

Scottish Good Practice Statement on ME-CFS: Comments on the Canadian Consensus Document

General Principles on Guideline Development

It is now generally accepted that clinical guidelines must have a demonstrable methodology and clear source of scientific evidence, based on the principles of systematic review of the literature, as developed and used by the Scottish Intercollegiate Guidelines Network (SIGN). There is no reference to any such methodology in the Canadian Consensus Document and the source of evidence appears to have been selective citation of the literature on the basis of expert opinion. Although the Canadian Consensus Document is lengthy, and heavily referenced, many of its assertions and recommendations are unreferenced and are not based on published clinical evidence

Specific Issues of Concern

This analysis does not seek to present a detailed critique of the Canadian Consensus document, but there are numerous matters with which one could take issue including:

- As noted above, the guideline was developed without reference to any standard methodology (eg SIGN).
- The guideline appears to have been at least part funded by Crystall (Biovail pharmaceuticals); a firm who claim to specialise in CNS niche placement products). Clinical guidelines development should be free of any commercial sponsorship.
- The guideline says that *ataxia, muscle weakness and fasciculations are common*'. The Scottish Neuroscience Council takes the view that the 'hard' neurological signs of ataxia or fasciculations never occur in ME. Where these signs do occur, they have very specific clinical implications. True fasciculations (as opposed to muscle twitches) are associated with degeneration of peripheral nerves and often are linked to a diagnosis such as Motor Neurone Disease (MND) and not with ME-CFS. Whilst the symptoms of dizziness or unsteadiness may be common in ME-CFS and accompanied by signs of being slow or clumsy, true cerebellar ataxia should trigger a search for an alternative cause. Similarly, whilst many people with ME-CFS complain of feeling weak and may have apparent weakness on examination, this is often variable over time and reflects variation in effort due to fatigue for example, rather than true muscle weakness as seen with diseases of the upper or lower motor neuron. There is a strong concern that by including these symptoms and signs in its core description of the condition, the statement would lead to misdiagnosis both of those with ME-CFS and with other unrelated serious neurological diseases.
- In the same section the guideline specifies impairment of short term memory consolidation. This is not technically possible- short term memory (also known as working memory or immediate memory) is a short term, capacity limited store which holds 7 (+/- 2 items of information) on a temporary basis, it does not consolidate or

'hold' them for later usage (ie the content of your immediate thoughts) - there is either immediate transfer to long term memory, where consolidation does take place, or they are simply forgotten.

- Confusion and disorientation are listed. Whilst colloquially commonly described and usually actually referring to depersonalisation, true confusion and disorientation do not occur in ME-CFS. If present, they would most commonly indicate delirium (toxic confusional state) or advanced neurodegenerative disease.
- The guideline divides symptoms up into a range of aetiological mechanisms autonomic, neuroendocrine and immune. These mechanisms are speculative and unconfirmed.
- The assertion (page 21) that ME-CFS patients have abnormal pupillary responses – the only published article examining the pupils of ME-CFS patients that we could locate on this subject, after extensive searching, found no difference between patients and controls.
- The recommendation to give vitamin B₁₂ (page 56). Detailed instructions for dose and schedule are given – but there has only been one very small published trial of B₁₂ in ME-CFS (Kaslow et al, Arch Int Med 149:2501, 1989) and no benefit was seen.
- Similar concerns apply to fludrocortisone (recommended on page 59, 67) - several published trials are all negative.
- The document also recommends the use of methylphenidate and dexamphetamine (page 57). Although there are small short term published controlled trials of both these agents showing increases in energy, it is hard to see UK physicians prescribing amphetamines for patients with ME-CFS, and we doubt that the government or medical regulators would wish to be supporting that.
- Ampligen is recommended (page 65). There have been no published trials of this antiviral agent in CFS since 1994 and it is not available in the UK. In 2000 the manufacturers were warned by the FDA to cease promotion of ampligen for ME-CFS. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLettersstoPharmaceuticalCompanies/UCM166046.pdf>. This compound has been 'in search of a disease' for over 15 years, and has been unsuccessfully promoted for a number of conditions, including HIV.
- *"Organic food is recommended ...or soak produce in water with 1 tablespoon of sea salt and one tablespoon of lemon juice for 20 minutes to help remove toxins..."*(Page 42). No evidence is presented for the involvement of pesticide residues in ME-CFS, nor for the efficacy of this procedure in removing any that may be there.

Conclusion

There is undoubtedly much in the Canadian Consensus Document that is true, but it is accompanied and often obscured by a great amount of material that is speculative and unproven. As a review of the literature as it existed in 2003, it is selective and unsystematic, and as a guideline for action either by care providers or researchers, it is unsatisfactory.

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(on behalf of the Clinical Quick Reference Guide Working Group)

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