

C'mon, CAM



“All who drink of this remedy are cured, except those who die. Thus, it is effective for all but the incurable.” — Galen

“I didn’t say it was good for you,” the king replied. “I said there was nothing like it.” — Lewis Carroll,

Through The Looking Glass

“What I tell you three times is true.” — Lewis Carroll,
The Hunting of the Snark

I’m a fan of Monday night football. A feature introduced in the past year or so has been “c’mom, man,” showing dramatically bad plays. Increasingly I’ve come to think about so-called “complementary and alternative medicine,” (CAM) this way^{1,2,3,4}. It would make my “c’mom, man” list if I were compiling medicine’s (or perhaps more correctly, society’s) “do-overs.” Why? And is there really nothing currently that might be of interest?

Let’s briefly examine certain recent literature about CAM and rheumatic disease, after which I will expand on my comments and elaborate. Briefly, type II collagen therapy has not emerged as clinically useful, despite a rationale to examine this⁵. *Tripterygium wilfordii* Hook F (the thunder god vine) appeared promising for rheumatic disease and was studied; while there was clinical benefit, side effects and costs precluded development for widespread use^{6,7,8}. Intraarticular botulinum toxin was suggested for refractory pain following knee arthroplasty⁹, and has been reported for tendonitis¹⁰. Antibiotics may indeed have a role for some patients with Chlamydia-induced reactive arthritis¹¹. Clarithromycin helped a patient with adult-onset Still disease¹². Pulsed electrical stimulation remained disappointing for knee osteoarthritis (OA)¹³. Low-intensity ultrasound is being studied for knee OA¹⁴. Yoga^{15,16}, tai chi¹⁷, massage¹⁸, and manipulation¹⁹ may help some patients with OA and back and neck pain. Classic Ayurvedic medicine can be formally studied^{20,21}. Leeches were used for knee OA²², again^{23,24}, and in an unblinded trial. Vitamin C may affect serum uric acid levels²⁵. The most interesting report was of the mechanism of massage therapy²⁶. This examined effects of massage after exercise-induced muscle damage. Massage activated mechanosensory sensors (the mechano-transduction signaling pathways focal adhesion kinase and extracellular

signal-regulated kinase), as might be expected. Massage also potentiated mitochondrial biogenesis signaling, mitigated the rise in nuclear factor κ -B nuclear accumulation caused by exercise-induced muscle trauma, and moderated production of tumor necrosis factor- α , interleukin 6 and heat-shock protein phosphorylation, all reflecting less cellular stress and inflammation and promoting recovery and healing. This offered a biologic explanation and mechanism for clinical effect, and represented a model approach for examining any putative therapy, whether CAM, traditional, mainstream, or non-mainstream. But the therapeutic value of massage remains limited.

C’mom, man. I find these observations underwhelming. They have not been and are not likely to augur “break-through” innovations. At present, I do not consider that diet or other CAM therapies have an important role in the routine management of rheumatic diseases. I think there is less here than meets the eye, as do others^{27,28}.

I had occasion to examine selected abstracts from the 2001 and 2009 scientific sessions of the American College of Rheumatology, which was instructive in this regard: CAM therapies were represented in 14 and 2 abstracts, respectively, those years; by comparison, glucosamine/chondroitin were in 3 and 3, those 2 years; herbs, none; familial Mediterranean fever, 8 and 4; amyloid, 10 and none; stem cells 16 and 2; Kawasaki disease 20 and 4; Behçet disease 28 and 11; Still disease 12 and 3; nanomedicine, 0 and 1; and genes/genomics, 184 and 70. CAM has not been prominent at our scientific meetings³. C’mom, man.

What is CAM? A term I and some others have come to prefer is “non-mainstream” therapies. Thus some CAM treatments will be supported by evidence of safety and efficacy while most will not. For example, sitting in abandoned uranium mines, which was once used to treat arthritis, is a CAM therapy that is unconventional, non-mainstream. Hopefully, and generally, most “mainstream” therapies will be acceptably and demonstrably safe and effective. But there have certainly been routine, mainstream practices that were not supported by evidence or proven safe; these included tonsillectomy and adenoidectomy, certain arthroscopic and back operations, irradiation for acne or ankylosing spondylitis, and iced saline lavage for gastrointestinal bleeds; consider too the recent popularity and use of nonsteroidal antiinflammatory

drugs, now fraught with hazards; and there are others that are evidence-based but eschewed by given cultures (e.g., balneotherapy). Consumption of glucosamine for arthritis became a mainstream therapy but has been shown to be of disappointingly little value. A new, more popular term for all this has become “integrative medicine,” implying use of whichever therapies are supported by scientific evidence — regardless of CAM or conventional origin. I don’t particularly like the terms “complementary” or “alternative,” or even “integrative,” as they tend to euphemize concepts about treatments. Although I prefer the simpler “mainstream” and “non-mainstream” designations, for purposes of this discussion I will abide by convention and largely use “CAM.” Certainly anything offered patients should be proven effective and safe, whether mainstream or not^{1,2,3,4}.

CAM has been through several phases of varying disfavor and favor in the past decades. It wasn’t that long ago that this was all termed “quackery” and dismissed categorically as nonsense. Slowly, many became persuaded that “there are more things in heaven and earth, Horatio, than are dreamt of in your philosophy” (Hamlet 1.v.166), that “to a scientist nothing is incredible” (Michael Crichton), and perceived the growing interest in what came to be called CAM as opening new frontiers in medicine and science, likening this to the starship *Enterprise* exploring the universe. While my own interest in this has waned, I respect the persistent enthusiasm and hope of those colleagues scientifically examining certain CAM therapies. As Camus said, “There is no sun without shadow and it is essential to know the night”; some aspects of this merit selective study. And, when done properly, such investigations may advance our knowledge^{1,2,3,4}.

Contemporary interest in these therapies, I think, reflects more an altered societal perspective and the inadequacies of our current understanding and management of rheumatic and musculoskeletal (and other) chronic diseases — despite our very significant progress — than any inherent value of CAM. I believe, like Bertrand Russell, that “what science cannot tell us, mankind cannot know,” that more and better science will relegate certain CAM therapies to the margins of medicine and/or to history; perhaps some (a few) will be adopted into mainstream medicine^{1,2,3,4}.

There has been a societal paradigm shift in attitudes toward health and healing. Perspectives about complementary and alternative medicine and CAM therapies, particularly for the rheumatic diseases, have changed dramatically. Their usage has exploded, popularity increased, costs risen, and terminology changed. They have become acceptable, credible, and some mainstream. CAM is in vogue, embraced by millions, thriving in the hallowed halls of the National Institutes of Health, and featured in scholarly publications. Data found more annual patient visits to CAM practitioners than to primary care physicians in the United States. In Mexico some patients received up to

19 CAM remedies, discontinued their formal treatment 11 times, visited CAM providers up to 180 times, and spent the equivalent of 1.3 days’ wages on CAM, all in 1 year². The United States spends c. \$34 billion annually on CAM products and practitioners, \$121.92/person/year, accounting for 1.5% of total healthcare expenditure and 11.2% of total out-of-pocket expenditure on healthcare². And all this despite little documentation of clinically important benefit for most of these for the treatment of patients with rheumatic diseases. Hardly the high-value, cost-conscious, evidence-based care to which we now aspire. C’mon, man.

Who uses CAM and why? Most patients do, particularly those with chronic diseases such as RA. There are several reasons for the appeal. Some patients fear conventional medications. Some worry about, or have experienced, problematic adverse effects from medicines. Some find costs daunting. Some have not fared well on routine treatments. Some prefer “natural” or holistic therapies. For others, CAM appeals to their lifestyle. Studies have shown that patients with emotional or psychological distress tend to favor CAM. Some patients like the notion that CAM treatments offer them more control over illness. And for others, CAM connotes a simpler, safer, cheaper approach to managing disease, although this is naive. Cynics might liken the appeal of CAM to Samuel Johnson’s statement about the widower who remarried — “it represents the triumph of hope over experience”^{1,2,3,4}.

Are there CAM therapies that may be of value for patients with rheumatic diseases? Here I list those that could be considered: glucosamine, yoga, tai chi, massage, manipulation, acupuncture, balneotherapy, fish and botanical oils, and minocycline. I use some of these, occasionally, usually adjunctively. I reiterate what I’ve already proposed — I don’t think not recommending these to patients would deprive them of demonstrably clinically important benefit. C’mon, man.

Most physicians today recognize the public interest in CAM. Patients curious about CAM therapies should responsibly discuss this with their physicians, and physicians, regardless of their views, must encourage and participate in this dialogue. All need also remember that just because something is called complementary or alternative that does not necessarily mean it is safe (or inexpensive). Some CAM therapies are dangerous and some have killed patients. Certainly patients should not neglect their regular treatments for CAM therapies^{1,2,3,4}.

I perceive CAM as a challenge and opportunity for us. Its popularity tells us we need to be more sensitive, responsive, and empathetic to our patients and their needs. Patients’ interest in CAM reminds us, too, that we still need to do better to find the causes and cures for rheumatic diseases. “When we believe in magic we have lost our way” (Nietzsche). The answers, I believe, will come from improving our art and our science. And then there no longer will be such a thing as CAM, only good medicine.

“A foreboding I have — maybe ill-placed — of an American in my children’s generation, and my grandchildren’s generation... when, clutching our crystals, our critical faculties in steep declines, unable to distinguish what’s true and what feels good, we slide, almost without noticing, into superstition and darkness... science requires an almost complete openness to all ideas. On the other hand, it requires the most rigorous and uncompromising skepticism.” — Carl Sagan

“When I speak of science, I refer not to the work of a group of people with special training but to a habit of thought that refuses to accept any propositions about the natural world without objective and verifiable evidence.”

— Marcia Angell, MD

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