

## References

1. Adatia F, Bedard PL. "Palm reading": 2. Hand-held software for physicians. *CMAJ* 2003;168(6):727-34.
2. Privacy policy. ePocrates. San Mateo (CA): ePocrates Inc.; 2003. Available: [image.epocrates.com/company/privacy.html](http://image.epocrates.com/company/privacy.html) (accessed 2003 Apr 27).

Competing interests: None declared.

## Investigating CAM

John Hoffer invokes homeopathy as an example of how medical scientists set a higher bar for proof of efficacy for complementary or alternative medicine (CAM).<sup>1</sup> Rather than describing this as a "complication," it might be better understood as an entirely appropriate response to extraordinary claims of any sort. "Evidence" of effectiveness can be found for any treatment, no matter how arcane. The question is how good the evidence is, in light of well-established scientific principles. In the case of homeopathy, we must ask whether chance and poor experimental design can explain positive results obtained in randomized controlled trials (RCTs) of homeopathy or whether RCTs with negative results (usually done by non-advocates of this type of therapy) but accompanied by a vast and well-established body of scientific evidence are in fact in error.

Hoffer also mentions St. John's wort and glucosamine as therapies of established efficacy. However, although positive RCTs of St. John's wort exist, the most rigorous studies (placebo-controlled and randomized, with proper case definitions and a treatment-responsive population) indicate no benefit.<sup>2-6</sup> Glucosamine enjoys the support of over 14 RCTs,<sup>7</sup> but critical reviewers will be concerned about the fact that almost all of these were conducted with funding from purveyors of this compound. Publication bias therefore appears to play a role.

Hoffer's call for funding to be directed to case reports and series on CAM therapies as a way of "grooming" them as candidates for RCTs may simply result in a situation in

which nothing new is learned. Why? Because uncontrolled and nonrandomized trials are poorly suited for investigating the subjective or "soft" outcomes that CAM therapies so often promise to deliver. Randomization, placebo control and blinding limit the effect of precisely those biases that are likely to explain the "effects" of CAM therapies.

A brief glance through PubMed reveals a plethora of clinical CAM trials. The fact that so many have been done (over 2000 in the case of acupuncture) without producing any clear examples of valid new therapies not only indicates that research money is available but also that it might be better directed.

Why the evaluation of scientifically implausible therapies should be a priority of any magnitude remains an open question. One could argue that some funds should be spent to ensure that prevalent therapies be investigated for safety and drug interactions. Yet research funds are scarce as it is, and the public would be poorly served if money were deliberately funnelled into treatments already recognized as implausible.

### Lloyd B. Oppel

Physician

University of British Columbia Hospital  
Vancouver, BC

## References

1. Hoffer LJ. Complementary or alternative medicine: the need for plausibility [editorial]. *CMAJ* 2003;168(2):180-2.
2. Shelton RC, Keller MB, Gelenberg A, Dunner DL, Hirschfeld R, Thase ME, et al. Effectiveness of St. John's wort in major depression: a randomized controlled trial. *JAMA* 2001;285:1978-86.
3. Deltito J, Beyer D. The scientific, quasi-scientific and popular literature on the use of St. John's wort in the treatment of depression. *J Affect Disord* 1998;51:345-51.
4. Field HL, Monti DA, Greeson JM, Kunkel EJ. St. John's wort. *Int J Psychiatry Med* 2000;30:203-19.
5. Khan A, Leventhal RM, Khan SR, Brown WA. Severity of depression and response to antidepressants and placebo: an analysis of the Food and Drug Administration database. *J Clin Psychopharmacol* 2002;22:40-5.
6. Hypericum Depression Trial Study Group. Effect of *Hypericum perforatum* (St. John's wort) in major depressive disorder: a randomized controlled trial. *JAMA* 2002;287:1807-14.
7. Kayne SB, Wadson K, MacAdam A. Is glucosamine an effective treatment for osteoarthritis? A meta-analysis. *Pharm J* 2000;265:759-63.

## [The author responds:]

I applaud Lloyd Oppel's objection to wasting money testing highly implausible therapies, but it seems to me that he is missing the bigger picture. Important new ideas often seem implausible at their inception. The goal of therapeutic research should be to generate important, novel (and hence, at the outset, implausible) ideas, find out which of them may actually be correct, and then gather definitive evidence one way or the other. My article<sup>1</sup> outlined a practical, low-cost strategy for determining which complementary and alternative medicine (CAM) approaches are plausible enough to justify a thorough and fair evaluation.

Government and nongovernment funding agencies have taken the position that CAM merits evaluation. Furthermore, CAM may infuse important new ideas into medicine at a time when much of our mainstream therapeutic research agenda serves the pharmaceutical industry.

Glucosamine sulfate is a safe, inexpensive and potentially useful therapy for osteoarthritis<sup>2</sup> that is especially interesting because it is clinically plausible but biologically implausible. We recently proposed that sulfate, rather than glucosamine, could mediate its beneficial effects.<sup>3</sup>

Oppel cites 2 negative RCTs of St. John's wort in depression. The first was restricted to patients with severe, chronic depression, and its authors suggested that people with milder and less chronic disease might have done better.<sup>4</sup> In the second trial, also restricted to patients with major depression, St. John's wort fared no worse than the established treatment, sertraline.<sup>5</sup> One might conclude that severely depressed patients — especially those referred to specialty units and in whom standard antidepressants fail — are unlikely to respond to St. John's wort.

Oppel misunderstands my point about the role of plausibility in setting standards of evidence. It is often said that there is no difference between