# Different Approaches to the Application of Science to Understanding and Treating Multiple Sclerosis – An Open Letter to Mark Freedman

Dear Mark,

I was recently forwarded a copy of an email which you had sent to one of your patients regarding the CCSVI issue. I was not surprised by your unwavering belief that CCSVI is nonsense but was slightly taken aback by your over-the-top view that all those who think that CCSVI treatment may be of value are nothing more than frenzied, cult members. I was also somewhat surprised that you mentioned me but was glad you asked an important question "***who am I to question the word of the many self-acclaimed experts who feed this frenzy like the rock doctor Embry whose lifelong study of lifeless objects has given him the wisdom to comment on such complex issues?"***

You are correct that my primary scientific research activity for the past 42 years has revolved around inanimate rocks, mainly those in the Canadian Arctic Archipelago. I'll be glad to send you some of my published geological papers if you have an interest in such things.

I must point out that it has not been my geological studies which have "given me the wisdom" to comment on complex issues associated with multiple sclerosis. My knowledge on MS comes from reading thousands of scientific papers and countless abstracts on MS and related subjects (e.g. nutrition, autoimmunity in general, and more recently vascular issues). My pursuit of scientific knowledge in regards to MS has been driven by a desire to ensure my son is doing everything he can to prevent the progression of his MS.

I would emphasize that I try hard to make sure any written comments I make on MS, especially recommendations on how to help control disease progression, are backed by solid science, including both empirical data and critical, rational reasoning. I suppose you could say that many years of geological research have instilled this hard-core, scientific approach so perhaps you are not entirely wrong with your statement that the source of my MS "wisdom" is my geological research.

I thought it might be useful if I discussed how we sharply differ on three important scientific issues which dominate decisions regarding the treatment of MS. These issues are CCSVI, vitamin D and the CRAB drugs. These differences show how we significantly vary when it comes to doing science and to using science to guide actions. Following this, I will wrap-up with a few possibilities on why such differences between us exist, despite the fact we both would claim we are scientists wanting to understand MS so as to allow us to make recommendations on how to treat it.

**CCSVI**

The first topic is CCSVI which continues to divide the MS community. As a scientist, I try to stay up to date on the literature but it wasn't until July, 2009 that I came upon Dr Zamboni's work, 4 months after he had published his watershed paper on CCSVI. After reading that paper, I immediately read all the available papers on CCSVI as well as major past references on vascular issues in MS. Once I had completed my literature research, which included carefully going through the Zamboni papers up to three times each, it was apparent that either impaired venous drainage was very likely an important factor in MS or that Dr Zamboni and his associates were incompetent or frauds. There basically was no middle ground given the apparent robustness of the Zamboni research.

A review of the extensive scientific contributions of Dr Zamboni and his colleagues over the past 25 years removed any doubt as to their impeccable scientific credentials and their solid competency when it comes to vascular research. Thus, their impressive clinical and theoretical studies on CCSVI, combined with past studies on vascular issues associated with MS, and the fact that CCSVI nicely explained some previously inexplicable features of MS (e.g. venocentricity of lesions, associated iron deposits, continued disease progression despite the complete destruction of the immune system), gave me no choice but to accept the proposition that it was very likely that CCSVI was an important factor in MS. This in turn led me to facilitate and encourage the dissemination of CCSVI information and to call for extensive research into CCSVI and MS in August 2009.

Since my initial immersion into the CCSVI literature, I have closely followed CCSVI research and this has included visiting with some of the researchers themselves. I have been most impressed with the CCSVI research being done at the University of Buffalo and their work, involving 500 subjects, has robustly confirmed the high association of CCSVI with MS. Such a high association, the plausible biological mechanisms which link CCSVI to the MS disease process, and the established nature of the venous problems associated with CCSVI, establish beyond a reasonable scientific doubt that CCSVI plays a role in the MS disease process.

I have also kept a close watch on the results of worldwide CCSVI treatments because such results, due to their high numbers, are important scientific data that cannot be ignored. Currently, there are at least 75 centres worldwide doing CCSVI treatment and between 100 and 200 procedures are now being done each day. These treatments involve the use of venography which is the gold standard for the identification of CCSVI and, of the 12,000+ patients treated so far, over 90% have had undoubted CCSVI. Furthermore, there have been thousands of well documented cases of substantial improvement of a variety of MS symptoms following CCSVI treatment.

As a scientist, I cannot ignore the CCSVI treatment data and to do so would be bordering on scientific incompetence/fraud. To sum up, the published scientific data on CCSVI and the many thousands of clinical procedures which have identified and treated CCSVI leave no reasonable doubt as to the existence of CCSVI and that it plays a role in the MS disease process.

I would contrast my objective, scientific appraisal of CCSVI with your emotional and non-scientific approach. I assume the first time you were exposed to the science of CCSVI was through the CTV documentary and that you had failed to read the papers which had been published on this topic before that time. Your public response to a group of MS patients that the Zamboni work was a hoax before you had read his papers, reveals a complete lack of scientific method and objectivity by you on this subject. Furthermore, your insistence on ignoring the results of many thousands of CCSVI procedures also underscores your inability to take an unbiased, scientific approach when it comes to CCSVI. I will discuss possible reasons for such a failure later.

The bottom line is that you have not spent time with the CCSVI researchers, you have not read most of the 200+ scientific papers which bear directly on the CCSVI question, and you have not taken the time to evaluate the results of the huge number of CCSVI procedures which have been done. Any claim that your comments regarding CCSVI are science-based is not supportable. Thus, when it comes to CCSVI my comments on the subject are given much more weight than yours simply because I know far more about the subject than you do and most importantly, I have taken an objective, scientific approach to CCSVI and MS, not an emotional, highly prejudiced one like you have. I can only encourage you to try to be more objective and scientific when it comes to CCSVI.

**Vitamin D**

The next topic is the role of vitamin D in MS. When I began my studies of the MS literature, my main goal was to identify environmental factors involved in MS. It seemed this would be the best approach for devising potential therapies for treating the disease. By 1999 there was enough solid and diverse scientific data to indicate that vitamin D deficiency was involved in MS. Given this, I advocated for the use of vitamin D supplements both as a strategy to prevent MS in the first place and to treat it. This was a classic case of a scientifically-backed therapy which offered nothing to lose (vitamin D is extremely low cost and completely safe) and all to gain in terms of prevention and treatment. At this time I also published a short note in Annals of Neurology on vitamin D and lesion formation (with a recommendation for a 4000 IU supplement) and I made available on the internet a comprehensive document on the science of vitamin D and MS.

Notably over the past 10 years there have been scores of studies on vitamin D and MS, all of which have supported and confirmed what we knew back in 1999 – there is a good chance adequate vitamin D will prevent MS in many cases and that it will have therapeutic value for those with MS. I would say that I have read

at least 750 papers on vitamin D with at least 250 of those directly related to vitamin D and MS. Given that my scientific abilities and literature research allowed me to identify vitamin D as a useful therapy for MS in 1999, the question becomes what did your scientific approach achieve for you regarding vitamin D and MS.

You may recall in November,2006 we both attended an AAN MS Guideline meeting in Boston. I gave a presentation on vitamin D and MS and the potential value of developing a guideline on such a topic. Following my talk, you made light of the concept of vitamin D for MS calling it alternative medicine that had no place in the meeting. It was very obvious you had not read any of the vitamin D literature or you would not have made such an unsupportable and revealing statement.

I have also learned that you do not recommend adequate vitamin D (enough to raise one's 25D level to between 125-175 nmol/l) to your MS patients and you do not let your patients know that there is a reasonable chance that adequate vitamin D from birth onwards will prevent MS. It is clear that you have not taken a scientific approach when it comes to vitamin D and MS and your patient care has consequently suffered. Again, I can only suggest you take some time to review all the vitamin D and MS literature in an objective and comprehensive fashion.

**CRAB drugs**

The CRAB drugs (Copaxone, Rebif, Avonex, Betaseron) is one topic I am sure you know lots about given your involvement in clinical trials and your very strong and lucrative financial ties to the drug companies that manufacture these drugs. I also have a great interest in these drugs because they represent a potential therapy for my son.

When it comes to such drugs, the key question is whether or not they affect the progression of the disease or not. If they do, then they would be a reasonable therapeutic option despite their high cost and adverse side effects. However, if they do not slow progression, then I would say they are possibly worse than useless. So the obvious scientific question, which we both are interested in, is whether or not any of the CRAB drugs slow MS progression.

Given that you prescribe such drugs to your newly diagnosed patients and give talks (often for money) advocating the use of such drugs, I can only presume that you firmly believe that the drugs do slow disease progression. I am not sure what you base such a belief on but I have to assume it is mainly based on the clinical trials which tested the effect of the drugs using frequency of MS relapse and number of new MS lesions as proxies for determining if a given drug affected progression or not. You and I both know that there have been no clinical trials which have lasted long enough to directly determine if any of the CRAB drugs actually do slow MS progression or not.

From a scientific perspective, it became essential to determine if frequency of MS relapse and new lesion formation correlated to MS disease progression and were thus valid proxies in clinical trials. I have read most studies connected with the MS drugs and over the last few years have been impressed with the studies which have shown that those two proxies do NOT correlate with disease progression. In fact it was found those with fewer attacks progressed faster and farther!

To emphasize this critical point I have to quote Dr George Ebers, one of the premier MS researchers in the world on this. Dr Ebers states “Clinical trials of multiple sclerosis have been uniform in utilising invalidated outcome measures. This has occurred to a degree to which it is difficult to find parallels in medicine in general. It is quite clear from natural history studies that **relapses have very little if anything to do with long term outcome**. Similarly, **MRI measures have been thoroughly evaluated within large datasets and found to be similarly non-predictive for meaningful outcomes.”** These are conclusions from hard science and have to be respected and used when it comes to actions regarding the CRAB drugs.

I assume you have read the key papers which demonstrate that relapse rate and MS lesion formation cannot be used to determine if a given drug is of value for slowing MS. I trust you will agree that currently we have no good scientific evidence that the CRAB drugs slow MS progression. In fact, we now have a three long term studies which indicate that **the drugs do not slow MS progression** by showing that those on the drugs reached the same EDSS end points in the same time as those not on the drugs (Boggild et al, 2009; Veugelers et al, 2009; Ebers et al, 2010).

Given the above scientific evidence and reasoning, I have advised my son not to use a CRAB drug and I also advise others not to use a CRAB drug which provides no benefit and which has adverse side effects such as flu-like symptoms and painful injection site reactions. It is somewhat bothersome that **you claim to be a scientist and to follow the dictates of evidence-based medicine but continue to prescribe drugs for which we have no reliable scientific evidence that they do any good. In fact, the current data indicate they do not work.**

I have to again quote George Ebers on the problem of **“widespread embracing of dubious and poorly validated outcomes by some MS investigators, often in contexts where there are egregious conflicts of interest, threaten academic credibility not to mention long term professional autonomy.”** There is no doubt that many neurologists are prescribing the CRAB drugs, not because the science says they work, but because it is financially advantageous to do so. Given your “egregious conflicts of interest**”** when it comes to the CRAB drugs and your disregard for the science concerning these drug, I assume you can understand why you have no credibility on this subject.

**Summary**

I have pointed out three main differences between us when it comes to various factors and MS. I objectively follow the available science which tells us that:

1) CCSVI is highly associated with MS and is very likely an important part of the disease process,
2) Vitamin D deficiency is an important factor in the onset and progression of MS.
3) The CRAB drugs do not have any effect on MS disease progression.

These science-based conclusions have led me to the following science-based recommendations that anyone with MS:

1) Be tested and, if need be, treated for CCSVI.
2) Take an adequate vitamin D supplement and ensure any first degree relative also takes such a supplement.
3) Do not use any of the CRAB drugs.

On the other hand you ignore much of the current science and, on the basis of blind faith rather than scientific analysis, tell your patients that:

1) CCSVI does not exist and persons with MS who see potential value in CCSVI treatment are frenzied cult members.
2) Vitamin D supplementation represents alternative medicine and has no place in MS treatment or prevention.
3) The CRAB drugs are of value and should be used by persons with RRMS.

Finally we are left with the question of why I have chosen an unbiased scientific path whereas you have gone in the opposite direction. My only hypothesis to explain this is that your financial ties to the drug companies have prejudiced you against any non-drug therapy such as adequate vitamin D and CCSVI treatment and made you blind to the robust data which demonstrate the drugs do not slow MS progression. On the other hand, with my son having MS, I have all to lose and nothing to gain by not ensuring that I carefully examine all scientific hypotheses for MS in a rigorous and unbiased manner. Perhaps also the fact I was trained as a scientist (PhD) whereas you were trained as an MD (ie engineer) might also come into play when it comes to the great difference in our application of science for helping persons with MS.

I hope this answers your question of why persons with MS trust what I have to say about various proposed therapies for MS far more than they trust you. They can tell the difference between an objective, science-based analysis and a self-serving, unscientific opinion every time.

Ashton Embry