

The Eternal Closure of the Biased Mind? The Clinical and Scientific Relevance of Biophysics, Infinitesimal Dilutions, and The Memory of Water

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UK GENETICIST PROFESSOR STEVE JONES' aphorism about science that it is "a broad church full of narrow minds trained to know even more about even less"¹ could be considered an apt description of the recent commentary that appeared in the *American Journal of Medicine*.² In it, the biomedical community was urged to adopt a closed mind toward homeopathy. Quite early on, however, by referring to manipulative physical therapies as "some of the more plausible aspects of alternative medicine," one of the commentary's authors seems to contradict his published stance on chiropractic.³

Then, in describing homeopathy as "among the worst examples of faith-based medicine . . .",² the commentary neglects the *conventional* medical and scientific literature on some of homeopathy's core tenets. Thus, hormesis (a biphasic dose response to an environmental agent (e.g., toxin, drug, remedial agent, etc.), characterized by a low-dose stimulation or beneficial effect, and a high-dose inhibitory or toxic effect)⁴ is a concept with a long history in medicine, precisely because of its association with a core tenet of homeopathic practice, namely, the potency of the minimum dose. Nevertheless, "the hormetic dose-response is far more common and fundamental than the dose-response models . . . used in toxicology and risk assessment . . . Acceptance of the possibility of hormesis has the potential to profoundly affect the practice of toxicology and risk assessment."⁵

Additionally, high-quality laboratory studies suggest infinitesimal dilutions agitated, or succussed in the manner used to make homeopathic preparations, may well exert biological effects.^{6–9} Indeed, most recently, very low doses of cytokines interleukin-12 and interferon- γ were reported by Gariboldi et al.¹⁰ to be much more effective in a mouse asthma model when the cytokines had been prior subjected to what is described as "sequential kinetic activation"; in other words, serial dilution and agitation.

Much as a 2005 *Lancet* meta-analysis¹¹ is repeatedly cited as conclusive proof that homeopathy is nothing more than placebo, it has, in fact been shown to be biased by several independent authors,^{12–15} and contains significant scientific flaws.^{16,17} Not only does this meta-analysis have an unusual paucity of literature references, but also it violates the *Lan-*

cet's own strict guidelines on methodological and publication transparency.¹⁸ So, perhaps it is not the "genuine and humble wish to explore the limits of our knowledge using the scientific method"² that the *American Journal of Medicine* commentary suggests itself to be.

Equally, the assertion in the commentary that the results of homeopathic prescribing lack efficacy beyond what might be expected of a placebo response² relies heavily on just two systematic reviews, both by one of the commentary's authors.^{19,20} This could be interpreted as suggesting that the author's systematic reviews alone are the only well-designed high-quality studies, and that those of others^{7,8,10,21–23} considered to be at least of equally high quality, if not more, should be discounted.

The commentary goes on to suggest that the scientific validity of homeopathy must exist in a "parallel universe," because if it were correct, it would mean that "much of physics, chemistry, and pharmacology must be incorrect."²

However, in the commentary's "parallel universe" of "gold standards" and systematic reviews, all is not well with evidence-based medicine. In fact, many conventional medical procedures are well known to lack scientific evidence;²⁴ fraud in biomedical and pharmacological research has been exposed recently and objectively referenced,^{25,26} while clear evidence exists for the harm that can result from routine conventional medical practice and prescribing.^{27,28} It would no doubt have been to the commentary's credit if its authors had campaigned for an open mind to the shortcomings of conventional biomedicine. Instead, they assert that "[t]he true sceptic . . . takes pride in closed mindedness when presented with absurd assertions that contravene the laws of thermodynamics,"² a reference to the Memory of Water hypothesis, as a possible explanation for the efficacy of remedies prepared by the method of serial dilution and succussion as in homeopathy.

Though the Memory of Water hypothesis cannot yet be taken as providing definitive evidence supporting the tenets of homeopathic medicine,²⁹ it is factually incorrect to assume that it contravenes basic scientific principles. There is now a growing body of evidence²⁹ from chemistry,^{30–33} physics,^{34,35} and materials science,³⁶ suggesting that the properties of water may well depend on its dilution history.³⁰ The question now is how?

The Memory of Water may be considered an *emergent* property of bulk liquid water (i.e., the whole is greater than the sum of its individual molecular parts). This defies explanation in terms of high-school chemistry, or the notion that water molecules move completely randomly in relation to one another. Certainly, the long-range ability of water molecules to affect each other via dynamic switching of hydrogen bonds may be crucially important here, as may be weak intermolecular interactions, called van de Waals forces.²⁹ From these may arise coherent supramolecular behavior (i.e., possibly involving huge numbers of water molecules) that the *equilibrium* laws of thermodynamics one learns at school, and the known short lifetime of hydrogen bonding in aqueous solutions,²⁹ cannot explain.

To understand the Memory of Water hypothesis requires a knowledge of systems operating far from chemical equilibrium, as described by Professor Ilya Prigogine's Nobel Prize-winning work on *nonequilibrium* thermodynamics in near-chaotic chemical reactions, and importantly, as exists in all living organisms.³⁷ Here, it has been suggested that microscopic points of local instability may act as dynamic "attractors" of the whole macroscopic system, leading to long-range coherent supramolecular behavior.³⁸

More than 20 years ago, a theoretical mechanism for Memory of Water was advanced by del Guidice et al.³⁹ that modeled the effects of sequential kinetic activation (as performed in making a homeopathic medicine) in terms of the continued formation and dissolution of dynamic supramolecular structures.²⁹ These so-called "coherent domains" (the equilibrium concentrations of which are governed by thermodynamics) recur long after all traces of the original dissolved substance have been removed. Indeed, a recent article authored by Professor Luc Montagnier (winner of the Nobel Prize for Medicine, for his discovery of the human immunodeficiency virus) has demonstrated memory effects in aqueous DNA solutions that depend on interactions with the background electromagnetic field.⁴⁰ Consequently, the Memory of Water hypothesis is not only plausible, but it also contravenes no known scientific laws and principles.

In conclusion, therefore, it would appear that the *American Journal of Medicine* commentary² exhibits a significant degree of bias in its expressed position on the science of homeopathy and related phenomena (especially in its neglect of the literature on these subjects),^{4-10,12-17,29-41} such that its authors' stance must be considered unscientific. In addition, and the science aside, the commentary ignores not only expressed concerns over the intolerance exhibited toward therapeutic pluralism in health care services⁴² by overzealous application of the principles of evidence-based medicine,^{43,44} but also ignores advances in our understanding of the meaning and possible purpose of disease to the health of the individual.⁴⁵

Though the form of discourse deployed in the commentary² might be considered better suited to media reportage than to a serious scientific journal, its call for "*the adoption of a closed mind to homeopathy*"² is reminiscent of the attitude of those inhabiting a desert island threatened with inundation. As the "atoll" on which the inhabitants sit shrinks before a rising tide of clinical, biological, and basic scientific evidence for the (sequential kinetically activated) effects of infinitesimal dilutions, one wonders whether the denunciation of homeopathy in the commentary is evidence of the authors "angrily waving, or desperately drowning"^{7,46}

References

1. Jones S. *The Single Helix: a Turn around the World of Science*. London: Little, Brown Book Group, 2005.
2. Baum M, Ernst E. Should we maintain an open mind about homeopathy? *Am J Med* 2009;122:973-974.
3. Ernst E. Chiropractic for paediatric conditions. Substantial evidence? *BMJ* 2009;339:b2766.
4. Mattson MP. Hormesis defined. *Ageing Res Rev* 2008;7:1-7.
5. Calabrese EJ. Toxicological awakenings: The rebirth of hormesis as a central pillar of toxicology. *Toxicol Appl Pharmacol* 2005;204:1-8, and references therein.
6. Linde K, Jonas WB, Melchart D, et al. Critical review and meta-analysis of serial agitated dilutions in experimental toxicology. *Hum Exp Toxicol* 1994;13:481-492.
7. Belon P, Cumps J, Ennis M, et al. Histamine dilutions modulate basophil activation. *Inflamm Res* 2004;53:181-188.
8. Witt CM, Bluth M, Albrecht H, et al. The in vitro evidence for an effect of high homeopathic potencies: A systematic review of the literature. *Complement Ther Med* 2007;15:128-138.
9. Milgrom LR. ". . . Macavity's not there!" *J Altern Comp Med* 2009;15:1051-1053, and references therein.
10. Gariboldi S, Palazzo M, Zanobbio L, et al. Low dose oral administration of cytokines for treatment of allergic asthma. *Pulmonary Pharmacol Therapeut* 2009;22:497-510.
11. Shang A, Huwiler-Müntener K, Nartey L, et al. Are the clinical effects of homeopathy placebo effects? Comparative study of placebo-controlled trials of homeopathy and allopathy *Lancet* 2005;366:726-732.
12. Bell IR. All evidence is equal, but some evidence is more equal than others: Can logic prevail over emotion in the homeopathy debate? *J Altern Complement Med* 2005;11:763-769.
13. Frass M, Schuster E, Muchitsch I, et al. Bias in the trial and reporting of trials of homeopathy: A fundamental breakdown in peer review and standards? *J Altern Complement Med* 2005;11:780-782.
14. Kienle H, Kienle GS, von Schön-Angerer T. Failure to exclude false negative bias: A fundamental flaw in the trial of Shang et al. *J Altern Complement Med* 2005;11:783.
15. Shang PD, et al. Carelessness, collusion, or conspiracy? *J Altern Complement Med* 2005;11:779-780.
16. Ludtke R, Rutten ALB. The conclusions on the effectiveness of homeopathy highly depend on the set of analyzed trials. *J Clin Epidemiol* 2008;61:1197-1204.
17. Rutten ALB, Stolper CF. The 2005 meta-analysis: The importance of post-publication data. *Homeopathy* 2008;97:169-177.
18. Moher D, Cook DJ, Eastwood S, et al. Improving the quality of reports of meta-analyses of randomised controlled trials: The QUOROM statement. *Quality of Reporting of Meta-analyses*. *Lancet* 1999;354:1896-1900.
19. Ernst E. A systematic review of systematic reviews of homeopathy. *Br J Clin Pharmacol* 2002;54:577-582.
20. Altnuc U, Pittler MH, Ernst E. Homeopathy for childhood and adolescence ailments: Systematic review of randomized clinical trials. *Mayo Clin Proc* 2007;82:69-75.
21. Spence D, Thompson E, Barron S. Homeopathic treatment for chronic disease: A 6-year university hospital-based outpatient observational study. *J Altern Complement Med* 2005;5:793-798.
22. Witt C, Keil T, Selim D, et al. Outcome and cost of homeopathic and conventional treatment strategies: A comparative

- cohort study in patients with chronic disorders. *Complement Ther Med* 2005;134:79–86.
23. Witt CM, Lüdtke R, Baur R, Willich SN. Homeopathic medical practice: Long-term results of a cohort study with 3981 patients. *BMC Public Health* 2005;5:115.
 24. BMJ Clinical Evidence web-site. Online document at: <http://clinicalevidence.bmj.com/ceweb/about/knowledge.jsp> Accessed November 2, 2009.
 25. Fanelli D. How many scientists fabricate and falsify research? A systematic review and meta-analysis of survey data. *PLoS ONE* 2009;4:e5738.
 26. Titus SL, Wells AJ, Rhoades LJ. Repairing research integrity. *Nature* 2008;453:980–982.
 27. Leigh E. A safer place for patients: Learning to improve patient safety. 51st report of session 2005–06 report, together with formal minutes, oral, and written evidence. House of Commons papers 831 2005–06, TSO (The Stationery Office). July 6, 2006.
 28. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients. *JAMA* 1998;279:1200–1205.
 29. Chaplin M. Water structure and behaviour. Regularly updated online document at: www.lsbu.ac.uk/water/ Accessed November 24, 2009.
 30. Samal S, Geckler KE. Unexpected solute aggregation in water on dilution. *Chem Commun* 2001;21:2224–2225.
 31. Elia V, Niccoli M. Thermodynamics of extremely diluted aqueous solutions. *Ann NY Acad Sci* 1999;879:241–248.
 32. Demangeat J-L. NMR water proton relaxation in unheated and heated ultrahigh aqueous dilutions of histamine: Evidence for an air-dependent supramolecular organisation of water. *J Mol Liquids* 2009;144:32–39.
 33. Wolf U, Wolf M, Heusser P, et al. Homeopathic preparations of quartz, sulfur, and copper sulfate assessed by UV-spectroscopy. *Evid Based Complement Alternat Med* 2009; May 27:e-pub ahead of print.
 34. Rey L. Thermoluminescence of ultra-high dilutions of lithium chloride and sodium chloride. *Physica (A)* 2003;323:67–74.
 35. Bell IR, Lewis DA, Brooks AJ, et al. Gas discharge visualisation evaluation of ultramolecular doses of homeopathic medicines under blinded, controlled conditions. *J Altern Complement Med* 2003;9:25–38.
 36. Roy R, Tiller WA, Bell I, Hoover MR. The structure of liquid water: Novel insights from materials research. Potential relevance to homeopathy. *Mat Res Innov* 2005;9:557–608.
 37. Prigogine I, Stengers I. *Order out of Chaos*. London, UK: Fontana, 1985.
 38. Hankey A. Are we close to a theory of energy medicine? *J Altern Complement Med* 2004;10:83–86.
 39. Del Guidice E, Preparata G, Vitiello G. Water as a free-electron dipole laser. *Phys RevLett* 1988;61:1085–1088.
 40. Montagnier L, Aissa J, Ferris S, et al. Electromagnetic signals are produced by aqueous nanostructures derived from bacterial DNA sequences. *Interdiscip Sci Comput Life Sci* 2009;1:81–90.
 41. Vallance AK. Can biological activity be maintained at ultra-high dilution? An overview of homeopathy, evidence, and Bayesian philosophy. *J Altern Complement Med* 1998;4:49–73.
 42. Holmes D, Murray SJ, Perron A, Rail G. Deconstructing the evidence-based discourse in health sciences: Truth, power and fascism. *Int J Evid Based Healthc* 2006;4:180–186.
 43. Rawlins M. De Testimonio: Harveian Oration Delivered to the Royal College of Physicians, London 16th October 2008. Online document at: www.rcplondon.ac.uk/news/news.asp?PR_id_422 Accessed November 1, 2008.
 44. Sikora K. Complementary medicine does help patients. *TimesOnline*, February 3, 2009. Online document at: www.timesonline.co.uk/tol/life_and_style/court_and_social?article5644142.ece Accessed February 18, 2009.
 45. Jobst KA, Shostak D, Whitehouse PJ. Diseases of meaning, manifestations of health, and metaphor. *J Altern Complement Med* 1999;5:495–502.
 46. Smith S. *Not Waving, but Drowning. The Collected Poems of Stevie Smith*. London: Penguin, 1972.

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