

## **Reflections on the US ME/CFS Research Symposium Report**

**Eileen Marshall and Margaret Williams**

**5<sup>th</sup> November 2004**

Attention is drawn to the November 2004 issue of Neuroimmunomodulation which contains the Report of the Research Symposium on ME/CFS convened by the CFIDS Association of America and co-sponsored by the US Centres for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) (ref: Immunologic Aspects of Chronic Fatigue Syndrome. Timothy R Gerrity et al Neuroimmunomodulation 2004:11:351-357).

This Report is important, not least because it sets out the necessary direction of future research into ME/CFS which differs significantly from the recommendations that currently prevail in the UK.

The symposium was organised in October 2001 and took place at the same time as the UK Chief Medical Officer's Working Group on "CFS/ME" was in existence.

During the life of the UK Chief Medical Officer's Working Group on "CFS/ME", detailed representations were repeatedly put before the Working Group by Emeritus Professor of Medicinal Chemistry Malcolm Hooper and his associates; those representations addressed three main areas: (i) the extent of the existing international knowledge-base on ME/ICD-CFS that militated compellingly against a psychiatric causation: (ii) the need for non-psychiatric centres of excellence that would carry out advanced investigations of those with ME/ICD-CFS because basic screening tests were known to be insufficient for such a complex multi-system disorder and (iii) the need for sub-groups to be studied instead of the heterogeneous population covered by the catch-all "CFS". These representations were in due course placed in the public domain and can be accessed at [www.meactionuk.org.uk](http://www.meactionuk.org.uk)

Because it became obvious from pre-publication drafts that the Working Group had consistently ignored or dismissed the bona fide evidence that had been provided for its use, Hooper et al legitimately queried the stance taken by the then Medical Adviser to the UK ME Association Dr Charles Shepherd and by Professor Tony Pinching, then Professor of Immunology at St Bartholomew's Hospital, London, both of whom could have been expected to argue the case on behalf of the best interests of people with ME/CFS by rigorously opposing the psychiatric lobby that dominated the decision-makers on the Working Group.

However, documentary evidence from Shepherd himself confirmed that he was advising the CMO that it was neither necessary nor appropriate for any investigations other than basic screening to be carried out on patients with "CFS/ME", whilst Pinching was advising the CMO that the issue of subgroups was simply a matter of personal preference and semantics. Moreover, whilst Deputy Chair of the Working Group and before publication of its Report, Pinching published an article endorsing the views of psychiatrists of the "Wessely School", claiming that the treatment of choice for "CFS" was cognitive behavioural therapy and graded exercise (Prescribers' Journal 2000:40:2:99-106, published by the Department of Health). He is currently overseeing the Government's investment of £8.5 million into the twelve newly-funded centres that will employ CBT and graded exercise regimes and is now Associate Dean for Cornwall at the Peninsula Medical School where he will head one of the newly-funded centres, and he is also Medical Adviser to the charity Action for ME.

Not only was Hooper publicly vilified (on the internet and elsewhere, including attempts by Dr Shepherd to enforce the withdrawal of an invitation for Hooper to address the Scottish Parliament) but both Hooper personally and also the Vice Chancellor of his university were relentlessly harassed by Shepherd and Hooper was threatened with legal action by the campaigning organisation to which Shepherd and Professor Simon Wessely both belong (HealthWatch).

In the interests of accuracy, the same information was provided for the members of the MRC Research Advisory Group who on 17<sup>th</sup> December 2002 released their “Draft Document for Public Consultation” concerning the direction of future research into “CFS/ME” and in May 2003 produced their report on “CFS/ME Research Strategy” (which as anticipated, favoured CBT and graded exercise).

Hooper particularly argued the need for immune profiling and for nuclear medicine imaging for those thought to have ME/ICD-CFS, since these areas were delivering hard evidence of an organic pathology, and one investigation specifically asked for by Hooper was the study of the 2-5A RNase L pathway, to which Shepherd was opposed.

In a letter dated 17<sup>th</sup> July 2001 to the Chief Medical Officer (which Shepherd himself circulated widely and placed on the internet), Shepherd stated “I acknowledge that I have opposed the inclusion of testing for RNase L activity (an antiviral marker) --- all the published information so far comes from researchers who have a financial interest in their promotion – a situation which involves a clear conflict of interest. I would also point out that much of the scientific argument being put forward by Hooper and ‘Montague’ to justify the use of the investigations they advocate (eg immunological, endocrine and virological screening) is very seriously flawed”.

For the avoidance of doubt, the published evidence put forward by Hooper et al included work by the people who have now published the US Research Symposium Report.

The Report advocates exactly what Hooper and Montague advocated and it addresses the following issues:

1. What is the evidence that there is dysregulation of the immune system in CFS?
2. What is the evidence of the involvement of infectious agents in CFS?
3. Are there examples or models of immune dysfunction that could lead to the symptoms of CFS?
4. What can we learn from the existing data on interactions among the immune system, hypothalamic-pituitary-adrenal (HPA) axis and autonomic nervous system about the clinical presentation of CFS?
5. (a) What are the recommendations for future research?

(b) What are the recommended opportunities for research collaboration?

(c) What methodological barriers are there to the careful study of these recommendations?

The following are quotations from the Report:

“Chronic fatigue syndrome (CFS), also known as chronic fatigue and immune dysfunction syndrome (CFIDS) and myalgic encephalomyelitis, is a serious health concern (with

estimated) prevalence of approximately 422 per 100,000 adults in the US. To put (this) prevalence into perspective, systemic lupus erythematosus affects 50 per 100,000 (and) multiple sclerosis affects 104 per 100,000 American adults.

“There are as yet no specific diagnostic markers for (ME) CFS. To exclude other mental and physical causes of their symptoms, persons with CFS often must undergo an extensive battery of tests.

“The CFIDS Association of America organized a symposia series to explore and assess in-depth the role of cardiovascular, neuroendocrine, immune and nervous systems in the onset, control and progression of CFS.

“There is substantial evidence that a large proportion of patients has some immunologic abnormalities, including decreased natural killer cell activity, an increase in the percentage of T cells expressing activation markers, decreased lymphocyte stimulation by certain mitogens and soluble antigens, and increased production of certain pro-inflammatory cytokines. The humoral immune system has also shown frequent abnormalities, including hypergammaglobulinemia, increased titres of various antibodies, and the presence of immune complexes. These changes support the conclusion that dysregulation of cellular and humoral response are associated with CFS.

“However, the ability to understand the role of these changes is constrained by (the fact) the CFS patient populations studied have been highly heterogeneous (with) considerable heterogeneity in the methodologies used to assess immunologic parameters (and) a paucity of data to associate the type or magnitude of immunologic abnormalities with the nature or severity of symptoms of CFS.

“However, the pattern of immune abnormalities suggests that the immunologic factors may contribute to the pathogenesis of the chronic fatigue and other symptoms (and) the overproduction of some pro-inflammatory cytokines contributes to the fatigue. The recent demonstration of activation of the 2-5A synthetase pathway (associated with interferon - $\alpha$  signal transduction) in some CFS patients provides support for this hypothesis.

“Direct and indirect evidence exists that infections play a significant role in the pathogenesis of CFS for certain patients subsets....Coxsackie virus activity in CFS cases in Great Britain may suggest endemic virus reactivation (and) some evidence exists for Coxsackie (but) the infectious theory of CFS fell out of favour for a period of time. The reasons for this include the design of studies without adequate follow-ups.

“A good experimental model, in our opinion, should utilize well-characterized and homogenous subject populations.

“A subset of individuals with acute mononucleosis go on to develop a more chronic disease state with manifestations closely similar to CFS.

“Immunologists have used a measure of the body's early defence system, natural killer cell activity, as a potentially reproducible parameter. It has been hypothesised that a shift in immunity from a cell-mediated Th-1 bias to a predominantly antibody-dominated Th-2 response, associated with slightly elevated levels of circulating immune complexes and mildly positive ANA (anti-nuclear antibody) values, is characteristic of this condition. This

is also evidenced by increased IL-4 production and manifest by increased allergy symptoms, as well as some evidence of autoimmune phenomena in patients with CFS.

“Reproductive hormones may also exert an influence on inflammatory cytokine production and may account for the clear gender differences in CFS prevalence.

Under **recommendations for future research**, the Report recommends the implementation of longitudinal studies that include the following key elements:

- The use of adequate numbers of subjects to assure robust statistical power
- Well-characterised cases
- Blood samples drawn at specified times
- Assays designed to measure immune function: (a) natural killer cell activity; (b) percentage of peripheral blood lymphocytes expressing activation markers; (c) pro-inflammatory cytokines and soluble receptors; (d) Th-1 and Th-2 response; (e) activity of the 2-5A synthetase pathway and (f) serum immunoglobulin levels
- Selected measure of autonomic nervous system and neuroendocrine functioning
- Because data from several serological studies suggest that reactivation of latent infectious agents may play a role in the genesis of CFS, further studies are needed to demonstrate the presence or absence of viral / microbial genetic materials from multiple, prospectively collected specimens (and) the association of each infectious agent with the immunological profile seen in CFS.

“Intervention trials in well-defined subsets of the CFS population may identify useful therapeutic modalities. These therapies would be designed to improve the quality of life of CFS patients. Possible candidates for such intervention trials include anti-inflammatory cytokine antibodies or soluble receptors, antivirals, antibiotics and immunomodulatory agents.

“This panel encourages a new emphasis on multidisciplinary research into CFS, involving the collaboration of specialists from fields such as immunology, microbiology and infectious diseases, neurology, endocrinology, electrophysiology, psychology, epidemiology and rehabilitation. The use of interdisciplinary longitudinal studies to explore potential links between the variations noted in CFS patients’ immune, neuroendocrine and cardiovascular systems is critical to developing an understanding of relationships among causal factors (and) symptom progression. Furthermore, including children and adolescents in studies of pathophysiology may help to overcome the problem of confounding factors.

“Three primary methodological barriers impair the investigation of CFS: poor study design, the heterogeneity of the CFS population, and the lack of standardised laboratory procedures and resources.

“A key issue in CFS study design is the need for larger, carefully defined populations. Such studies enable the identification and characterisation of subgroups within the heterogeneous CFS population. Identifying such subgroups may lead to the development of therapeutic interventions.

Furthermore, the addition of resources such as blood, serum and tissue repositories will enhance future studies by providing a source of specimens from well-characterised patients for use with new investigative techniques.

“It is our obligation to identify and overcome the methodological barriers outlined above (and) it is well within our capabilities to accomplish this through interdisciplinary co-operation and collaboration”.

As these very issues have already been put before but rejected by the UK Chief Medical Officer and the Medical Research Council (both of whom were overly-influenced by the “Wessely School” psychiatric lobby) and as the National Institute for Clinical Excellence (NICE) is about to consider the direction of future research in ME/CFS, if UK government bodies are not to be seen yet again to be denying reality (as in the case of Gulf War syndrome, where US studies have shown the assertions of psychiatrist Professor Simon Wessely to be less than credible --- see [“US in U-turn over Gulf war syndrome”: New Scientist, 4<sup>th</sup> November 2004](#)), is it not time for the UK to reconsider the evidence and engage with reality?

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*Statement about unfounded allegations made about Professor Hooper*

*Malcolm Hooper, Eileen Marshall and Margaret Williams*

*6 November 2004*

*For the avoidance of doubt, Professor Hooper and his associates wish it to be publicly known that, contrary to the unfounded allegations made on Co-cure by Miss Ellen Goudsmit PhD ([Co-Cure: Villification and scapegoats, 6 November 2004](#)), neither he nor they have "on several occasions written untruths" about anyone.*

*The matter to which Miss Goudsmit refers in her Co-cure post was supported by genuine documentary evidence and that evidence is extant.*

*Where is Miss Goudsmit's evidence that Professor Hooper has "on several occasions written untruths"?*

*As has previously been made clear, neither Professor Hooper nor any of his associates is responsible for anything but the authorised versions of any of their documents, nor is he nor any of his associates accountable for any unauthorised modification of their original documents.*

*Miss Goudsmit appears to take exception to the use by professionals of a pseudonym, whilst claiming that she herself used a pseudonym in the past, asserting about one of Professor Hooper's associates: "You are not a journalist using a pen name like I did during my time at InterAction". In this respect, it is to be noted that Miss Goudsmit has never been a professional journalist, although she has certainly used various pseudonyms over the years, as several people know and can testify.*

*The legitimate reason for the use by Professor Hooper's associates of a pseudonym was placed on the internet on 7 July 2001 and the stated reasons remain valid.*

*Another assertion made by Miss Goudsmit also requires correction (ie. where she states about one of Professor Hooper's associates that "You are not a professional"): this assertion is untrue and without foundation. In contrast to Miss Goudsmit's own formal employment status, Professor Hooper's associates to whom she is referring either currently are or formerly were employed in professional NHS posts and working as medical scientists, researchers or directly in the clinical field.*

*By comparison, it is understood that whilst unwell and unemployed, Miss Goudsmit obtained a PhD but remains unwell and formally unemployed. Notwithstanding, she often refers to herself as though she were a professionally employed clinician, describing herself on the internet as "an ME specialist" (for example, on 8 December 2000 and on 27 July 2001).*

*The facts must speak for themselves and people must judge those facts, and Miss Goudsmit's motives, for themselves.*

*No further statements on this matter will be issued by Professor Hooper or by any of his associates.*

*Malcolm Hooper, Eileen Marshall and Margaret Williams*

*6 November 2004*

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**8th November 2004**

**A few facts for the record**

**Margaret Williams**

1. Ellen Goudsmit has no idea what qualifications Margaret Williams obtained or where they were obtained, nor does she know the nature of Margaret Williams' post-graduate work or at which university it was undertaken (in fact it was the University of Oxford);
2. Ellen Goudsmit has no idea what professional posts Margaret Williams has held, or in what capacity, nor does Ellen Goudsmit know with which law firms Margaret Williams worked as a medico-legal researcher or for how long;
3. Ellen Goudsmit's assertion that "The court case which provided the reason for the initial use of the pseudonym by Ms Williams was completed some years ago" is erroneous: the reason for Margaret Williams' continued use of a pseudonym is precisely because the Court case (on ME) is still alive and her legal team insist on no publicity, which could be detrimental to the proceedings. Miss Goudsmit's implication that Margaret Williams uses a pseudonym to "hide behind" when "attacking people and needed to avoid brickbats or law suits" is pure fabrication by Miss Goudsmit and has no basis in fact, because Margaret Williams does not "attack" people, she simply states facts that can be verified;

4. No-one is claiming that Ellen Goudsmit's "contribution to life was useless": this is yet another illustration of her own misinterpretation of the facts;
  5. What people object to is Ellen Goudsmit's repeated portrayal of herself as something she is not (i.e. as a bona fide employed clinician who sees patients with ME). People object to her claims that imply her own superiority in ME matters (including her patronising references to "patients" as distinct from professionals such as herself) and to her many internet posts in which she clearly equates herself with genuine international ME experts, and to her claims that they are her "colleagues" and that, as the "only ME specialist" in the UK, she has "advised" these experts;
  6. Ellen Goudsmit states (about herself) "It is perfectly acceptable to use pen names to write in non-medical publications", so what is her objection to Margaret Williams doing so? The Statement from Professor Hooper, Eileen Marshall and Margaret Williams pointed out that Ellen Goudsmit was not a professional journalist and that is a statement of fact. That Miss Goudsmit has been paid for some articles she has written, whether she asked to be paid at Medical Journalists' Association rates or not, does not make her a professional journalist, any more than Margaret Williams is a professional journalist;
  7. Since it is Dr Charles Shepherd of the ME Association who organises the Melvin Ramsay Society, it is to be expected that Ellen Goudsmit would be involved, although her involvement apparently ceased when Professor Simon Wessely was invited: in her [post on ResAct](#) (posted before her [reply on Co-Cure](#)) she states "I specialise in ME and was an invited member of the Melvin Ramsey Society until they invited Wessely";
  8. Ellen Goudsmit states in her Co-Cure reply: "I wrote my PhD on ME", yet the title of her dissertation is "The psychological aspects and management of chronic fatigue syndrome" (Brunel University, July 1996). As a psychologist who knows the extent of the psychiatric bias towards ME and who claims to be a specialist in ME, one might wonder why Miss Goudsmit focused solely on the psychological aspects of a disorder that has been classified as neurological since 1969;
  9. The issues surrounding HealthWatch are detailed in Hansard (Lords) and it is the case that whilst on the CMO's Working Group, Dr Charles Shepherd did not declare his membership of and active involvement with HealthWatch until it was brought to the attention of the ME community by Montague and Hooper;
  10. In her Co-Cure reply Ellen Goudsmit finishes by again insinuating that Professor Hooper and his associates cast doubts "on good people which they do not deserve" and she continued: "To the untruths in relation to Dr Shepherd and HealthWatch, I can now add the errors in relation to myself". If she includes herself as a "good" person, perhaps she is unaware that such accolades are normally awarded by others, not oneself.
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