue syndrome...

“But their resistance to psychotherapy, medication and exercise – the most effective medical regimen for chronic fatigue does not stop ME women from

eagerly embracing the full range of crack-pot treatments, quack nostrums, alternative medicines, vaguely religious rituals and junk therapies of the Nineties. They try homeopathy, reflexology, Chinese herbs, acupuncture, Shiatsu massage, Jin Shin Jyutsu, astrology, anti-candida diets, aromatherapy, kombucha fungus, organically-grown vegetables.

“They are also convinced that they have allergies to wheat, sugar, salt, dairy products, chocolate, coffee, red meat, fizzy drinks and white bread.

“Most of all, Duvet Women ‘give in to their bodies’, stay in bed, sometimes for months or years, and often abandon outside relationships in the interests of what they regard as a healing focus on the self.

“I am sorry to see the Women’s Press publishing and endorsing this sentimental, superstitious tripe about a serious, if psychosomatic, epidemic”.

ME is not a cosy ‘duvet’ illness - and it doesn’t just afflict women  
Ian Purser. *Independent on Sunday*, 1 February 1998

In his response to Showalter’s diatribe (*above*), Ian Purser writes:

“As she goes on to call ME a psychosomatic epidemic among women, would she mind telling me, and other male sufferers from ME, what she thinks is wrong with us?

“But then, a ‘cultural historian’ who can...explain the experiences of Gulf War veterans...as being of the same order and cause as the claims of UFO ‘abductees’ is clearly beyond embarrassment.

“Ms Showalter is entitled to her prejudices and her sloppy thinking, but those of us who (unlike her) have to live with this condition are fed up with being exploited as part of some all-encompassing theory of pre-millennial hysteria.

“If she were more interested in real history than modish theorising, she might discover that before doctors had a greater understanding of multiple sclerosis it was referred to as ‘hysterical paralysis’.

“For someone supposedly commenting on the modern condition, Ms Showalter’s views are strangely out of date”.

And so it goes on.... and on, this spuming attack on those for whom medical science does not yet have any answers.

Wessely would be justified in thinking he had done a good job, as clearly his influence is such that unscrupulous exhibitionists like Showalter can

capitalise and profit from it, whilst at the same time promoting Wessely's own cause.

As the founding fathers of the mass hysteria theory of ME, history is likely to reveal that the two psychiatrists McEvedy and Beard (who in 1970, having never examined a single ME patient and purely as a vehicle for a PhD thesis, published their re-appraisal of the medical notes of patients who had been involved in the 1955 Royal Free outbreak, and who concluded that the outbreak was nothing more than "epidemic hysteria" (*Royal Free Epidemic of 1955: a Reconsideration. Colin P McEvedy; AW Beard. BMJ 1970;1:7-11*) have much to answer for.

One further and significant impact of Wessely's influence is that the Department of Health has admitted it has not commissioned any research on ME / CFS and that it has no present plans to do so (*see p. 76 above*).

From this it follows that people who are chronically and severely affected with ME must look forward to a bleak future, as NHS commissioning officers can justifiably rely on the recommendation of the joint Royal Colleges' report CR54, which in chapter 12 (Facilities and service provision) states unequivocally at paragraph 12.1:

"We see no reason for the creation of specialist units for the majority of cases"

and at paragraph 12.4:

"We do not think that specific guidelines on the management of CFS should be issued for general practitioners at present. Appropriate clinical practice is not to be defined by special interest groups"

and in their Summary under Implications for commissioners, Wessely et al state:

"CFS...is likely already to be consuming significant resources...much of the expenditure of no benefit to the patient and some of it positively harmful.

The authors of CR54 plainly state that existing specialist units should be identified and a review should take place with those units to ensure that those units have the knowledge and understanding of the issues raised in the joint Royal Colleges' report. This can only be interpreted as the authors' determination that their preferred triad (ie. cognitive behavioural therapy and forced graded exercise programmes, together with antidepressants even when there is no clinical depression) should form the mainstay of any therapeutic intervention or support.

In their Summary at paragraph 16, Wessely et al make the specific point that

“The above course of action has no resource consequences”.

The effects of Wessely et al’s specific recommendation about there being no need for the provision of specialist care for people with CFS is already apparent.

In an April 1998 report into people suffering from CFS / ME in just one county, the findings are alarming (*Long Days of Pain. A Report into People Suffering from Chronic Fatigue Syndrome / ME in Gloucestershire. Westcare, Bristol, April 1998*).

The main findings of this report are:

1. There are a minimum of 1,500 people with CFS / ME in Gloucestershire.
2. There are no specialist services provided by the Health Authority or by any other agency.
3. The average length of time people have CFS / ME is nine years.
4. One in four sufferers is severely affected.
5. Seven out of ten GPs are sympathetic and supportive.
6. No GP is able to put into practice the recommendations of the report of the National Task force on CFS / ME because the facilities do not exist, particularly for the services of occupational therapists, physiotherapists, nutritionists and counselors. Training needs to be offered to social workers to increase awareness and understanding of the impact of the illness upon patients and their families.

The Conclusions of the report include the following:

- the report shows a disturbing picture of a group of people suffering from a serious and disabling disease.
- the survey highlights the lack of primary and secondary services available to GPs and patients.

- sufferers are being left alone to cope with the illness as best they can with minimal access to relief from their symptoms and no hope of being offered a clear route to recovery.
- there is general agreement within the medical profession that early diagnosis and an holistic approach to treatment can contribute significantly towards recovery. These crucial elements are absent in Gloucestershire.
- Many people with CFS / ME are living alone and because of the illness have withdrawn from normal social life. They are socially isolated and suffer severely from being cut off in this way. This can have devastating effects.
- Access to proper support from social services or the voluntary sector would be a vital service that could be offered to both patients and those around them.

As a direct result of the recommendations contained in the joint Royal Colleges' report CR54, provision of any such support remains a forlorn hope for most people.

However, a glimmer of change appeared in the Daily Telegraph on 23<sup>rd</sup> October 1999, when it was reported that the country's first clinic for the treatment of ME had been opened at Wareham Hospital, Dorset by the Duke of Kent the previous day.

In an item entitled "First clinic for treating ME opened by Duke", Matt Born writes:

"The Duke, who has been patron of the ME Association since the Duchess of Kent was diagnosed with the debilitating illness in 1996, met patients during a brief ceremony at the clinic.

"It aims to be one of the world's leading centres for research into (ME and chronic fatigue syndrome) for which there are currently no accepted cures.

"The clinic, which has been granted funding for three years from the Dorset Health Authority and the county branch of the ME Association, has been holding monthly out-patient clinics since opening a year ago".

*(Note that the National ME Centre at Harold Wood, Essex, was the first such clinic, so this news item is inaccurate in that respect).*

## **Considerations**

In his book “Toxic Psychiatry” (Fontana, London, 1993), psychiatrist Peter Breggin states that psychiatrists’ main function is not treatment, but control, and that they are “agents of the State”.

Is this applicable to the psychiatrists of the “Wessely School”?

Wessely’s tactics --- which have been his trade-mark since 1987 --- are to trivialise, summarily dismiss or to ignore completely any research findings with which he does not agree.

He is often simply wrong, as can easily be shown from just three illustrations:

### 1. Cognitive behavioural therapy

Wessely et al endlessly promote CBT as the treatment of choice for what they term “functional somatic syndromes”, which include CFS / ME, Gulf War syndrome, multiple chemical sensitivity (MCS), fibromyalgia, irritable bowel syndrome, pre-menstrual tension and chronic low-dose organophosphate poisoning.

However, the “Wessely School” ignore the *facts*.

Apart from their own studies, there is little published evidence to support the notion that CBT actually *works* in CFS / ME etc, and their own studies have been the subject of criticism on the grounds that many of those studies are deemed to be methodologically flawed, principally because of the authors’ selection bias (ie. they are not studying cases of true ME, but are then claiming that their results relate to ME).

Due in no small measure to Wessely’s ubiquitous control over what gets published on CFS / ME in the UK, the medical journals frequently publish highly uncritical assessments of CBT which focus on the few studies which support its use, whilst ignoring those controlled trials which did not find CBT to be effective (and which warned about the dangers of exercising beyond fatigue).

This point is the subject of an article entitled “A Subgroup Analysis of Cognitive-Behavioral Treatment Studies” by Fred Friedberg (JCFS: 1999: 5: 3-4:149-159; co-published simultaneously as “Chronic Fatigue Syndrome: Advances in Epidemiologic, Clinical and Basic Science Research” - (ed). Roberto Patarca-Montero, Haworth Press Inc. 1999).

Friedberg, clinical professor in the Department of Psychiatry at the State University of New York, makes the following points:

“Several studies of graded activity-oriented cognitive behavioural treatment for CFS, all conducted in England, have reported dramatic improvements in functioning and substantial reductions in symptomatology.

“On the other hand, cognitive behavioural interventions conducted in Australia and the United States have not found significant improvements in functioning or CFS symptoms.

“Furthermore, descriptive studies of CF patients in England, the US and Australia suggest that the CFS population studied in England shows substantial similarities to depression, somatization or phobia patients, while the US and Australian research samples have been clearly distinguished from primary depression patients and more closely resemble fatiguing neurological illnesses.

Friedberg notes the “widely divergent clinical presentations” and he notes specifically that because all the apparently successful CBT studies have all been conducted in England, a replication of these findings in a well-designed US study would be necessary before a general recommendation for CBT could be made.

He also observes that CBT appears to be most appropriate for low functioning patients with a phobic fear of symptom exacerbation.

He points out that other subgroups “may show a much more limited response”.

Friedberg observes that there may be an upper limit of functioning, ie. an “activity ceiling” for many CFS patients, as outcome results of CBT have begun to decline 17 months after treatment termination.

Notably, in his presentation at the 1998 Boston Conference on CFS, Michael Sharpe himself conceded that the difference between the CBT treated patients and the untreated controls disappeared after time.

Thus Wessely’s inflated claims for the gratifying success of his CBT treatment cannot be substantiated.

It must therefore be surmised that Wessely appears to have lost his objectivity, and that this has led him to a selective blindness which has resulted in over-simplification, which has nothing to do with “evidence-based “medicine.

## 2. The Camelford Drinking Water Contamination Incident

In July 1988, 20 tonnes of aluminium sulphate were accidentally pumped into the drinking water supplies of the small town of Camelford in Cornwall.

Despite the delay in informing the public of what had happened, residents and visitors immediately suffered distressing symptoms such as nausea and vomiting, diarrhoea, skin rashes and mouth ulcers; these were followed by musculoskeletal pains, malaise and impairment of memory and concentration. In some cases, hair, skin and nails turned blue.

In some cases, bone biopsy showed stainable aluminium over six months later.

In other instances of aluminium exposure (patients undergoing haemodialysis who were in end-stage renal failure as a result of aluminium contamination of the water used to prepare the dialysate), the importance of gastrointestinal absorption was clearly established (*Gastrointestinal absorption of aluminium from aluminium-containing antacids. Kaehny WD et al. NEJM 1977;296: 1389-1390*).

In the Camelford catastrophe, seven people died; 25,000 suffered serious health effects, and 40,000 animals were affected. (*The Politics of Poisoning: The Camelford Aluminium Sulphate Scandal. (Douglas Cross). The Ecologist: 1990;20:6:228-233*).

An article by Bernard Dixon entitled Still waters was published in the BMJ on 5<sup>th</sup> August 1995 (311:395); it informed readers that “mass hysteria was largely responsible for the furore”.

Dixon’s article is based on a “re-assessment” of the Camelford incident by psychiatrists Anthony David and Simon Wessely which was published in the Journal of Psychosomatic Research (1995;39:1-9). Dixon claimed that this article “helps to sort out facts from fiction”.

Dixon notes that David and Wessely support the findings of the two Clayton reports into the Camelford incident, which found that anxiety was the cause of the long-term symptoms suffered by up to 400 people, and that the verdict was unambiguous ie. there was no evidence of long-term adverse effects on health as a consequence of the water contamination.

Dixon states “David and Wessely’s wide-ranging review contains nothing to alter this verdict”

As ever, “sensational reporting” by the media was held to be a significant factor.



However, it seems that David and Wessely's confident assertion that mass hysteria and / or anxiety were responsible for the supposed suffering of those in the Camelford area at the time of the incident has now been shown to be wrong.

In an article entitled Disturbance of cerebral function in people exposed to drinking water contaminated with aluminium sulphate: retrospective study of the Camelford water incident (*Paul Altmann et al. BMJ 1999;319:807-811*), it is conclusively shown that Camelford residents who were exposed to aluminium sulphate-contaminated drinking water suffered considerable damage to cerebral function which was not related to anxiety, and that there is objective evidence of organic brain damage which is compatible with the known effects of exposure to aluminium.

The study clearly revealed that the residents had suffered considerable organic brain damage as opposed to psychological trauma only, and the suggestion that anxiety led to those abnormalities is effectively rebutted.

The authors note that previous psychological studies on victims of the Camelford incident concluded that the most likely explanation was that 'the perception of normal and benign somatic symptoms (physical and mental) by both subjects and health professionals was heightened and subsequently attributed to an external cause, such as poisoning'.

The current authors conclude: "Our study suggests that this is not the case".

They note that many of those originally affected still have symptoms eleven years later.

Altmann's study was commissioned by lawyers acting on behalf of the Camelford plaintiffs and was funded through Legal Aid, not through the Department of Health.

This is an illustration of proven mis-attribution by Wessely.

### 3. Gulf War Syndrome

In their official report on GWS published in the *Lancet* in January 1999 (see pp 160-163 above) David and Wessely et al conclude that there is no such thing as Gulf War syndrome and that “associations of ill-health with adverse events and exposures...may not be...causally implicated in Gulf War-related illness”. They conclude that although some of the exposures were unique to the Gulf War, the *mechanisms* linking those exposures to ill health might not be specific, and that one pathway of subsequent illness could be the “perceived” risk of chemical attack, and that this *psychological* effect might be contributing to the increased level of ill health in Gulf War veterans.

At approximately 2.20 am and at 4.20 am on 20<sup>th</sup> October 1999, the BBC World Service announced in its main headlines details of a new study which did not support Wessely’s conclusions: listeners were informed that when it was advised of the report’s findings, the Pentagon changed its policy and had that day released a statement.

The new study was carried out for the US Defence Department by the well-respected independent Rand Corporation; as a result, the Pentagon now admits that there could be a link with GWS and the use of pyridostigmine bromide (PB or anti-nerve-gas) tablets which the UK, US and Canadian troops were forced to take during the conflict in the Gulf.

Dr Beatrice Golan, author of this two-year study, concedes that PB tablets were not licensed by the FDA to be given to the troops and that the study found that links between PB tablets and GWS could not be ruled out.

Gulf War veteran Paul Sullivan of the National Gulf War Resource Centre was interviewed on the BBC World Service and said the Gulf War veterans had long suspected the PB tablets and in this respect he mentioned two previous studies, one at Duke University in the US and another in Scotland.

Sullivan said that the Gulf War veterans now wanted “aggressive and immediate research programmes to determine the link”.

He also said that the veterans had already forced the Clinton administration to make it law that if such a causal link is found, then the veterans will automatically get research examinations *and* compensation, and that this law had been signed by President Clinton himself.

Thus it can be seen that doubt has now been cast on the reliability of Wessely’s findings on Gulf War syndrome.

*(For details of Gulf War research which were presented at the Brussels International Congress in September 1999, see pp 250-254 below).*

## **Conclusions**

The aim of this Update is identical to that of the original review of Wessely's role in the perception of ME, namely to promote a much wider and multidisciplinary scrutiny of Wessely's work, which hopefully will lead to serious questioning as to whether his undoubted influence is justified.

Sadly, the conclusions are also identical to the 1996 conclusions, in that Wessely's tactics, power and influence continue unabated -- at least in the UK -- despite important research advances in the understanding of ME from the US and Australia.

For over a decade the "Wessely School" has used the same pattern of tactical strategies, which briefly are as follows:

1. Wessely and his like-minded associates limit themselves to a highly selective choice of the available published literature on ME and they continue to use the simple expedient of not including for consideration any research findings with which they do not agree.

They ignore peer-reviewed international papers which contradict their own construct of ME, and this means that they never provide a balanced view of the evidence.

When he cannot ignore a much-acclaimed paper, Wessely (as does Anthony David in particular) trivialises or dismisses outright findings which do not conform to his own preferred theory of causation.

For example, Wessely does not accord due consideration to many aspects of ME, including the nature and *severity* of it, nor does he afford due regard to areas such as the neurological problems in ME; the immunological problems in ME; the virological aspects of ME; precipitating factors such as acute trauma in ME; allergies and hypersensitivities in ME; multiple chemical sensitivities in ME; contra-indications of anaesthesia in ME; adverse drug reactions in ME; vertigo and chronic dysequilibrium in ME; hypo-perfusion of the brain stem in ME; ocular problems in ME; laboratory findings in ME; endocrinological findings in ME; cardiac problems in ME; respiratory problems in ME; autonomic problems in ME; vasculitis in ME; fibromyalgia in ME; the relationship between the post-polio syndrome and ME; hair loss in ME; the *type* of cognitive dysfunction in ME; the many *helpful* psychological papers on ME and papers dealing with the quality of life in ME.

All of these are well-documented in the ME / CFS literature, but Wessley mostly ignores

them or – in a cavalier and unscientific manner -- relegates them to the realms of functional somatic syndromes.

Good science thrives on open debate; it is only those who promote suspect and weak theories who need to suppress divergent scientific opinion.

Such lack of balance and such bias by Wessely in the presentation of what is known about ME can only mean that he is deliberately influencing and manipulating the perception of ME / CFS which his readers – particularly medical and legal practitioners – will acquire.

In effect, he is purposefully setting out to mislead influential professional decision-makers by mis-representing what is known about ME.

He achieves this by deception and by his selective and biased use of available texts and references, a technique of which he is master on the grand scale.

This should not happen in science.

2. Wessely persists in exaggerating the (unproven) role of psychopathology in ME, despite increasing evidence which challenges such a partisan view.

For example, the ME literature abounds with evidence of viral activity in ME patients and there is much evidence of a *chronic* viral infection; in particular, there is an abnormality in an antiviral lymphocyte enzyme system called the 2-5A pathway, which has been found to be chronically activated in patients with ME; overall, there is strong evidence of an *ineradicable* infection (see *Chronic Fatigue Syndrome: an Update*. AL Komaroff, DS Buchwald. *Ann Rev Med* 1998;49:1-13). This paper, by two of the world's leading and most respected authors on ME / CFS, discusses the evidence that abnormal, objective biologic processes are present in ME / CFS; in particular, these are subtle abnormalities of the central nervous system (CNS), chronic activation of the immune system, and re-activation of latent viruses.

There is also abundant published evidence of multiple abnormal immunological (mostly hyper-immune) and neuroendocrine laboratory findings in ME, and these abnormalities are consistent with those seen in viral infections. (see *Chronic fatigue syndrome: clinical condition associated with immune activation*. Landay AL, Jessop C *et al*, *Lancet* 1991;338:707-712).

In other studies (see those of Hassan & Weir *et al* and Wagner & Klimas on page 36 above), the most important association with greater disease severity involved elevation of T-helper cells and the CD4:CD8 ratio.

Further, it is widely acknowledged by ME experts with actual experience in the discipline that there is an increase in the CD8+ cytotoxic T cells bearing antigenic markers of

activation on their cell surface (see *Chronic fatigue syndrome: an Update*. AL Komaroff, DS Buchwald. *Ann Rev Med* 1998;49:1-13).

Overall, the elevated levels of immune complexes, the abnormalities in Ig subclasses (especially IgG3) and in autoantibodies and the universal finding of decreased NK cells are known to be consistent with evidence demonstrating chronic, low-grade immune activation in ME.

Further, there is the well-established and universal evidence of neuroendocrine changes consistent with a degree of dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis.

In particular, there is nuclear magnetic evidence on PET / SPECT scans which shows reduced blood flow through the brain stem in ME patients: to date, this exact finding has never been found in any other illness or disease process apart from ME.

(see *Brainstem perfusion is impaired in patients with chronic fatigue syndrome*. Costa DC, Tannock C and Brostoff J. *QJM* 1995;88:767-773).

Also, there is firm laboratory evidence which demonstrates delayed muscle recovery from fatiguing exercise; this demonstrates conclusively that in ME, there is *continued* loss of post-exertional muscle power (giving an *additional* loss of power), with delayed recovery for at least 24 hours (whereas sedentary controls recovered full muscle power after 200 minutes). (see *Demonstration of delayed recovery from fatiguing exercise in chronic fatigue syndrome*.

Paul L et al. *European Journal of Neurology*: 1999;6:63-69).

### 3. Wessely urges that people with “medically unexplained symptoms” should not be “over-investigated”.

Wessely is being highly unscientific in attempting to prevent the progress of medical science, but from his own preferred perspective, if such patients are never fully investigated, his allegation that their symptoms are “functional” cannot easily be disputed.

By his promotion of this limited and narrow perspective, Wessely is attempting to remove discourse on ME from the realms of medical science: if unexplained symptoms remain uninvestigated, they remain unexplained.

As yet, there is no single, definitive laboratory test for ME, but there *are* certain tests which ME clinicians use which, taken together, are highly indicative of a diagnosis of ME. These include the following:

- (i) higher frequencies of low-levels of various autoantibodies, especially antinuclear and smooth muscle antibodies

- (ii) elevated CD4:CD8 ratio (as in multiple sclerosis, this increased ratio always corresponds with disease severity)
- (iii) decreased (very low) levels of cytotoxic activity of NK cells
- (iv) circulating immune complexes (CICs) are found (at fairly low levels)
- (v) IgE is increased (not very high levels, but definitely increased)
- (vi) salivary IgA (SIgA) is positive at low levels
- (vii) IgG3 is present at low levels. *(sceptics assert that the significance of this is unknown and therefore irrelevant, but this is not so: there is a known linkage with lung disease and with gastrointestinal tract disorders. The IgG3 laboratory baseline range is extensive – from 14 to 240 – and there is a huge range of methodologies, so it is essential to ascertain the patient's individual baseline for future comparison. Most low IgG3s are associated with primary immune deficiency and with low IgG2 and IgG1 in malignancies)*
- (viii) HLA phenotyping shows 46% of those with ME to be HLA DR4 +ve This is very suggestive of a genetic component and suggests a genetic susceptibility in ME involving antigen presentation *(see the work of Dr Paul Terasaki from UCLA School of Medicine, who is one of the world's leading experts in HLA typing; see also Chronic fatigue syndrome: A Diagnostic and Treatment Guide for Patients and their Physicians. Jay A Goldstein. Pub. The CFS Institute, 436 N.Roxbury Drive, Beverly Hills, California, 1990, p59).*
- (ix) the water-loading test is abnormal (+ve) in ME patients
- (x) the buspirone / prolactin challenge test is abnormal in ME patients
- (xi) there is hard evidence on polymerase chain reaction (pcr) of muscle abnormality in ME patients
- (xii) nuclear imaging shows specific and definite patterns of abnormality in ME patients
- (xiii) mast cells are often +ve in ME patients
- (xiv) there is low (or very low) pancreatic exocrine function in ME
- (xv) copper response test results are low, indicating abnormal liver function in ME: following the oral administration of zinc sulphate, the copper response from the liver should be around 200; in ME it can be zero

- (xvi) there are anomalies in the trace element metabolism, especially low *red blood cell levels* of magnesium, zinc, chromium and potassium
- (xvii) non-invasive Doppler scans show peripheral vascular problems in ME, with low peripheral oxygenation levels, and poor perfusion and pulsatilities
- (xviii) some patients with ME have positive electronystagmography and caloric testing results, indicating the presence of a vestibular lesion
- (xix) a significant percentage of people with ME show flattened or even inverted T-waves (which are not picked up on a straight 12 lead ECG, but are seen to occur in the presence of concurrent tachycardia on 24 hour Holter monitoring).

In addition, there are characteristic patterns in various other laboratory parameters, with particular problem areas being thyroid function, adrenal function, bone density, cholesterol levels and high density / low density lipoprotein ratios (HDL / LDL ratios).

Whilst not requiring laboratory facilities, the following clinical signs should not be overlooked:

- a) 20% of ME patients have obvious (non-androgenous) hair loss
- b) there is frequently visible fasciculation in ME
- c) patients with ME often have obvious, significant and recurrent mouth ulcers.
- d) patients with ME have a +ve Romberg sign
- e) patients with ME have a discrete gait pattern.
- f) ataxia is commonly observed in ME
- g) nystagmus (often jelly-like and intermittent) is almost invariably present
- h) discolouration of the skin is often present, particular on the forearms and hands
- i) Raynaud's phenomenon is very common in ME and fibromyalgia
- j) there is often an observable tremor present.
- k) according to Professor Jonathan Brostoff of UCL medical school, candida / candidiasis is present in about 50% of ME patients
- l) patients with ME bruise easily and often show peri-articular bleeds, especially in the digits

(See also page 146 above).

It is unacceptable to attempt to dismiss, ignore or deny a reality which can be scientifically measured, yet Wessely (and the joint Royal Colleges' report CR54) advocates that people with ME should not be comprehensively investigated.

4. Wessely and colleagues continue to perpetuate their own version of the ME "myth", ie. that "ME" is nothing more than a belief that one is suffering, and that ME does not exist as a nosological entity

By promulgating the dissemination of such misinformation, Wessely undermines the understanding of what ME really is: a formally classified neurological condition, and he appears to be guilty of deliberately halting further understanding.

By the deliberate widening of the baseline definition criteria (the Oxford criteria) to include *all* medically unexplained “fatigue”, and by *excluding* from the diagnostic criteria manifestations of neurological disease, Wessely and his close psychiatrist colleagues have paved the way for him to achieve his often-stated objective, namely, the disappearance of “ME” from medical nosology.

Given this deliberate dilution of the criteria, of course Wessely can now claim that present “CFS” is not past “ME”, because the definition criteria have been altered (although when it suits him, he claims that they *are* the same).

This altering of definitions, and the combining of separate and distinct subgroups, has been criticised in the Report of the National Task Force on ME / CFS.

That Wessely consistently fails to study patients who have ME as distinct from those who are simply “tired” or “fatigued” (and then claims in his published work that ME does not exist) has caused international concern, and the Task Force Report found that progress in understanding ME / CFS has been hampered by:

- the use by researchers of heterogeneous study groups
- the lack of adequate comparison groups
- the invalid comparison of contradictory research findings stemming from the above

*(see Report from The National Task Force on Chronic Fatigue Syndrome (CFS) Postviral Fatigue Syndrome (PVFS) Myalgic Encephalomyelitis (ME). Westcare, Bristol 1994 / supported by The Department of Health and The Wellcome Trust).*

That such failure by this group of psychiatrists to ensure accuracy is a matter of world-wide concern can be seen from the following extract from the journal MPWC News, (Medical Professionals With CFIFS / ME), Summer 1999, written by Byron Hyde of The Nightingale Research Foundation, Ottawa, editor of the standard textbook on ME (*see footnote 46 on page 145 above*), entitled “Are ME and CFS synonymous?”

“This ME definition is important in that unlike the CDC definitions of chronic fatigue syndrome, the Wallace (*sic*: *Wallis*) and Ramsay definitions of ME observe the importance of the initial acute variable infectious type illness associated with subnormal



temperature.

“They then note the important secondary and resulting chronic illness characterized by CNS and the autonomic nervous system features and intellectual and muscle dysfunctions and their chronic persistence.

“Enlarged cervical lymph nodes and pharyngitis are almost never observed in the chronic phases of ME and yet by definition they form part of the characteristic findings in CFS.

“ME is also distinguished from CFS in that multiple organ involvement, seizure activity, death and autonomic nervous system dysfunction occur in ME and by definition these simply do not occur in CFS.

“Perhaps the most important difference is that chronic fatigue is not an essential factor, but rapid CNS and muscular fatiguability, with a pathologically slow recovery or loss of stamina is an essential finding.

“In ME, the illness, the disease process, its investigation and pathology start on the day the patient ceases to be well.

“In CFS, the Atlanta-based CDC has decreed that the disease process starts only on the first day of the sixth month.

“It is my belief that the initial CDC definition was created by a group (of researchers and physicians) who...had never...seen or examined CFS patients (and) who were so compliant in believing that EBV (Epstein Barr virus) was the cause of CFS that they simply incorporated diagnostic features of infectious mononucleosis (glandular fever) into the CDC CFS definition.

“It is also important to note that three of the physicians who had the longest experience with ME / CFS patients withdrew from the initial CDC definition committee.

“Good definitions are good because they correspond closely to the disease state being described. It is thus important that those who attempt to define any disease or illness have long-term clinical experience with patients with this illness.

“I believe that the inclusion of psychiatrists in the defining of an epidemic (and disease) of obvious infectious origin simply muddies the waters for any serious understanding of that disease.

“The UK (Oxford) definition of CFS was developed by a panel of physicians who were primarily psychiatrists with few if any physicians who had ever looked at an epidemic of CFS.

“A serious effort must be made to look at epidemic disease....this has not been done by those who have defined CFS in the USA nor in the United Kingdom”.

Wessely, however, deems that ME and CFS should not be distinguished, as he believes that they are all one “functional somatic syndrome”.

5. Wessely continues to flood the medical literature with repetitious claims about the efficacy of his choice of psychotherapy (especially graded exercise and cognitive behavioural therapy) in chronic fatigue syndrome.

Most of the articles claiming success for the supposed efficacy of GA/CBT in CFS are written by the (mostly British) authors themselves, so their conclusion comes as no surprise. (*see the criticism of this practice by Friedberg F. on pp 202-203 above*).

6. Wessely makes assumptions and takes for granted what still needs to be explained.

In many of his published studies, Wessely appears to form his conclusions before he has generated the data to support those conclusions.

One of his tenets is that what *precipitates* ME / CFS is not what *perpetuates* it: as yet, he has produced no *evidence* of when the supposed change from precipitation to perpetuation occurs in ME, nor of what *causes* the supposed change.

He *believes* this change is brought about by psychosocial factors (including his claim that there is secondary gain), but that is not evidence which scientifically supports his own ideas.

For example, Wessely claims that people with ME *benefit* from having what they believe is a “legitimate” diagnostic label, so he spends much effort attempting to demolish any such legitimacy of a diagnostic label for ME.

He maintains that people with ME *benefit* by “adopting the sick role” and that once their incapacity has been “legitimised”, they can then manipulate those around them to do their bidding (for supposed “secondary gain”).

However, Wessely has never produced even a shred of evidence which supports his opinion that there is secondary gain .

He has made no scientific study of individual cases for which he claims secondary gain: if he wishes to claim that there are benefits, then he needs to show that patients *are* benefitting from adopting the sick role for what they can get out of it, and this needs to be *proved* before it can be stated as *fact*.

He does not do this, most probably because even a cursory attempt to discuss their losses with ME patients would rapidly demonstrate the absurdity of his conclusions about

“gains”.

For example, where does Wessely consider the *losses* experienced by virtually all those who have ME?

He rarely, if ever, discusses the loss of a fulfilling professional career, nor the loss of any kind of employment, nor the loss of status, nor the inevitable financial loss (including the loss of pension), nor the loss of financial security arising from being reliant upon meagre state benefits, nor the loss of dignity and self-respect and independence, nor the loss of relationships, including marriage, nor the loss of friends, hobbies, holidays, social life, community involvement.

He has seemingly made no study of the number of suicides by those with ME.

He pays scant regard to the impact of such profound illness, pain and relentless suffering with which those with ME must live on a daily and even hourly basis, often with incredible but unremarked courage. *Wessely* has never carried out a study of the quality of life of those with ME, but others have; their conclusions are chilling.

*(See page 18 above, and see also Quality of Life in Chronic Fatigue Syndrome. Robert Schweitzer et al. Soc Sci Med 1995;41:10:1367-1372, which found that CFS sufferers had more dysfunction than those with multiple sclerosis, and that their impairment was more extreme than that found in end-stage renal disease and heart disease. Only in terminally ill cancer patients was the sickness impact profile (SIP) greater than that found in ME / CFS. The two pervasive consequences were found to be social isolation and the loss of highly valued roles.*

*See also Testimony Before The FDA Scientific Advisory Committee, February 18, 1993, by Paul R.Cheney, in which Cheney testifies as follows: “I have evaluated over 2,500 cases of chronic fatigue of which over 2,000 cases meet the CDC case definition. At best, it is a prolonged post-viral syndrome with slow recovery. At worst, it is a nightmare of increasing disability with both physical and neurocognitive components. The worst cases have both an MS-like and an AIDS-like clinical appearance. We have lost five patients in the last six months. The most difficult thing to treat is the severe pain. Half have abnormal MRI scans.*

*80% have abnormal SPECT scans, 95% have abnormal cognitive-evoked EEG brain maps. Most have abnormal neurologic examinations. 40% have impaired cutaneous skin test responses to multiple antigens. Most have evidence of T-cell activation. 80% have an up-regulated 2-5A antiviral pathway. 80% of cases are unable to work or attend school. We admit regularly to hospital....with inability to care for self.*

*“CFS is a poorly understood disorder with a distinctive clinical presentation.*

*“This disorder is a socio-economic as well as medical catastrophe that will not end.*

*“This disease is too complex to rely wholly on standard medical orthodoxy to explain it”.*

Note that in the United States, ME/ CFS research is now being treated as a priority, and that in the year 1995-6, the US government voted \$11.8 million to ME research.

In the UK, as a result of Wessely’s adverse influence, the government is funding absolutely no research whatever (*see page 76 above*).

In the light of what is known about ME, it is surely curious that, whilst adducing absolutely no supportive data, Wessely has concluded that adoption of the sick role confers “secondary gains”.

One further illustration of Wessely’s tactic of generating his conclusion before he has generated the supporting data can be found in his paper Vitamin B status in patients with chronic fatigue syndrome (*LC Heap, TJ Peters, S Wessely. JRSM 1999;92:183-185*); having found evidence of reduced functional vitamin B status, particularly pyridoxine, in CFS patients, the final sentence reads “But clearly, many patients with CFS are currently taking vitamin B and other supplements with little evidence of benefit”, yet nowhere in his data does he provide any evidence that “many” patients with CFS are taking supplements “with little evidence of benefit”, so his final conclusion once again fails to follow from the data, especially as his study consisted of only 12 patients and 18 controls. (*See pp. 127-128 above*).

7. Wessely et al wilfully mis-use the published data on ME / CFS and manipulate it so that it appears to support their own views, when the source article does not support them

On 27<sup>th</sup> April 1997 a senior American clinical psychologist said of Wessely’s work (quote) “It is one of the worst jobs I’ve seen of mis-using psychological research” (*personal communication*).

For illustrations of this, see the critiques of the joint Royal Colleges’ report CR54 on CFS (*see pp 60-62 and page 65 above* and see also Dr Hedrick’s letter in the QJM (*see pp 81-83 above*).

8. Wessely et al are highly selective in the patient cohorts they purport to study

It is a matter of international concern that Wessely never includes in his research studies

anyone who is too sick with ME to get to a clinic, which means that there is an unrepresented sub-group who are bed- or house-bound who are continually excluded from his study groups.

This is hardly impartial science, but it has enabled Wessely to be on public record as aiming to “eradicate” ME (see *Eradicating ‘Myalgic Encephalomyelitis’ (ME). Report of the meeting held on 15<sup>th</sup> April 1992 at Belfast Castle, Pfizer / Invicta Pharmaceuticals, pp 4-5*), and see also *Denigration by Design? pp 121-123 for the report of his Eliot Slater Memorial Lecture given on 12 May 1994*), which he believes can be achieved by psychotherapy (by altering the way patients think) and by the administration of antidepressants.

When untold numbers of such patients become too sick to continue in his trials, his usual tactics appear to be never to follow them up at home, but simply to claim a high drop-out rate, which appears to be ethically and methodologically corrupt.

It is only those who really know the literature who are able to pick this up; busy clinicians and government officials certainly do not do so.

9. Wessely continues to be overtly patronising in his encounters with ME patients, whilst continuing to denigrate and mock them in print and in his behaviour with his colleagues, where those with ME are the subject of his ill-concealed ridicule

At the Spring meeting of the British Society for Allergy, Environmental and Nutritional Medicine held at the Royal College of General Practitioners in April 1998, Dr Gordon Skinner from Birmingham gave a lecture entitled “Identification of endocrine and other disorders in chronic fatigue syndrome” in which he described his treatment regime for hypothyroidism in ME, which over five years he had found to be the most common concurrent diagnosis.

Dr Skinner then announced that his funding for treating ME patients had been withdrawn, whereupon Wessely was observed to be visibly amused.

At this same meeting, Wessely’s own talk consisted mainly of jokes and newspaper cuttings. He told the audience that ME was not due to a virus, and that his approach was to stop patients thinking they have a virus infection, which he does by talking to them for two hours to gain their confidence, followed by cognitive behaviour therapy, which he claimed was safe.

Wessely then said that 50% of ME patients are maladjusted.

His preferred focus was on “misjudged psychiatrists” rather than on the plight of ME patients.

*(For an illustration of how Wessely mocks those with ME, see pp 84-85 above, and for examples of how he patronises patients with ME, see p 88 above and p.101 above, also pp 109-110 above. See also Denigration by Design?, pp 121-123, which reports on Wessely's mockery of those with ME contained in his Eliot Slater Memorial Lecture given on 12<sup>th</sup> May 1994).*

10. Wessely continues to contribute to the on-going stigmatisation of psychological illness (in which he includes ME / CFS)

Despite his lip-service to the need for the mind / body dualism to be discarded as no longer apposite, Wessely's decade of denigration of those with ME has resulted in patients with ME being stigmatised on an unprecedented scale; this has taken the form of defamation of character; damage to their credibility; loss of state benefits; loss of legal aid so that common justice could not be pursued, all of which have led to a consequential increase in suffering, isolation, despair and suicide. *(see page 191 above for Dr Shepherd's response to the article by Elaine Showlater, in which as Medical Director of the UK ME Association, he stated that there is now one ME suicide per month).*

In an article entitled Stigma and chronic fatigue syndrome (Green J, Romei J and Natelson BH: *JFCS* 1999;5:2:63-75), the authors found that significantly more male doctors labelled symptoms as psychological, and that doctors reconstructed reality to signify that the illness of the patients was "not real".

The authors found that with ME, doctors played a potentially damaging role in legitimising the illness experience; they also found that there was a subtle infantilization of patients with ME / CFS and that interactions with sceptics have a greater influence on stigmatisation.

Bearing in mind Wessely's many attacks on the credibility of ME patients, there can be little doubt that he has personally contributed to this on-going stigmatisation of those with ME.

Such stigmatisation seems likely to continue, for it is Wessely's own data base at King's College Hospital which is to be used as the basis for the systematic review of the CFS / ME literature currently being carried out for the NHS by the Centre for Review and Dissemination (CRD) at York university.

The CRD collaborates with a number of health research and information organisations across the world and is a member of the International Network of Agencies for Health Technology Assessment (INAHTA) and is a sibling of the Cochrane Collaboration *(see Denigration by Design? page 26)* which is an international body set up to prepare a database to encompass the results of all clinical trials, and whose database will form an internationally available meta-analysis of what is considered to be the most effective

treatment / management in all medical disciplines. Its' results will thus become the definitive worldwide medical database on all medical conditions.

Wessely offered himself to and was accepted by the Cochrane Collaboration (then based in Oxford); he is in charge of the working party on CFS / ME on this collaboration.

As the CRD plays an important part in disseminating the contents of the Cochrane Reviews to the NHS, it seems inevitable that stigmatisation of those with ME will continue for as long as Wessely exerts such influence.

#### 11. The continued effect of Wessely's influence

Wessely's tactics appear to be an intentional and co-ordinated campaign to obliterate the history and existence of ME as it has been documented in the medical literature since the 1930s, and to denigrate and destroy those who resist his forceful coercion techniques, ie. those who refuse to be brain washed into relinquishing their belief that they are physically, organically ill and that they are suffering from a serious and devastating condition which cannot be effectively controlled or successfully managed by psychotherapy.

At the same time, Wessely disparages and diminishes those researchers and clinicians who try to support and help patients with ME.

As a result, one sector of medicine seems to have become very ugly indeed.

Patients severely ill with ME are being subjected to harsh and often unsuitable therapy, often with the inappropriate administration of antidepressants or psychotropic drugs as if they were somehow deviant. (*see The Organic Basis of ME / CFS, presented to the Chief Medical Officer Sir Kenneth Calman on 11<sup>th</sup> March 1998 by The Countess of Mar, Dr EG Dowsett and DM Jones MSc*).

Wessely's own ideology is being enforced with a ruthless tyranny: quite certainly, sick people have been left with the unmistakable impression that if they do not co-operate by complying with psychotherapy, then they are deemed not to *wish* to get well, so their benefits will cease; equally certainly, children and adolescents have been threatened with forcible removal from their parents and home.

One area health authority ( West Kent Health Authority) insists that all patients diagnosed as having ME / CFS must be compulsorily referred *only* to Wessely's CFS clinic at King's College Hospital, London, with his known bias and preference for a psychological cause of ME / CFS.

These are nothing other than bullying tactics which are far removed from the concept of caring for the sick.

## 12. The question of whether or not Wessely is guilty of scientific misconduct

It seems that to Wessely and his closest associates, the belief of the moment represents the only truth.

He would do well to recall that in the early 1600s, King James of England wrote a book called “Demonology” and this book helped to send to their death women known as the Lancashire witches (from Pendle in East Lancashire).

Countless women – often Catholics – were persecuted, tortured and executed as witches, having been forced into admitting things which they did not do, the majority being people suffering from mental illness.

Incredibly, it was not until the 1950s that the Witchcraft Act was repealed in the UK.

This must surely serve as a salutary reminder that the belief of the time is not necessarily the truth, even though it might be promoted as the truth.

The question of whether or not Wessely is guilty of scientific misconduct has already been published (*see Appendices I and II*).

Given the extent and nature of what is now known about ME / CFS, it is a matter of extreme concern that patients with “functional somatic syndromes” have been described as “unavoidable, untreatable and unattractive” and that Wessely himself has written about CFS patients as follows:

“The description given by a leading (doctor) at the Mayo Clinic remains accurate: ‘the average doctor will see they are neurotic and he will often be disgusted with them’ “. (*Chronic fatigue and myalgia syndromes. Wessely S. In: Psychological Disorders in General Medical Settings. Eds: N. Sartorius et al. Hogrefe & Huber, 1990*).

It is therefore not in doubt that Wessely is of the view that the above description of those with CFS (ie. that they are neurotic and that doctors are often disgusted with them) is an *accurate* description.

It is fair to state that Wessely and his close colleagues are held in contempt by many people – medical and lay alike – who have to deal with the reality and severity of ME.

At the beginning of the 21<sup>st</sup> century, it cannot be acceptable that whenever medicine does not have a definitive test, a disorder is assumed to be “psychological” simply by default.

For those who *do* have a psychological illness, as such illnesses are now known to be caused by organic disturbances in the brain, it is imperative to remove the totally



unjustified stigma which psychological illnesses still engender. One way to start the process of de-stigmatisation would be for the state to grant parity of financial support for both physical *and* psychological illnesses, but whilst Wessely acts as adviser about the nature of CFS / ME to the Benefits Agency, any hope of this remains nothing more than a dream.

However, it needs to be noted that the Courts of Law do not now distinguish between physical and psychiatric injury per se.

*(See Page - v - Smith, Court of Appeal: Civil Division. Sir Thomas Bingham MR, Morritt and Auld LJJ. 3 All ER 1996: 272-280, in which Ronald Page won his case that the road traffic accident in which he was the innocent party had grossly exacerbated his quiescent ME and had converted it into chronic illness. Although in this landmark case ME has been reported as being “psychological”, in the actual Judgments there is repeated reference to the plaintiff’s ME as a physical illness as opposed to a psychological one by Lords Browne-Wilkinson and Lloyd of Berwick, who ruled that it should not make any difference that the physical illness which the plaintiff undoubtedly suffered as a result of the accident “operated through the medium...of the nervous system”).*

On the medical and social fronts however, very significantly because of Wessely, injustice for those with ME continues, and cases of untold suffering and despair continue to accumulate.

One can but pray that his power and influence – unlike that of demonology – will not prevail for the next 350 years and that medical science will soon have the ability to right the wrongs which Wessely has done so much to perpetrate.

## APPENDICES

### **Short summary of some of the findings presented at the Second World Congress on Chronic Fatigue Syndrome and Related Disorders, Brussels, 9-12 September 1999**

*These findings refute Wessely's incessant claim that ME / CFS is a "somatisation" (psychiatric) disorder.*

This was the second international conference arranged by Professor Kenny de Meirleir and his team in Brussels, Belgium; medical experts from around the world, including some well-known and respected researchers, presented their most recent findings.

At the previous international congress held in Brussels in November 1995, Simon Wessely attended by invitation; at the 1999 congress, he was not an invited participant and he chose not to pay for himself, so he did not attend.

Indeed, there was a veritable dearth of psychiatrists at the 1999 congress, a fact noted by Professor Daniel Peterson of the USA, who commented that at one conference, 99% of the presenters were psychiatrists, and that he was amazed at the misconceptions which existed about CFS.

Peterson said that ten years ago he believed CFS would be resolved by science; he had now changed his mind, and believed that it could only be resolved by politics.

### **Biochemistry of fatigue and pain**

Dr Neil McGreggor from the Department of Biological Sciences, Callaghan, New South Wales, Australia, spoke about The Biochemistry of Chronic Pain and Fatigue.

He presented data from four separate investigations of CFS using metabolite profiling techniques; several types of chronic pain and fatigue disorders were discerned.

Chronic pain was associated with reductions in serum sodium levels, changes in urinary volume, output of amino acids and other urinary metabolites, and increases in enzyme markers of tissue damage (ALT, AST). Increases in tyrosine / leucine ratios indicated changes in protein turnover, and were significant.

Fatigue was associated with alterations in the excretion of amino and organic acids associated with the tricarboxylic (citric) acid cycle.

Levels of RNase-L correlated with chronic fatigue and related symptoms.

Carriage of toxin-producing coagulase-negative staphylococci (which correlated with increased tyrosine / leucine ratios) was evident in 89% of CFS patients.

Changes in nitrogen homeostasis were associated with pain and fatigue symptoms.

Dr Henry L. Butt, a medical microbiologist from the University of Newcastle (Australia) research team discussed The Association of Staphylococcal Membrane - damaging Toxin and Chronic Fatigue / Pain, and reported that the increased prevalence of multiple carriage of coagulase - negative staphylococcus (which produces membrane-damaging toxins) was associated with increases in the tyrosine / leucine ratio, and that this indicated changes in the balance of proteolysis and protein synthesis, resulting in increased urinary excretion of the excitatory amino acid glutamic acid, which correlated with musculo - skeletal symptoms, mood and cognition functions, and with an inverse association with temperature.

The toxin is hexameric and may function as an ion channel.

Overall, dysregulated proteolysis and increased excitatory amino acids are events associated with chronic muscle pain.

In a separate lecture, Butt spoke about The Development of Laboratory-based Tests in Chronic Fatigue and Pain: Faecal Microbiology and Biochemistry. He reported that 60% of patients with chronic fatigue and pain have gastrointestinal problems, which supported the hypothesis of an altered gastrointestinal microbial flora.

These alterations in the microbial composition of the gastrointestinal tract may adversely affect the normal symbiotic processes.

There were also distinct differences in the faecal lipid composition in CFS patients, which showed significant correlation with gastrointestinal symptoms and in changes in the gut microflora.

Dr Hugh Dunstan, another member of the Newcastle, Australia research team spoke about The Development of Laboratory-based Tests in Chronic Pain and Fatigue: Essential Fatty Acids and Cholesterol.

He reported that EFAs are important for nerve functions, cell integrity, communications and membrane functions.

The mitochondria and myelin are affected.

CFS patients have significantly different fatty acid and sterol fasting plasma profiles from controls, and patients could be divided into different sub-groups on the basis of the profiles; in contrast, the control group was homogenous in their lipid profiles.

CFS patients have lower levels of cholesterol, which would adversely affect the membrane integrity and functioning, as well as steroid hormone synthesis, energy metabolism and bile production.

Viral infection can affect the nature of lipid-based anomalies in CFS patients.

Discriminant analysis showed clear differences between different CFS symptom indices.

This analysis provides a basis for treatment by lipid and micronutrient supplementation -- fish oils are less suitable (high arachidonic acid content) than vegetable oils. Division into biochemical sub-groups may provide a basis for individually-tailored management and treatment. His team recommends EFA supplementation, plus zinc, magnesium, manganese and vitamins A,C,E and B6.

In some CFS patients there is poor absorption as a result of a highly compromised gastrointestinal tract.

In a second paper, Dunstan spoke about The Development of Laboratory-based Tests in Chronic Pain and Fatigue: muscle catabolism and coagulase - negative staphylococci which produce membrane - damaging toxins.

In particular, he spoke about urine analysis, which is affected by the toxic chemical load, occult infections and altered homeostasis.

Their research data showed that CFS patients had reductions in total organic acid excretion.

Sub-groups of CFS patients could be delineated on the basis of their urine excretion and symptom presentation.

Muscle catabolism resulted in dramatic changes in urinary amino acids, particularly increases in tyrosine and 3-methylhistidine, with significant decreases in leucine, aspartate and phenylalanine. Pain severity was related to the tyrosine / leucine ratio and could be identified based on analysis of urine excretion and presented symptoms. Succinate levels were also reduced.

Membrane-damaging toxins (MDT -CoNS - coagulase negative staphylococci) were strongly correlated with catabolic responses and pain severity.

An unknown marker molecule (UM 27 –*urinary metabolite 27*), was elevated, and there was a positive correlation of pain with the levels of UM27, indicating that this may play a significant role in the aetiology and sustenance of chronic pain / fatigue disorder.

Dr H.Kuratsune from the Department of Haematology and Oncology, University Medical School and Department of Neuroscience, Osaka Bioscience Institute, Japan, spoke on Brain Regions Responsible for Fatigue Sense? --reduced acetylcarntitine uptake with PET into Brodmann's Area 9 + 24 in patients with CFS.

They found that most Japanese and Swedish CFS patients have a serum acetylcarnitine (ACC) deficiency and that this correlates with rating scores of fatigue.

They studied regional cerebral acetylcarnitine metabolism (rCMRac) and regional cerebral blood flow (rCBF) in CFS patients and in controls: there was deficient uptake in certain areas of the brain in CFS patients, particularly in Brodmann's areas 9 and 24, but also in the thalamus and other Brodmann areas 44,43,39,19,18, and in the anterior cingulate, the left temporal parietal cortices and basal ganglia, and this was correlated with rCBF.

Areas 9 and 24 are associated with cognitive, attentive and autonomic functions.

They concluded that biosynthesis of glutamate, aspartate and GABA in these areas may be impaired due to ACC deficiency, and this may explain the fatigue experienced by CFS patients.

Professor Tim Roberts from Australia presented details on Biochemical Abnormalities Associated with Visual Processing Disability (Scotopic Vision) in CFS.

Apart from fatigue, many other important problems are reported by CFS patients.

Disorders of visual processing in CFS patients include fatigue, lack of concentration (especially while reading), decreased visual span, abnormal pupil response, saccades and disturbed pursuit eye movements.

Similar anomalies have been identified in dyslexia.

Such problems are known as Scotopic Sensitivity / Irlen Syndrome (SSIS), and show an association with alterations in amino acid homeostasis, indicative of proteolysis, and changes in lipid metabolism.

He tried to ascertain whether biochemical anomalies in CFS may be related to these visual problems: preliminary investigation of urine excretion data show several metabolic abnormalities which may be associated with these symptoms and reported symptoms appear to correlate with the finding of protein catabolism, which suggests an underlying infective aetiology.

## **Immunology**

Professor Nancy Klimas from the Clinical Immunology Laboratory, University of Miami School of Medicine, USA, gave a comprehensive and authoritative overview entitled Immunological Abnormalities in CFS.

She started by listing various factors affecting the immune system in CFS:

- (i) genetic predisposition (51%)
- (ii) triggering events (infections)
- (iii) mediators (endocrinological and psychological factors)

and observed that the health outcome in any individual depends on how all these interact.

The role of the immune system in illness is twofold:

- (i) it plays a direct role in contributing to the symptom complex: immune competence decides effective or defective prevention of reactivation of infections. When turned on, the lymphocyte antigen-driven response may generate a Type I response (CD4+, Th1, IL 2 / IL 12, INF - gamma, with activation of CD8+ cells that kill viruses). Lymphocytes play a vital role: They function through a messenger system -- cells have memories; they are antigen-driven and recognise infections, transplants, toxins, foods etc.
- (ii) it plays an indirect role, because it interacts with the brain (it has receptors for neurotransmitters) and with the endocrine system (cortisol reduces inflammation through down-regulation of immune activation -- low cortisol in CFS could play a role in chronic immune activation. *(See Appendix IV for differences in cortisol levels in CFS and in true ME)*. Stress has a profound impact on the immune system. Interaction with the hypothalamic / pituitary axis affects neurotransmitters and impacts on sleep. The Type II response (Th2, IL6, IL10, activation of B cells, and antibody production, (which prevents / clears infection) comes to dominate as the illness extends.

The importance of the 2-5RNase -L (a product of INF- gamma activation) leads to an up-regulation of RNA synthesis and pro-inflammatory cytokines, TNF -alpha and IL 1, which also disturb circadian rhythms.

Specific oligoclonal and not polyclonal antibodies are involved.

The effects of stress and negative life events were similar in CFS patients and in controls, but the long-term outcome depends on the shift from Th1 to Th2.

There is evidence of chronic immune activation: enzyme systems are up-regulated (eg. interferon, 2-5A RNase L activation, mRNA (cytokines).

With regard to oligoclonal versus polyclonal activation, Klimas observed that there is a

lack of abnormal serology to most latent viruses, suggesting that immune activation was antigen-specific.

There is evidence of cytokine abnormalities – cytokines change over time and with illness severity: TNF-alpha receptor expression increases with flares of the illness, and there is increased evidence of Type II expression as the illness persists for years.

Longterm, stress results in immune dysfunction illness (eg. reduced numbers of CD8 (suppressor) cells, blunted growth hormone (GH) response and thyroid releasing factor (TRF), and increased corticotrophin releasing factor (CRF),

ACTH and cortisol, which Klimas pointed out was the *opposite* of what Demitrack claimed.<sup>2</sup> (*See Appendix IV for differences in cortisol in CFS and true ME*).

Of interest is the fact that Klimas has found an *enlarged* adrenal mass, which is the opposite of Dinan's findings, where the right and left adrenals were found to be reduced in size by 50% (*see page 34 above*).

Klimas said CFS was an excellent model of neuroendocrine-immune interaction and restated the PNI (*psychoneuroimmunological*) paradigm as a basis for understanding the complex relationships which underlie the extensive changes occurring in CFS patients.

She concluded by confirming that immune abnormalities play an integral role in the pathogenesis of CFS and that they contribute to the symptom complex, and that they interact with the autonomic and endocrine systems; the pattern and type of immune activation are equal to "cause and effect".

Professor Jonathan Brostoff from University College, London discussed Allergy in CFS.

He started by saying that it might be useful and practical to look at the 'total load' in CFS and try to alleviate the burden.

25% of ME / CFS patients are allergic, and this can be mistaken for CFS. In contrast, it was rare to see an allergic diabetic. Common culprits giving rise to food allergies are chocolate, grains, dairy products, coffee and citrus fruits, which can give rise to migraine, arthralgias, lethargy, myalgia, irritable bowel syndrome and vivid dreams. Hyperventilation is common and gives rise to breathlessness, pins and needles, scotopic vision, alkalosis and reduced blood magnesium.

Multiple chemical sensitivity was another add-on problem, where patients become extremely sensitive to drugs and inhaled chemicals.

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<sup>2</sup> Evidence for Impaired Activation of the Hypothalamic-Pituitary-Adrenal Axis in Patients with Chronic Fatigue Syndrome. Mark A. Demitrack et al. *Journal of Clinical Endocrinology and Metabolism*. 1991;73:6:1224-1234

All these provide add-ons to CFS and should not be mistaken for it.

If these add-on problems are treated (by an elimination diet, by micro-nutrient supplementation and by correcting breathing patterns), the total load would be less.

Brostoff believes that the IBS / opioid theory is not valid for more than 20% at most of ME / CFS patients.

He commented that almost 30% of the general population suffer from some form of food intolerance (*which is his area of speciality*).

Dr L.Lambrecht , from the Department of Nuclear Medicine, University Hospital, Ghent, Belgium, spoke about The Chronic Fatigue Syndrome: Clinical, Immunological and Neuro-imaging Correlations in 500 patients.

He outlined results from an extensive battery of tests done on 500 consecutive CFS patients between January 1991 and May 1999. The tests included routine laboratory parameters and erythrocyte magnesium levels; lymphocyte phenotyping (CD8+ / CD38+ and associated T8 cell percentage); pulmonary function evaluation and maximal exercise tests; vital capacity and forced ventilatory capacity and inspiratory ventilatory capacity. Brain SPECT scans were performed (on 200 patients) and MRI scans were performed (on 30 patients). Polysomnographic results (on 250 patients) were related to SPECT scan findings.

SPECT scans revealed 294 lesions (mostly involving the left temporal lobe) in 148 patients.

MRI scans showed 17 lesions (demyelination foci) in 30 patients.

SPECT anomalies were more frequent and occurred in higher numbers compared with MRI scans.

Karnofsky scores (KS) were negatively correlated with significant neurospect anomalies, and also with CD+ / CD38+ cells, and with erythrocyte magnesium levels (which were reduced in 37% of cases).

A neurospect scan showed no perfusion in the brain stem of one patient, and an iodine tracer indicated glial cell inflammation.

Tiffeneau index and peak flow index were significantly decreased.

2% of patients showed a significant increase in airway resistance.

Lymphocyte phenotyping was significantly increased in 52% of cases and decreased in



0% of cases.

Splenomegaly was reported in 29% of cases (*see page 37 above*).

Patients with CFS had significant psychomotor dysfunction (*eg. dizziness, vertigo, lack of balance, inability to judge and control distance and speed of own movements, inco-ordination*) and sleep disturbances.

All this supports the encephalomyelitic pathogenesis of CFS and illustrates the mutisystem involvement in CFS disability.

Dr Byron Hyde from The Nightingale Research Foundation, Ottawa, Canada spoke on Immune Abnormalities in 16 ME / CFS Patients.

This was a small study on 13 female and 3 male patients who were treated with isoprinosine.

These patients underwent extensive immune investigations.

Investigations showed that these subjects had significant and persistent abnormal immune changes in CD4, CD8 and NK cells, and in immune memory; key cytokines (IL-2) were increased, while IL-12 was almost zero. Others which were significantly decreased were IL-10 and IFN gamma. CD8 cells and NK cells were also decreased.

Each patient had one or more abnormal brain SPECT scan results which showed perfusion abnormalities ie. a vasculitis pattern, particularly in the left parietal frontal lobe in right-handed people. This pattern is found in two thirds of autistic cases and resembles the HIV-encephalitic pattern found in one third of patients.

### **Epidemiology**

Professor Paul Levine from George Washington University School of Public Health outlined details on Chronic Fatigue Syndrome and Cancer: is there a relationship?

Immune dysfunction was an important aspect for one subtype of CFS and fatigue was arbitrary.

Grufferman's earlier study on cancer in a North Carolina symphony orchestra had persuaded them to research a cancer link in CFS more systematically.

Their aim was to see if CFS predisposes to cancer.

Details of the study were presented, and their results showed an increase in malignancies,

notably brain tumours, non-Hodgkin's lymphoma, B-cell lymphoma, adenoid cystic carcinoma of the breast, transitional cell carcinoma of the bladder and uterine cancer. This pattern of cancers differs from the usual most common population cancers.

They tentatively concluded that a subgroup of CFS patients may be prone to develop cancer.

They propose to establish a register of those with CFS who develop cancer.

### **RNase-L in Chronic Fatigue Syndrome**

Professor Bernard Lebleu from the Molecular Genetics Institute, Montpellier, France first presented The Interferon-Activated 2-5A / RNase L Pathway: An Overview.

In this excellent overview, Lebleu explained that interferons are the most efficient agents in defending the body against pathogens, especially viruses, and are closely involved with the function of cell mechanisms. IFN-gamma (acting through membrane receptors) activates up to 20 different genes leading to a double stranded RNA which activates 2-5A synthetase.

It is associated with a variety of viral diseases.

2-5A is an unstable molecule with a half life of minutes. In successive transformation stages, this pathway becomes impacted in CFS. This also happens in other viral disease, eg. myocarditis and HIV viruses.

In CFS patients, this is degraded into a low molecular weight enzyme (RNase-L) which can exist in either an active or inactive form.

A natural inhibitor molecule (RLL) controls the balance between the active and inactive forms.

The active molecule degrades cellular RNA leading to inhibition of viral protein synthesis.

The 2-5A binding site requires a cystine-rich environment for RNA cleavage.

*(Cysteine is the reduced form of cystine, which is a key amino acid important for maintaining the three-dimensional structure of all enzymes: in order for the substrate to react with the enzyme –ie. the RNA cleavage—it is necessary for the cystine-rich environment to be preserved, otherwise the three-dimensional enzymatic properties are lost. The disorder of the 2-5A antiviral pathway in CFS is in finding the low molecular weight enzyme.*

*The possibility of this disordered pathway being a response not only to viral presence*

*but also to foreign chemicals such as organophosphate and fluoride ions (or to a deficiency of important mineral ions such as magnesium) is worthy of further investigation.*

*This has already been studied by Vojdani and Lapp<sup>3</sup> who set out to develop biomarkers for possible differentiation between viral-induced CFS -- . ie those without sensitivity to chemicals – versus chemically-induced CFS. They concluded that 2-5A and PKR (protein kinase RNA) are not only biomarkers for viral induction of CFS, but biomarkers for other stressors in CFS, including certain chemicals).*

There are now good techniques for identifying RNase-L in CFS patients.

In a second paper, Lebleau spoke of the new Low molecular weight RNase-L molecule (a 37KDA 2-5A binding protein) as a potential biochemical marker for CFS.

The identification of this new low molecular weight molecule was achieved in French / Belgian collaboration.

This particular binding polypeptide was found in 88% of CFS patients (in the peripheral blood mononuclear cells – PBMCs).

This 37 KDalton form of the enzyme was found only in CFS patients and not in controls, where the relative amount of 37KDA was very low.

Over-expression of this 37KDA protein leads to significant changes in cell and mitochondrial metabolism.

This appears to be another objective biochemical marker which accords with most of the many other markers presented at this Conference and may be a diagnostic marker for distinguishing CFS patients from healthy individuals.

Professor R.J.Suhadolnick from Temple University School of Medicine, Philadelphia, USA spoke about the Diagnosis of Chronic Fatigue Syndrome: Determination of a Low Molecular Weight 37KD 2-5A-Dependent RNase-L in Peripheral Blood Mononuclear Cell Extracts.

This was a joint US / Belgian / French / German study.

Suhadolnick explained that in HIV infections, the 2-5A RNase-L pathway was shut down, but in CFS it was upregulated.

Two methods for determining the presence of RNase in peripheral blood mononuclear lymphocytes was described: the American group used a photochemically labelled azide

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<sup>3</sup> Interferon-induced proteins are elevated in blood samples of patients with chemically or virally induced chronic fatigue syndrome. Vojdani A, Lapp C. *Immunopharmacol Immunotoxicol* 1999;21:2:175-202

probe, whilst the French group used a radiolabelled probe coupled with periodate oxidation of the ribose ring.

Both methods had a high degree of specificity and sensitivity: one method had 98% accuracy, the other was 100% accurate.

In both methods, statistically significant agreement with clinical diagnosis was demonstrated.

This represented a significant breakthrough: it took them deeply into the biochemical origin of CFS, indicating kinetic properties and possible regulation of this dysfunctional pathway, and it provided a possible diagnostic marker.

Although the methodologies are complex, they have been shown to be reproducible in different laboratories and to identify patients accurately.

Professor Kenny de Meirleir of the Free University, Brussels continued by outlining the Low Molecular RNase-L Pathway Abnormalities in Chronic Fatigue Syndrome: Its Use in Clinical Practice.

The presence of the LMW RNase-L 37KDA 2-5A binding protein appears to correlate well with the clinical diagnosis of CFS.

They therefore decided to study the abundance and presence of this LMW RNase- L in relationship to the following:

- (i) the 1988 CDC criteria for CFS
- (ii) bronchial hyper-reactivity
- (iii) post-Ampligen treatment.

In test (I), they found that in 705 CFS patients, there was a clear correlation between the binding protein and the clinical symptomatology in patients who fulfilled both the 1988 *and* the 1994 CDC criteria for CFS

In test (ii), they found that in 162 patients with bronchial hyper-responsiveness to 2mg of histamine, patients were three times more likely to have a LMW RNase-L ratio greater than 1.

In test (iii) they found that a positive outcome after Ampligen treatment was inversely correlated with LMW RNase-L ratio in 24 out of 26 cases.

They concluded that a more pronounced RNase-L enzyme dysfunction correlates well with the original (1988) CDC definition of CFS (which related more to an acute *viral* onset).

## **Diagnosis**

Dr Byron Hyde from The Nightingale Research Foundation, Ottawa, Canada spoke on The Technological Investigation of ME / CFS Patients, and stated that after 16 years, he still had problems in deciding what they are dealing with.

He gave a critical analysis of the failure of the CDC criteria, and of the CDC's failure to suggest types of investigations that would be helpful in elucidating ME / CFS.

Despite this, the following techniques have produced evidence to help the practising physician.

These include SPECT and PET scans, total blood cell and plasma volumes, and immune function studies.

SPECT scans have indicated deficiencies in cerebral blood flow, whilst brain pathology was found in cadavers.

In about 60% of patients, abnormally low RBC volumes were found: only proportions of red blood cells and plasma volumes are normal.

The 1992 CDC definition specifically stipulates glucose and TSH (thyroid stimulating hormone) tests – 40 -50% of patients develop thyroid problems.

A total cardiovascular work-up reveals that frequently there are CNS vascular occlusions.

Vasculitic patterns are identical to those in HIV patients.

There may be major valve pathology.

SPECT and PET scans show that huge areas of the brain are injured.

ME and CFS **are not the same**.

Determining disability in North America was very important – he often went to Court, and settlements are huge for this illness : between \$0.5 million and \$4 - 5 million, but physical changes must be demonstrated.

Professor Tim Roberts from the Newcastle, Australia research team spoke on The Development of Laboratory-Based Tests in Chronic Fatigue Syndrome: Investigation of Erythrocyte Oxidative Damage in CFS.

They investigated CFS patients by full blood counts, ESR, CRP haematinics, and markers for oxidative stress.

Their results showed that two markers of oxidative stress were identified in CFS patients: methaemoglobin (metHb) and malondialdehyde (MDA) markers were identified, and increased mean erythrocyte volume compared with controls, with significantly different blood parameter profiles.

Erythrocyte distribution width was the primary factor differentiating CFS patients from controls.

Statistical analysis showed that these parameters were associated with symptom expression and indices in CFS.

The MDA and metHb groups were associated with different symptoms and symptom indices.

*In vitro* studies demonstrated that RBCs reduced the interaction between activated neutrophils initiating chromium release from target cells by free radical mechanisms involving active oxygen species and nitric oxide.

Free radicals can cause much damage, to DNA and elsewhere.

Treatment to maintain the integrity of membranes, particularly RBCs, should be helpful in CFS / ME.

Dr G.Moorkens from the Department of Internal Medicine & Endocrinology, Antwerp, Belgium spoke about Characterization of Pituitary Function in 73 Patients with Chronic Fatigue Syndrome.

These researchers performed comprehensive hormonal testing, investigating growth hormone (GH), ACTH and cortisol responses to insulin-induced hypoglycaemia, arginine and clonidine stimulation. Nocturnal GH secretion and serum levels of IGF-1, free thyroxin and TSH were measured.

Their very detailed results showed that there were subtle but significant changes in the pattern of GH secretion in CFS patients, which need further study.

In particular, serum prolactin, TSH and visceral fat levels were all increased in these patients.

Such changes were observed only during insulin tolerance testing and nocturnal GH secretion.

Increases in visceral fat indicate GH deficiency.

They concluded that increased prolactin, TSH and abnormal GH secretion fit into the theory of dopamine deficiency and adrenal axis dysfunction.

### **Clinical Observations**

Dr N.Posner from the Department of Social and Preventive Medicine, University of Queensland, Australia spoke about Patterns of Functional Impairment in CFS.

Using the SF 36 health status survey from 530 responders, the means for the eight dimensions were found to be markedly lower than in population norms.

The overall results indicated a marked pattern of impairment; it was similar to that found in the USA studies, but was dissimilar from other disease profiles, particularly depression.

There is a very significant functional impairment in this group of patients.

The researchers concluded that CFS / ME patients are severely disabled, needing home support.

Dr Katherine Rowe from The Royal Children's Hospital, Melbourne, Victoria, Australia discussed Does the Symptom Complex of Chronic Fatigue Syndrome Occur in Adolescents?

This was a very detailed, elegant and well demonstrated study involving 189 young people, in which it was shown that the symptom pattern and reported frequencies were consistent in all 189 subjects.

The reported symptoms were similar to those seen in adults, but prolonged fatigue after physical exercise, headaches, problems in concentration, sleep disturbances, abdominal pain and myalgia were particularly pronounced.

Careful conical assessment and extensive statistical analysis provided an excellent fit to the data for 24 symptom items by identifying one second order syndrome factor and five correlated first order factors (muscle pain and fatigue; neurocognitive; abdominal, head and chest pain; neurophysiological and immunological respectively).

The immunological symptoms had significant direct and indirect effects on the four other factors.

“In this sample, an alternative hypothesis of somatisation disorder could not be supported”.

Dr G.C.Scroop from the Exercise Physiology Research Unit, University of Adelaide,

### Australia outlined Normal Exercise Capacity in Chronic Fatigue Syndrome

He described detailed results of an incremental exercise test on CFS patients and on sedentary controls.

They concluded that CFS patients are not deconditioned, and that graded exercise programmes are unwarranted.

### Patients' Day

In the morning session, there was a debate on Name Change for Chronic Fatigue Syndrome, chaired by Vicki Walker of CFIDS Chronicle.

This clearly showed that everyone was dissatisfied with the term 'chronic fatigue syndrome', which was easily misunderstood: it stigmatised patients and focused on 'fatigue' only, when fatigue was not the most disabling problem.

There was no support for an eponym (ie. named after a person, eg Ramsay).

Both the Holmes 1988 and Fukuda 1994 definitions of CFS had muddled the waters.

Multiple sclerosis is well-defined, yet can have very differing characteristics.

"ME" still existed: there have been 60 epidemics this century.

"ME" offered greater legitimate recognition, and was accepted by the World Health Organisation. There was strong support for the term myalgic encephalomyelitis in the UK, Holland and New Zealand.

The US Congress would not consider the term myalgic *encapalopathy*.

There was general consensus that this is a **brain dysfunction disease with a biochemical basis**: a new descriptive name should indicate the most significant aspects, ie. brain, muscle pain, lack of energy and a dysfunctional immune system (affecting the neuroendocrine system).

The afternoon session took the form of a CFS patients' meeting, when about 500 patients (mostly Belgian) filled the lecture hall. A summary of the Congress was given – much of it in Flemish—and some experts addressed the audience.

### International lobby group

At this afternoon session, Simon Molesworth, a barrister from Australia and Chairman of



the Australian National Trust (who is the father of a teenage boy with severe ME) made a passionate speech.

He said CFS /ME offered challenges in many forms --- first of all there is the question of *credibility*: having ME recognised as an illness presented more problems than with other illnesses. The physical nature was doubted by authorities, governments, pension agencies etc, and this doubt undermined essential support for those with ME / CFS.

Stories from around the world were the same – no government was comfortable with the concept of ME / CFS, and therefore patients were let down.

People fought battles with authorities all over the world.

There is an urgent need for stronger advocacy.

Politicians and governments *must* know that people with ME / CFS share the same view.

Molesworth announced that it had been decided that day to form an international lobby group as a voice for all concerned, and this idea had come from Professor Kenny de Meirleir.

A Charter would be drawn up to incorporate the following points:

1. Provide an international voice to represent ME / CFS people to national and international organisations
2. Ensure services are provided under Human Rights Laws
3. Secure support from governments, medical and social services
4. Sponsor sensible medical research and treatment for ME / CFS
5. Represent those in jeopardy
6. Ensure public education about ME / CFS as an illness; provide information and advocacy.

International groups (not merely the major patients groups and not individuals) would be members of this lobby group.

Professor Daniel Peterson from the USA said big changes were taking place and it was easier for the disability to be recognised.

Internationally we are all talking about the same thing and it is ridiculous to have different guidelines. All it needed was a one-line change in law: declare CFS / ME to be a **“medically determined disease”** (*which is already acknowledged by the World Health Organisation in the 10<sup>th</sup> International Classification of Diseases*).

With CFS, everyone was their own advocate, said Peterson.

Both Canadian and US representatives confirmed that CFIDS / CFS is now considered to lie somewhere between HIV / AIDS and Alzheimer's Disease.

The overall impression of Congress delegates is that there is a rapidly growing body of objective and physical measurements, which mean that (quote)  
 "ME / CFS has now been taken out of the hands of the psychiatrists".

Particularly important and impressive is the evidence of the urinary metabolite profiles and plasma lipid profiles which, in extensive and objective statistical analysis, correlated with five different sub-groups of ME.

The infection - immune basis of ME has been strengthened.

Both SPECT and MRI scans clearly provide objective evidence of underlying central disorders in ME.

Many cross-links between earlier studies and the conference reports are now apparent.

The CDC definition of CFS is clearly not adequate.

It should be possible to sharpen the classification of ME into various sub-groups; this will help research, diagnosis and treatment.

### **Evidence presented on Gulf War Syndrome at the Brussels Congress**

The Congress opened with the consideration of Gulf War Illness / Syndrome and with its relationship to ME and related disorders such as fibromyalgia syndrome.

Professor Ben Natelson from the DVA Medical Centre, East Orange, New Jersey discussed findings in Gulf War veterans of inadequate cardiovascular support.

Professor Paul Levine, a Veterans' Association epidemiologist from George Washington School of Public Health, Washington DC confirmed that his study  
 "supports the possibility that environmental factors could be responsible for some of the complaints of Gulf War veterans".

Professor Garth Nicolson from the Institute of Molecular Medicine, Huntington Beach, California spoke on mycoplasma in GWS; his team have used cycles of antibiotics, but the response differs widely and there have been 600 reports of anaphylaxis in Marines after the Gulf War.

Professor Malcolm Hooper from the Department of Medicinal Chemistry at the University of Sunderland, UK, gave a most impressive and well-received lecture entitled  
"Towards a fuller understanding of Gulf War Illness / Syndrome" in which he explained

that although lasting for a mere five weeks, the Gulf War conflict had been the most toxic war in military history.

UK soldiers were given 10 vaccines plus five or six undeclared (and unknown) injections, all records of which had been destroyed or were being kept by the MOD.

US soldiers had 17 vaccines by injection which included biological warfare agents (BWAs), eg. anthrax, plague, botulin, Rickettsia, aflatoxins, plus NAPS (Nerve Agent Protection Sets) tablets (ie. pyridostigmine bromide -PBs); they were exposed to organophosphates (OPs), carbamates, organochlorines (OCs, eg. Lindane), pyrethroids, and DEET (an insect repellent as distinct from an insecticide).

The administered vaccines included several live vaccines, including typhoid, polio, Yellow Fever and measles.

The UK soldiers also received injections of Hepatitis A-Ig, *but this should never be used in conjunction with live viruses.*

When they were ordered to take the NAPS tablets, some troops experienced classic autonomic effects such as sweating and uncontrollable diarrhoea, which meant that their protection suits were soiled with their own excrement.

Deployed personnel were also exposed to chemical warfare agents such as mustard gas, and to the organophosphate analogues sarin, tabun and soman and Vx.

No informed consent was given by the soldiers.

Squalene was used as an adjuvant in experimental vaccines: HIV envelope genes have been found by Professor Nicolson in association with mycoplasma, indicating a possible gene modification of the mycoplasma, thereby enhancing their pathogenicity, which has a worrying potential.

Human endogenous retroviruses can re-arrange DNA – this can be detected in myeloma patients.

In addition there was toxic smoke from oil well fires, and there were problems with the troops' protection suits (quite apart from personal soiling).

The soldiers were exposed to solvents used in preparing vehicles; these and toxic fumes from oil fires are immunosuppressant and carcinogenic, affecting the respiratory and gastrointestinal tracts.

There were also biohazards such as malaria, Leishmaniasis, fleas, scabies, lice and other insects, including sand flies and mosquitos.

A list published in JAMA in 1997 mentioned not only the biological warfare agents but

also bacteria like brucella species, pseudomonas species and *Francisella tularensis*.

It was easy to design studies which give the desired result, said Hooper, but there was little doubt that the Gulf War veterans had received a cholinergic “triple whammy”; there was bound to be some synergism and it was to be expected that some esterases would be knocked out.

Hooper pointed out that almost the entire cholinergic system would be wiped out.

Could a person still function? he asked. The answer was No.

The central nervous system was affected, as were the autonomic and peripheral nervous systems --- under stress, substances and biological agents get transported across the blood brain barrier (BBB).

Of particular interest to Hooper was depleted uranium (DU), which is associated with Radioactivity alpha, beta and gamma. DU shells have high penetration and are pyrophoric; when fired, they produce respirable uranium dust, which blows around. Some 300 tons of respirable uranium dust was created, which could travel up to 25 - 30 miles in a light breeze.

Some 1,200,000 rounds were fired from Tomahawk tanks and aircraft.

Helicopter pilots and VTOs were wearing casual clothes.

This dust persists: externally it can cause skin rashes; when respired, one third is excreted rapidly through the kidneys but two thirds accumulate in the throat, lungs and respiratory tract.

It gets into the bones, resulting in stem cell exposure, causing blood dyscrasias and cancer.

All the toxic substances to which the Gulf War veterans were exposed affect the central nervous system, and with the exception of DU, they also all affect the peripheral nervous system; some affect the autonomic nervous system and some affect the cardiovascular system and the blood.

Hooper discussed various diagnostic tests which ought to have been carried out on the Gulf War veterans; clinically these include neurological, immunological (IgA + cortisol), cardiovascular, renal and liver function tests, with tests for genetic markers.

RNA screening should be used to look for pesticide contamination and for evidence of depleted uranium.

SPECT scans should be used to look for brain perfusion levels.

Urine should be tested for levels of IAG (indolylacroylglycine); this test may show peaks of small peptides which indicate a “leaky gut”, which is associated with a compromised digestive system and with ensuing disruption of central nervous system and endocrine function.

Batteries of tests to assess oxidative status should be performed (eg GSH, selenium, zinc etc) and specific enzyme systems should be tested, eg. paroxonase activity, SOD, sulphur transferase and esterases; membrane stability should be assessed.

Levels of nutrients and micro-nutrients should be assessed and monitored, including a Niacin flush test (for vitamin B3); gut function and permeability should be assessed, as should pancreatic function.

Endocrine responses should be assessed.

**NB. On his own admission, in his official study of Gulf War veterans Wessely performed no clinical examination or laboratory investigations (*see page 160 above*). He worked only from a self-report questionnaire which was sent only to selected veterans, yet he confidently concluded that there is no such thing as Gulf War Syndrome and the MOD accepts his study.**

Hooper said that a pattern is emerging: there is a primary insult, which may be neurological. Vaccines are primarily immunological insults, thus the immune and endocrine systems are affected, which in turn affect the gut and brain tissue. The blood brain barrier is crossed, and an entire cascade of processes ensues, affecting the central nervous system, the pineal complex, opioids, the endocrine system (gonads, thyroid and adrenals); through the olfactory system the limbic system is affected, which in turn affects the central nervous system: there is a direct link between the immune system and the CNS.

Despite Wessely’s view that there is no evidence of birth defects in Gulf War veterans, reports from America indicate that in one state alone (Mississippi), 67% of children born to Gulf War veterans have birth defects.

Hooper provided statistics showing that 9,000 Gulf War veterans were now dead (and these were previously fit and healthy young men); there are 230,000 medical cases, of which 203,000 have filed claims.

From the UK alone, 53,000 troops were involved in the Gulf War, but we do not know how many are ill or how many are dead, because the only epidemiological study on UK veterans is the one done by Wessely.

Hooper strongly challenged the official UK stance.

He also pointed out that syndromes which overlap with Gulf War Syndrome include ME.

*This Appendix has been compiled in collaboration with Professor Malcolm Hooper and Doris M.Jones MSc, to both of whom grateful acknowledgment is made.*

## **Recommended Reading**

Research shows clear differences between subgroups of “chronic fatigue syndrome” (CFS).

### **Chronic Fatigue Syndrome**

The term CFS was coined in 1988 by Dr Gary Holmes of the CDC as a replacement for the term Chronic Epstein Barr Virus Disease (the name used by some USA physicians until it was realised that EBV was not the only virus associated with this illness). It was based on a single symptom found in those affected by the 1984 outbreak of ME at Lake Tahoe, Nevada.

“CFS” has since become an umbrella term much favoured by certain psychiatrists, particularly those of the “Wessely School” and by others who find it a less challenging option.

The term “CFS” has given rise to much confusion, especially since Wessely et al broadened the definition criteria (Oxford, 1991) to include all categories of unexplained “fatigue”. In the UK, it encompasses disorders other than ME, including undiagnosed hypothyroidism, masked depression, and disorders related to lifestyle and nutrition. In America, stricter criteria select a more homogeneous population, so some US studies on CFS are undoubtedly looking at true ME.

*(For a more comprehensive explanation, see Appendix V to the original Denigration by Design?).*

Despite Wessely’s obsession with reductionism, on scientific grounds it is helpful and appropriate to consider the differences between sub-groups.

### **Myalgic encephalomyelitis (ME)**

This is one specific subgroup of the many chronic fatigue or post-viral syndromes.

It is a multi-system disorder and is primarily neurological (affecting not only the central nervous system but also the autonomic and peripheral nervous systems), with variable involvement of cardiac and skeletal muscle. There is also involvement of the liver, and of the lymphoid and endocrine organs. In CFS, the focus is on “fatigue”, whereas in ME the focus is on *post-exertional fatiguability*.

Whereas the 1988 Holmes / CDC definition placed great emphasis on symptoms such as mild fever, sore throat and tender lymph glands (ie. glandular fever), the definition criteria of true ME include the following:

- muscle fatiguability following minimal exertion, with prolonged recovery time

- evidence of neurological disturbances (CNS + ANS + PNS)
- evidence of impaired circulation
- a marked variability of symptoms (from day to day and even from hour to hour)
- an extended relapsing course, with a tendency to chronicity
- an increasing sensitivity to drugs (at the Dublin International Meeting on CFS presented under the auspices of The World Federation of Neurology, 18-20 May 1994, Professor Charles Poser of the Department of Neurology, Harvard Medical School, and the Neurological Unit, Beth Israel Hospital, Boston, Mass., said this is virtually pathognomonic of true ME).

Additionally, in The International Classification of Diseases, the World Health Organisation officially classifies ME as a **neurological disorder** (ref. G.93.3) whereas it officially classifies fatigue syndromes as **“other neurotic disorders”** (ref: 48.0).

It is therefore not an option for Wessely et al to seek to overturn such official classification.

Much of the work on the broadly-defined CFS has failed to find the type of abnormalities found in the more strictly-defined ME; this ought not to be surprising, given that the CFS criteria definition specifically does not *require* evidence of central nervous system dysfunction.

For those who look and who wish to see, there are clearly discernible differences between “CFS” and ME, most notably in the *pattern* of cognitive impairment; in the type and pattern of immune dysfunction; in the clinically unmissable circulatory impairment and in the endocrine abnormalities --- for example, in CFS there is usually a normal to low level of cortisol (Demitrack et al, 1991: Evidence for impaired activation of the hypothalamic-pituitary-adrenal axis in patients with chronic fatigue syndrome. *J Clin Endocrinol Metab.*

1991:73:1224-1234) whereas in ME, researchers report cortisol levels which are normal to high (Hilgers & Frank, 1992: Chronic fatigue immune dysfunction syndrome in 103 patients – diagnosis, test results and therapy. *Zeitschrift fur Klinische Medizin*, 1992:47:4:152-166: *In German*); Richardson 1995: (Disturbance of hypothalamic function and evidence for persistent enteroviral infection in patients with chronic fatigue syndrome. *Journal of Chronic Fatigue Syndrome* 1995:1:2:59-66).

Indeed, Wessely himself also found mean salivary cortisol concentration to be significantly higher in patients than in controls, concluding that:



“These findings are at variance with earlier reports that CFS is a hypocortisolaemic state and suggest that in CFS the symptom of fatigue is not caused by hypocortisolaemia”. (*Salivary Cortisol Profiles in Chronic Fatigue Syndrome*. Barbara Wood, Simon Wessely et al. *Biological Psychiatry*: 1998;37:1-4).

Wessely states that his patients in this study fulfilled both the UK and CDC criteria for CFS and that they had no history of neurological, cardiovascular or endocrine disease, so one wonders about the definition of his cohort.

Black <sup>4</sup> puts forward the observation that the immune system is turned on (or more appropriately, is not turned off) because of a hypothalamic defect in the synthesis and / or secretion of CRF. CRF mediates the central nervous system response to environmental, physiologic or psychological stress, thus an *on-going* immune response results in *elevated* levels of corticosteroids, catecholamines and certain endogenous opiates. (cf pp. 237-238 above).

For clarification, the following suggested additional reading has been listed in various categories.

#### A. DEFINITIONS of ME

(see also pp. 212-214 above)

- 1) Wallis A.L. An investigation into an unusual disease in epidemic and sporadic form in general practice in Cumberland in 1955 and subsequent years. *University of Edinburgh. Doctoral Thesis 1957*
- 2) Ramsay, A.M, O’Sullivan E. Encephalomyelitis simulating poliomyelitis. *Lancet*: 1956;1:761-766
- 3) A.Melvin Ramsay. Myalgic Encephalomyelitis and Postviral Fatigue States. 2<sup>nd</sup> edition. Gower Medical Publishing, London 1988 (1<sup>st</sup> edition 1986 entitled Postviral Fatigue Syndrome -- The Saga of Royal Free Disease. *Ramsay always said how much he regretted not standing firm about the title of the 1<sup>st</sup> edition, which he wished to call “Myalgic Encephalomyelitis”, not “Postviral Fatigue Syndrome”: in the 2<sup>nd</sup> edition, he stood firm*).
- 4) Dowsett EG, Ramsay AM. Myalgic encephalomyelitis – a persistent viral infection? *Postgraduate Medical Journal*: 1990;66:526-530

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<sup>4</sup> Immune system - central nervous system interactions: effect and immunomodulatory consequences of immune system mediators on the brain. Paul H.Black. *Antimicrobial Agents and Chemotherapy*: 1994;38:1:7-12.

- 5) Hyde, BM. The Definitions of ME / CFS. In: *The Clinical and Scientific Basis of Myalgic Encephalomyelitis / Chronic Fatigue Syndrome.* Ed: Hyde, BM, Goldstein J. & Levine P. Pub: The Nightingale Research Foundation, Ottawa, Canada, 1992
- 6) Dowsett EG & Welsby PD. Conversation Piece. *Postgraduate Medical Journal:* 1992:68:63-65
- 7) Hyde BM. Are myalgic encephalomyelitis and chronic fatigue syndrome synonymous? *MPWC:* 1999:3-17

## **B. EVIDENCE OF VIRAL TRIGGER**

The presence of enteroviral particles has been found in a significant number of muscle biopsies taken from ME patients. This was rare in healthy controls.

Enteroviral sequences have been detected in tissue samples taken from the hypothalamus and brain stem of a patient with ME. Such sequences were not found in samples from depressed patients who had not suffered from ME.

- 1) Innes SBG. Encephalomyelitis resembling benign myalgic encephalomyelitis *Lancet:* 1970:1:969-971
- 2) Gow JW, Behan WMH, Clements GB, Behan PO et al. Enteroviral sequences detected by polymerase chain reaction in muscle biopsies of patients with postviral fatigue syndrome. *BMJ:* 1991:302:692-696
- 3) Bowles NE, Lane RJM, Cunningham L & Archard LC. Persistence of enterovirus RNA in muscle biopsy samples suggests that some cases of chronic fatigue syndrome result from a previous, inflammatory viral myopathy. *Journal of Medicine:* 1993:24:145-160
- 4) McGarry F, Gow J & Behan PO. Enterovirus in the chronic fatigue syndrome. *Ann Int Med:* 1994:120:11:972-973
- 5) Clements GB et al Detection of enterovirus-specific RNA in serum: the relationship to chronic fatigue. *Journal of Medical Virology:* 1995:45:156-161

## **C. ABNORMALITIES IN MUSCLE TISSUE**

In a study of a fairly homogeneous population, 80% of the biopsies showed evidence of structural damage to the mitochondria.

A deficiency in the levels of carnitine and serum acylcarnitine have been found; researchers believe this may be involved in the muscular symptoms of ME.

Abnormalities in muscle function have been found and do not appear to be related to inactivity.

In people with ME, objective tests have found prolonged recovery rates following exercise.

- 1) Behan WMH et al. Mitochondrial abnormalities in the postviral fatigue syndrome. *Acta Neuropathologica*: 1991:83:61-65
- 2) Majeed T, Behan PO et al. Abnormalities of carnitine metabolism in chronic fatigue syndrome. *European Journal of Neurology*: 1995:2:426-428
- 3) Kuratsune H, Evengard B et al. Low levels of serum acylcarnitine in chronic fatigue syndrome and chronic hepatitis type C, but not seen in other diseases. *International Journal of Molecular Medicine*: 1998:2:1:51-56
- 4) Lane RJM, Archard LC et al. Muscle fibre characteristics and lactate responses to exercise in chronic fatigue syndrome. *JNNP*:1998:64:3:362-367

**D. THE FATIGUE REPORTED BY PATIENTS WITH ME AND STRICTLY DEFINED CFS IS VERY DIFFERENT FROM THAT EXPERIENCED BY THE GENERAL POPULATION. SCORES ON FATIGUE SCALES ARE MORE LIKE THOSE OF PEOPLE WITH OTHER NEUROLOGICAL DISEASES SUCH AS MULTIPLE SCLEROSIS.**

- 1) Krupp LB et al. An overview of chronic fatigue syndrome. *Journal of Clinical Psychiatry*: 1991:52:10:403-410
- 2) Ray C, Weir WRC et al. Development of a measure of symptoms in chronic fatigue syndrome: the profile of fatigue-related symptoms (PFRS). *Psychology and Health*: 1992: 7:27-43
- 3) Schwartz JE et al. The measurement of fatigue: a new instrument. *Journal of Psychosomatic Research*: 1993: 37:7:753-762

**E. EVIDENCE OF ON-GOING INFECTION AND IMMUNE ACTIVATION**

Many studies have found evidence of an overactive (up-regulated) immune system. The immunological changes documented in ME and in strictly-defined CFS are related to the severity of the illness and correlate with intensity of symptom expression.

These immune changes are generally more common in the severely affected.

The immunological changes are not the same as those documented in depression.

Some symptoms of ME may be related to an inflammatory process: findings are consistent with the view that fatigue in ME could be due to cytokine production within the central nervous system.

- 1) Klimas NG, Salvato FR et al. Immunologic abnormalities in chronic fatigue syndrome. *Journal of Clinical Microbiology*: 1990;28:1403-1410
- 2) Ho-Yen DO, Billington RW & Urquhart J. Natural killer cells and the post-viral fatigue syndrome. *Scandinavian Journal of Infectious Diseases*: 1991; 23:711-716
- 3) Landay AL, Jessop C et al. Chronic fatigue syndrome: clinical condition associated with immune activation. *Lancet*: 1991;338:707-712
- 4) Lloyd A, Hickie I et al. Cell mediated immunity in patients with chronic fatigue syndrome, healthy control subjects and patients with depression. *Clinical & Experimental Immunology*: 1992;87:76-79
- 5) Cheney PR. Evidence for T-cell activation by soluble IL-2-R and T8-R in the chronic fatigue syndrome. *In: The Clinical and Scientific Basis of Myalgic Encephalomyelitis / Chronic Fatigue Syndrome. Ed: Hyde BM, Goldstein J and Levine P. Nightingale Research Foundation, Ottawa, Canada, 1992*
- 6) Lugendorf S, Klimas NG et al. Relationships of cognitive difficulties to immune measures, depression and illness burden in chronic fatigue syndrome. *Journal of Chronic Fatigue Syndrome*: 1995;1:2:23-41
- 7) Patarca R, Klimas NG et al. Dysregulated expression of soluble immune mediator receptors in a subset of patients with chronic fatigue syndrome: cross-sectional categorization of patients by immune status. *Journal of Chronic Fatigue Syndrome*: 1995;1:1:81-96
- 8) Sheng WS, Chao CC et al. Susceptibility to immunologically mediated fatigue in C57/BL/6 versus Balb/c mice. *Clinical Immunology and Immunopathology*: 1996;81:2:161-167
- 9) Bennett AL, Chao CC, Buchwald D, Komaroff AL et al. Elevation of bioactive transforming growth factor- $\beta$  in serum from patients with chronic fatigue syndrome. *Journal of Clinical Immunology*: 1997;17:2:160-166
- 10) Cannon JG, Komaroff AL et al. Interleukin 1- $\beta$ , interleukin -1 receptor

agonist, and soluble interleukin-1 receptor type II secretion in chronic fatigue syndrome. *Journal of Clinical Immunology*: 1997;17:3:253-261

- 11) Hassan IS, Weir WRC et al. A study of the immunology of the chronic fatigue syndrome: correlation of immunologic parameters to health dysfunction. *Clinical Immunology and Immunopathology*: 1998;87:1:60-67

## **F. EVIDENCE OF HPA DYSFUNCTION**

Research has revealed a number of disturbances in the function of the hypothalamic-pituitary-adrenal axis. Some of these are different from the abnormalities documented in patients suffering from depression – indeed, some are the exact opposite.

Symptoms indicative of autonomic nervous system dysfunction are not related to psychiatric disorder.

Such symptoms cannot be explained by “de-conditioning”.

- 1) Behan PO, Bakheit AMO. Clinical spectrum of postviral fatigue syndrome. *British Medical Bulletin*: 1991;47:4:793-808
- 2) Demitrack MA et al. Evidence for impaired activation of the hypothalamic-pituitary-adrenal axis in patients with chronic fatigue syndrome. *Journal of Clinical Endocrinology and Metabolism*: 1991;73:1224-1234
- 3) Bakheit AMO, Behan PO et al. Possible up-regulation of 5-hydroxytryptamine receptors in patients with postviral fatigue syndrome. *BMJ*:1992;304:1010-1012
- 4) Cleare AJ, McGregor A, Wessely S et al. Contrasting neuroendocrine responses in depression and chronic fatigue syndrome. *Journal of Affective Disorders*: 1995;35:283-289
- 5) Majeed T, Dinan TG, Behan PO et al. Defective dexamethasone induced growth hormone release in chronic fatigue syndrome: evidence for glucocorticoid receptor resistance and lack of plasticity? *Journal of the Irish Colleges of Physicians and Surgeons*: 1995;24:1:20-24
- 6) Richardson J. Disturbance of hypothalamic function and evidence for persistent enteroviral infection in patients with chronic fatigue syndrome *Journal of Chronic Fatigue Syndrome*: 1995;1:2:59-66
- 7) Freeman R & Komaroff AL. Does the chronic fatigue syndrome involve the autonomic nervous system? *American Journal of Medicine*;1997;102:4:357-364

## **G. EVIDENCE OF HYPOPERFUSION IN BRAINSTEM**

MRI scans have revealed abnormalities in up to 80% of patients.

Researchers believe that these defects are probably caused by viral encephalitis.

There is a correlation between the areas involved and the symptoms experienced.

The number of defects are correlated with clinical status.

Abnormalities on SPECT scans provide further objective evidence of central nervous system dysfunction.

Studies published to date show patterns of reduced blood flow which are markedly different from those documented in depression.

The results on SPECT have been replicated using PET.

- 1) Daugherty SA, Peterson DL, Bastein S et al. Chronic Fatigue Syndrome in Northern Nevada. *Rev Inf Dis* 1991;13:Suppl 1: S39-S44
- 2) Buchwald D, Peterson DL, Gallo RC, Komaroff AL et al. A chronic illness characterised by fatigue, neurologic and immunologic disorders, and active Human Herpes Type 6 infection. *Annals of Internal Medicine*:1992;116: 2:103-113
- 3) Schwartz RB, Komaroff AL et al. Detection of intracranial abnormalities in patients with chronic fatigue syndrome: comparison of MR imaging and SPECT. *American Journal of Roentgenology*:1994;162:4:936-941
- 4) Schwartz RB, Komaroff AL et al. SPECT imaging of the brain: comparison of findings in patients with chronic fatigue syndromes, AIDS dementia complex and major unipolar depression. *American Journal of Roentgenology*:1994;162:4:943-951
- 5) Costa DC, Tannock C and Brostoff J. Brainstem perfusion is impaired in patients with chronic fatigue syndrome. *Quarterly Journal of Medicine* :1995: 88:767-773
- 6) Tirelli U, Tavio M et al. Brain positron emission tomography (PET) in chronic fatigue syndrome: preliminary data. *American Journal of Medicine*: 1998;105:3A: 54s-58s

## **H. EVIDENCE OF PROFOUND COGNITIVE IMPAIRMENT**

Neuropsychological tests on patients with ME / PVFS and strictly-defined CFS have

revealed abnormalities which are consistent with organic brain disorder.

These deficits have been found in both community and hospital samples.

The deficits were not the result of psychiatric disorders, such as depression.

Exercise has an adverse effect on cognitive functioning in ME / CFS.

- 1) Daugherty SA, Peterson DL et al. Chronic fatigue syndrome in Northern Nevada. *Rev Inf Dis:1991;13: Suppl.1: S39-S44*
- 2) Riccio M, Lant AF et al. Neuropsychological and psychiatric abnormalities in myalgic encephalomyelitis: a preliminary report. *British Journal of Clinical Psychology:1992;31:111-120*
- 3) Smith AP. Chronic fatigue syndrome and performance. *In: Handbook of Human Performance. Vol 2. pp.261-278. Ed: AP Smith and D.Jones. London, Academic Press, 1992*
- 4) Marcel B, Komaroff AL et al: Cognitive deficits in patients with chronic fatigue syndrome. *Biological Psychiatry:1996;40:535-541*
- 5) DeLuca J, Johnson SK, Natelson BH et al. Cognitive functioning in patients with chronic fatigue syndrome devoid of psychiatric disease. *JNNP:1997;62:151-155*
- 6) LaManca JJ, DeLuca J, Natelson BH et al. Influence of exhaustive treadmill exercise on cognitive functioning in chronic fatigue syndrome. *American Journal of Medicine:1998;105:3A:59s-65s*
- 7) Scholey A et al: A comparison of the cognitive deficits seen in myalgic encephalomyelitis to Alzheimer's Disease. *Proceedings of the British Psychological Society, 1999, 12 January*

# **I. PSYCHIATRIC STUDIES: FINDINGS DO NOT SUPPORT A PSYCHIATRIC DIAGNOSIS**

It should be noted that there is no evidence of maladaptive beliefs, nor of phobic avoidance of activity in patients with ME.

In contrast to claims made by the "Wessely School", other more rigorously controlled studies have found low rates of depression.

The depression experienced by patients with ME / strictly-defined CFS is different from

that found in psychiatric patients and is closely related to the severity of other symptoms.

The fatigue is not due to a lack of motivation or effort.

Evidence indicates that most patients with ME / CFS do not spend the whole day resting, and that a number of coping strategies are used.

Longitudinal studies using appropriate measures have shown that patients' attributions to a physical cause do not affect outcome; moreover, research on patients with ME indicate that a belief in a biological cause is not associated with poor mental health.

Graded exercise (where activity is increased according to a pre-set plan irrespective of symptom severity) is not appropriate for all patients with ME / CFS: over-exertion can lead to relapse.

There has been no study assessing the effectiveness of graded exercise or cognitive behavioural therapy in ME or in strictly-defined CFS.

The documented links between CFS and psychiatric disorders may reflect the overly-broad diagnostic criteria and the researchers' choice of measures for assessing psychiatric morbidity.

- 1) Hickie I, Lloyd A et al. The psychiatric status of patients with the chronic fatigue syndrome. *British Journal of Psychiatry*:1990:156:534-540
- 2) Hickie I, Lloyd A & Wakefield D. Chronic fatigue syndrome and depression. *Lancet*:1991:337:992
- 3) Yeomans JDI & Conway SP. Biopsychosocial aspects of chronic fatigue syndrome (myalgic encephalomyelitis). *Journal of Infection*:1991:23:263-269
- 4) Landay AL, Jessop C, Lenette ET and Levy JA. Chronic fatigue syndrome: clinical condition associated with immune activation. *Lancet*:1991:338:707-712
- 5) Lloyd A, Gandevia S and Hales J. Muscle performance, voluntary activation, twitch properties and perceived effort in normal subjects and patients with chronic fatigue syndrome. *Brain*:1991:114:85-98
- 6) Lloyd AR, Hickie I, Dwyer J, Wakefield D et al Immunologic and psychologic therapy for patients with chronic fatigue syndrome: a double-blind, placebo-controlled trial. *American Journal of Medicine*:1993:94:197-203
- 7) Friedberg F & Krupp LB. A comparison of cognitive behavioural treatment for chronic fatigue syndrome and primary depression. *Clinical Infectious Diseases*: 1994:18: (Suppl 1) S105-S110



- 8) Jason LA et al: Politics, science, and the emergence of a new disease, *American Psychologist*:1997:52:9:973-983
- 9) Lawrie SM, Pelosi AJ et al: A population-based incidence study of chronic fatigue. *Psychological Medicine*: 1997:27:343-353
- 10) Ray C, Jeffries S & Weir WRC. Coping and other predictors of outcome in chronic fatigue syndrome: a one-year follow-up. *Journal of Psychosomatic Research*:1997:43:4:405-415
- 11) Packer TL et al: Fatigue and activity patterns of people with chronic fatigue syndrome. *The Occupational Therapy Journal of Research*:1997:17:3:186-199
- 12) Lindal E, Bergmann S et al: Anxiety disorders: a result of long-term chronic fatigue – the psychiatric characteristics of the sufferers of Iceland Disease. *Acta Neurologica Scandinavica*:1997:96:3:158-162
- 13) Lapp C. Exercise limits in chronic fatigue syndrome. *American Journal of Medicine*:1997:103:83-84
- 14) Sisto SA, Natelson BH et al: Physical activity before and after exercise in women with chronic fatigue syndrome. *QJM*:1998:91:7:465-473
- 15) Heijmans MJWM. Coping and adaptive outcome in chronic fatigue syndrome: importance of illness cognitions. *Journal of Psychosomatic Research*:1998:45:1:77-83
- 16) Saltzstein BJ et al: A naturalistic study of the chronic fatigue syndrome among women in primary care. *General Hospital Psychiatry*:1998:20:5:307-316
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**Note:** In her paper in ME Today (BRAME) 1999:9: pp 27-31 entitled Research into ME / CFS 1988-1998: Too much philosophy and too little basic science, Dr E.G.Dowsett (former President of the UK ME Association) states:

“Owing to severe problems in obtaining any adequate funding and in securing subsequent publication for ME research outside the psychiatric remit in the UK, most basic scientific work is performed with difficulty and published abroad”.

Dowsett observes:

“Previously reputable medical journals concur with therapies which compound psychological manipulation. A leading proponent of this approach has ensured that the very words of a leading article on this subject are now inscribed upon a wide variety of benefit agency, insurance, retirement and other official forms which doctors must sign on behalf of their patients.

“Compared with this bludgeoning of public opinion, the ‘mass hysteria’ allegation at the Royal Free Hospital seems little more than the mad buzzing of a demented fly”.

One must never forget that the recipients of this aptly-described bludgeoning are many extremely sick and disabled human beings.

It is worth recalling that in his address to the 1999 Sydney, Australia ME / CFS Conference, Simon Molesworth QC pointed out that “Litigation for misdiagnosis is a reality”, and he asserted that doctors are legally vulnerable if they dismiss CFS as somatisation disorder or as another manifestation of psychopathology.

It is hoped that if used as a compendium, the two volumes of Denigration by Design? will help to establish the prominent role played by Simon Charles Wessely in the dismissing of ME /CFS and related syndromes as somatisation, despite the enormous body of published research which indicates that such a view is inappropriate, unproven and harmful.

### **Notes on Human Herpes Virus Type 6 Research in ME**

1. There is continued interest in HHV6. It was discovered in 1986 by Dr Dharem Ablashi et al and has two sub-types: variants A and B. It is of the same herpes family as the Epstein-Barr virus (which is responsible for mononucleosis / glandular fever).
2. HHV6 is closely associated with cytomegalovirus (CMV) and with HHV7.
3. It has been found to interact with the human immunodeficiency virus (HIV) -- the GS strain is the one implicated in HIV infections; research has found HHV6 in 100% of AIDS patients tested. HHV6 is known to interact with other viruses, making those viruses more severe.
4. HHV6 has also been found in patients suffering from multiple sclerosis.
5. HHV6 has been linked to other known autoimmune conditions including systemic lupus erythematosus (SLE / lupus) and to Sjorgren's syndrome.
6. HHV6 can attack the brain, lymph system, bone marrow and lungs.  
  
(ref: ACFS Conference will report high HHV6 results. *ME Today / BRAME: September 1999:9:50-57*)
7. Variant B (found in childhood roseola) affects most people quite early in life and then remains latent unless reactivated.
8. Variant A is less common. In 1986 Ablashi was contacted by three of the leading US experts in ME / CFIDS / CFS (Drs Cheney, Peterson and Komaroff) and asked to test for HHV6 in ME / CFIDS. He found that 70% of those patients had variant A instead of variant B.
9. Ablashi is now working with Professor Robert Suhadolnik (*see pp.12 & 243 above*), as HHV6 is directly related to the low molecular weight protein which Suhadolnik hopes will become a marker for ME / CFIDS / CFS.
10. Other research has also shown that HHV6A is active in ME / CFIDS. Evidence of this was presented at the Fourth International AACFS Research and Clinical Conference on CFIDS (Massachusetts, October 1998) by Dr Konstance Knox of Herpesvirus Diagnostics Inc and the Institute for Viral Pathogenesis (Wiscconsin) (*ref: Abstract of Proceedings, page 38*).
11. Tests for HHV6 detect only *active* infection, so the tests need to be re-run over several months, as patients are only intermittently positive for HHV6.
12. A patient with ME or multiple sclerosis is most likely to show a positive HHV6 result if tested during a relapse / flare-up. (*Even the concept of a*

*relapse rarely features in papers by psychiatrists of the “Wessely School”).*

13. Some laboratories use pcr techniques (polymerase chain reaction) but this is not as reliable as using an early antigen assay.
14. A further herpes link with ME has been postulated by David Berg, Director of HEMEX Laboratories Inc, Phoenix, Arizona who at the Fourth International AACFS Research and Clinical Conference on CFIDS, Mass, October 1998 presented evidence that antibodies (caused by various antigens, including HHV6) attack capillary endothelial cells, thereby activating coagulation (with the formation of fibrin), resulting in increased blood viscosity.
15. This well-understood and serious blood disorder (known as disseminated intravascular coagulation or DIC) has been found in nearly 100% of tested ME / CFIDS patients; it has also been found in fibromyalgia patients; following silicone breast implants, and in Gulf War syndrome.
16. Berg’s data point to the immune system as activating this coagulation (by removing protective proteins and then by effectively agglutinating other proteins, resulting in fibrin deposition).
17. Whilst this process does not usually cause a thrombus in most ME patients, it does interfere with the body’s ability to transfer nutrients and oxygen via the capillary network.
18. Known as “Antibody Mediated Thrombosis”, this work was also presented at the International Society of Thrombosis and Hemostasis Symposium, Washington DC, in August 1999. (*ref: ME Today / BRAME: 1999:9:51-57*).

**Information about other virological aspects of ME / CFS supplied by The Chronic Fatigue Syndrome Research Foundation (formerly known as The Persistent Virus Disease Foundation)**

Chairman Professor John Hughes FRS stated that CFS / ME is a biochemical condition; the Foundation believes that it is now recognised as a serious organic illness.

According to Hughes, “Progress requires the close collaboration of neurologists, geneticists, molecular biologists and neurobiologists.....the technology is now available to measure gene transcription (phenotype) in a single nerve cell”.

From their press release, just two examples of on-going studies funded by the CFSRF include the following:

1. Alteration of gene expression in CFS (Dr Robert Powell from The University of Reading, with Professor Stephen Holgate, MRC Clinical Professor of Immuno-

pharmacology, University of Southampton.

Most diseases involve increases or decreases in the activity of specific genes. In some cases this may be found in the genes of the infectious agent but in many cases it is the genes of the affected individual which are altered.

More specifically, it is the genes involved in the immune system (the body's defence mechanism) that show such changes.

In CFS, the likely sites of these alterations are the lymphocytes.

These researchers believe it is likely that a number of infectious agents and / or toxic substances could be responsible in different individuals; assuming there is a common underlying mechanism as a result of these different assaults, a unifying disease process can be envisaged at the cellular level.

Extracts of genetic material are isolated, processed and examined by differential display: effectively this allows the identification of genes that are more or less active in one group of individuals than another.

Such altered gene expression could provide a consistent pattern of changes in CFS patients which could distinguish them from those not suffering from CFS.

## 2. Inhibition of mitochondrial function during Poliovirus infection (Dr Michael Carter, University of Surrey)

Carter and his team have been examining how a persistent virus infection could affect the functioning of the cell. Their most recent work has focused on the effect of poliovirus, a member of the enterovirus family, on the energy-producing compartment of cells.

Since many viruses could have a similar effect, this mechanism could offer a unifying explanation for CFS / ME.

Carter's team went on to determine at which stage of energy production the mitochondria were affected by poliovirus infection.

It is known that energy is released by a flow of electrons, so it is possible to find out at which step any blockage is occurring.

Carter has found that the effect of viral infection is blocking energy production mainly at (or just past) the second stage, ie. blocking the transport of electrons to the third stage.

Using special dyes, it was shown that mitochondrial function is dramatically altered by poliovirus infection.

These changes in cellular energy levels as a result of impairment of mitochondrial function could well explain the muscle fatiguability in ME / CFS, as it is possible that a variety of different viruses may be acting through similar mechanisms.

### **Postscript**

The sheer volume of international research into the virological aspects of ME makes it all the more remarkable that in the joint Royal Colleges' report CR54 on CFS, Wessely et al dismissed the virological aspect in a mere 2½ pages of the 58 page report.

For someone who claims to practice "evidence-based" medicine, such consistent and repeated failure even to consider for review the available evidence inevitably raises questions about Wessely's role in the perception of myalgic encephalomyelitis.

It is time that his role was addressed, exposed and examined, so that if there has been no scientific misconduct (and if no-one, including Government, has been misled by misinformation and by manipulation of the existing knowledge) the matter must be dropped; if however, the charge is found to be justified, then Wessely must surely be called to account. Too many people have been too damaged for too long, and someone is accountable; many informed people believe that it is Wessely who is accountable.