Chelation Therapy for Vascular Disease

To the Editor:

The review of chelation therapy for vascular disease by Ernst1 was flawed because of important omissions and inaccuracies. By omitting a discussion of the critiques of the studies he presented, which have been published in several journals,2,3 the author cannot convincingly conclude that those studies were “of out-standing methodological rigor.” By ignoring a vast body of literature4,5 that documents multiple mechanisms of action for EDTA on the vascular system, he has no basis to say that proponents of chelation therapy are “in overt discordance with our present knowledge.” By reporting on a few isolated incidences of adverse effects, he erroneously implies that chelation therapy is dangerous.

Both of the studies presented used inappropriate statistical analyses that distorted the fact that the EDTA groups did in fact improve more than the placebo groups, but neither study had enough subjects to draw significant conclusions.

The two Danish reports of the same study did not follow the published protocol6 as they claimed, which is taught to physicians by the medical societies for which we have served as presidents, the American College for Advancement in Medicine and the Great Lakes College of Clinical Medicine. Furthermore, the study was criticized by the Danish Council for Scientific Dishonesty because it was not properly randomized, the code was broken prematurely, and the study had an extremely high dropout rate.

The van Rij study had a much better design but was far too small to have power enough to support its conclusions. Only 15 patients were in the treatment group. Both the treatment and the control groups increased walking distance by 60%. After publication, it was discovered7 that the control group had a single outlier that accounted for almost all of the improvement in the placebo group. Without the outlier, the EDTA group clearly improved more than the control group.

The recent edition of Messerli’s textbook, Cardiovascular Drug Therapy,8 devotes an entire chapter to the use of EDTA, demonstrating removal of calcium from coronary arteries. Chelation therapy has also been shown to reduce oxidized LDL, increase the effectiveness of hydroxyl radical scavengers, reduce reperfusion injury, reduce platelet adhesiveness, and result in other beneficial effects.4,5

As long as the protocol is adhered to, EDTA has been shown to be safe,9 especially compared with more conventional cardiovascular treatments.

Not only did Ernst omit important information, he also listed an inaccurate reference for the meta-analysis9 by Chappell and Stahl. The meta-analysis contains reports from thousands of patients with vascular disease who have been successfully treated with EDTA chelation therapy, some of whom were told by cardiologists that there was nothing else that could be done to help them. This alone is sufficient reason to allow patients the option of receiving the therapy, and it should be a compelling reason for adequate clinical trials to be accomplished.

Proponents of chelation therapy and the leadership of our organizations have worked very hard and have spent much of their resources to try to get unbiased, randomized, controlled clinical trials preformed by appropriate researchers.

Fortunately, there are medical schools and governmental agencies in several countries that do not believe that chelation therapy has been fairly or accurately studied. New clinical trials have been planned, and hopefully they will have commenced by the time this letter is published.

L. Terry Chappell
Bluffton, Ohio

John Wilson
Asheville, NC


Response

Chappell and Wilson have misunderstood my article1 and the methodology of systematic reviews (SRs). SRs represent the attempt to objectively evaluate the evidence on a given subject. They follow a stepwise procedure of (1) identifying all trials fulfilling predefined inclusion/exclusion criteria, (2) critically evaluating all reports, and (3) drawing conclusions from the overall results (eg, Reference 2). Thus, my SR followed a protocol described in its Methods section. I also invited national organizations of chelation therapy to contribute material. “Studies were admitted . . . if they related to randomized, placebo-controlled, double-blind clinical trials.” The evidence cited by Chappell and Wilson does not stem from controlled clinical trials and was thus excluded. The trials included in my SR are “of outstanding quality” in that they are randomized, placebo-controlled, and double-blind, thus minimizing various sources of bias. Collectively, their results are dimensions more reliable than the evidence quoted by Chappell and Wilson. Regardless of what Chappell (president-elect of the American College for Advancement in Medicine, an organization that promotes chelation therapy and sponsors the Journal of Advanced Medicine, which published his “meta-analysis”)10 and Wilson state, chelation therapy is not based on good science.

A perhaps more important point relates to a repetitive pattern in the scientific investigation of “bogus” therapies. Proponents first manage to mobilize supporters to campaign in their favor. This brings financial gain. When skeptics ask about the evidence, the burden of proof is swiftly put on their shoulders, and the lack of evidence is made to look like a “conspiracy” of orthodoxy against the alternative. If scientists then decide to rigorously test the method, its proponents would celebrate this as a breakthrough for their method. Again, this amounts to financial gain. Subse-
Assessment of LV Mass by Echocardiography

To the Editor:

The data presented by Vasan et al.1 have clear and important implications in the way echocardiographic data should be reported and understood in routine practice because they make it possible to readily identify (hypertensive) patients with a “normal sized” heart in whom left ventricular (LV) mass is truly increased. In addition, it is likely that these data would help distinguish the dilated and thickened but otherwise healthy heart (so called “athlete from cardiomyopathy”). The general utility of the data, however, would be enhanced by displaying it as shown here in the Figure, which illustrates the relationship between LV mass, LV end-diastolic internal dimension (ID), and combined LV wall thickness, superimposed on the relations between LV mass, LV end-diastolic internal dimension and sum of the left ventricular wall thicknesses [septum plus posterior wall], respectively, using the Penn corrected American Society of Echocardiography deemed normal even though LV hypertrophy would not ordinarily be considered present on the basis of accepted normal values. In contrast, an otherwise healthy but taller individual with an LV ID of 6.0 cm would be recognized as having an LV mass within the 95% CI of normal even in the presence of a combined LV wall thickness of 2.3 cm, which by standard criteria would be reported as LV hypertrophy.

Furthermore, the Framingham data1 also indicate that there is a strong relation between LV ID and wall thickness, so that in general, when LV ID is ≤5.6 cm, LV mass will fall within the 95% confidence limits of normal when the ratio of LV ID to combined wall thickness is >2.7. In subjects with an LV ID >5.6 cm, however, this ratio should be >2.6. This rule of thumb may simplify the distinction between left ventricles with a normal and abnormal mass in the absence of reference tables or charts at the time of reporting.

Mark Nidorf, MBBS, MD, FRACP, FACC
Brendan McQuillan, MBBS
The Queen Elizabeth II Medical Centre
Nedlands, Western Australia

reference value. Thus, one should not interpret LVIDed, LVWT, or LVM, without reference to height and sex.

It should be noted that there is not a strong relation between LVIDed and LVWT. Although the 95th percentile values of LV mass, LVIDed, and LVWT seem to plot along a straight line, this does not suggest a strong relation between LVIDed and LVWT. Framingham data, on the contrary, suggest a very poor correlation of LVIDed and LVWT (r=0.042 [men] and −0.079 [women]).

We greatly appreciate Drs Nidorf and McQuillan’s efforts to increase the utility of our data by prompting us to provide a graphical representation of the relations between LV mass, LVIDed, and combined LVWT. We hope that the figure will enhance efforts to standardize the clinical interpretation of echocardiographic measurements.

Emelia J. Benjamin, MD, ScM
Ramachandran S. Vasan, MD
Martin G. Larson, ScD
Daniel Levy, MD
Jane C. Evans, MPH
National Heart, Lung, and Blood Institute’s Framingham Study
Boston University School of Medicine Framingham, Mass

Evolution, Cholesterol, and Low-Fat Diets
To the Editor:
Steinberg et al1 report that cholesterol, even at levels within the normal range, may cause endothelial dysfunction. This is hardly surprising. From an evolutionary perspective, which enhances the understanding of both human nutritional requirements2 and humankind’s metabolic physiology,3 there is no doubt that current standards for serum cholesterol values fail to match those of today’s hunter-gatherers, “whose experience represents the closest living approximation of ‘natural’ human lipid metabolism.”4 Whereas in Western countries serum cholesterol levels <200 mg/dL are considered “desirable,”4 the mean serum cholesterol level found in 5 hunter-gatherer groups was 123.2 ± 7.2 mg/dL,4 which suggests that the “desirable” level for serum cholesterol concentration is <150 rather than <200 mg/dL.4 This suggestion, notably, is in accord with the results of Steinberg et al.1 However, although these authors correctly point out that their findings have important clinical implications,1 they unfortunately fail to mention the most important recommendation that can easily be inferred from their study, namely, a drastic reduction in the currently widely advocated direction that 30% of energy should be obtained as fat.5 Such a drastic reduction, besides being theoretically well founded on evolutionary grounds,2–5 has been experimentally shown to represent an excellent tool for both lowering cholesterol levels and reversing coronary atherosclerosis.3

In view of the frequently reported association between low serum cholesterol and cancer, some physicians might be reluctant to recommend a substantial reduction in dietary fat. Their worries, however, are clearly unjustified, because no enhanced cancer mortality is seen in populations with low cholesterol levels.2–5 It is evident, therefore, that catabolic diseases cause low cholesterol levels instead of the reverse. On the other hand, it is conceptually untenable that humans can be killed by the same low-fat nutritional environment that both molded their lipid metabolism and kept their cholesterol levels physiologically low for millions of years.2–5

Richard Baschetti, MD
Retired Medical Inspector
Italian State Railways
Padua, Italy

Response
We appreciate Dr Baschetti’s comments in response to our publication in Circulation. The aim of our study was to extend to subjects who exhibit “normal range” cholesterol levels the observation that frankly hypercholesterolemic subjects display endothelial dysfunction. Our article was not intended to lead to nutritional guidelines. Clearly, cholesterol contributes to the development of macrovascular disease, and thus, a left shift in cholesterol levels on a population basis is desirable and should lead to lower rates of cardiovascular mortality. However, one needs to be cautious about assigning any teleologic significance to cholesterol levels achieved by primitive diets. Indeed, life expectancy is higher in industrialized populations compared with hunter-gatherers or populations of underdeveloped countries. Although advances in sanitation and disease prevention are undoubtedly important, it is conceivable that higher cholesterol levels than those exhibited by hunter-gatherer populations may confer some survival benefit. Thus, more research on the overall health consequences of different diets must be performed before we should recommend more drastic changes in the diet of healthy people than those already recommended by the AHA or similar organizations.

Alain D. Baron, MD
Professor of Medicine and Director
Division of Endocrinology and Metabolism
Helmut O. Steinberg, MD
Assistant Professor of Medicine
Indiana University School of Medicine

Marfan Syndrome, Not Marfan’s Syndrome
To the Editor:
I read with interest the case of infantile Marfan syndrome reported by Doroshow, Lin, and Milliken.1 But I wish they would not use the possessive form of Marfan syndrome.

Use of eponyms for diseases is a common practice in medicine. It often conveys a nice sense of historical tribute, by calling diseases by proper names such as names of physicians (for example, Osler-Weber-Rendu disease), patients (for example, Lou Gehrig disease or Christmas disease), or sometimes geographic regions (for example, Silk Route disease). The reason for use of the nonpossessive form is that the person or locale behind the eponym has no proprietary claim on the entity.3

The Council of Biology Editors’ manual4 has been strongest in its position: “It is recommended that the possessive form be eliminated altogether from eponymic terms so that they can be clearly differentiated from true possessives.” Certainly it would seem unnecessary to use the possessive before a sibilant, as in Marfan syndrome or Laennec cirrhosis. Furthermore, one avoids

Marfan Syndrome, Not Marfan’s Syndrome
To the Editor:

goofs such as “Grave’s disease,” “Homan’s sign,” “Wilm’s tumor,” and “Johns Hopkin’s president” when the apostrophe is put in the wrong place. Finally, just imagine how many trees could have been saved by eliminating all the unnecessary apostrophes and s’s.

Tsung O. Cheng, MD
Professor of Medicine
The George Washington University
Washington, DC

Robin W. Doroshow, MD
Associate Chief, Pediatric Cardiology
Henry J. Lin, MD
Division of Medical Genetics
Harbor-UCLA Medical Center
Torrance, Calif


Response

We couldn’t agree more with Dr Cheng and thank him for making the point so eloquently. In fact, our original title was Infantile Marfan Syndrome. Our concerted efforts in that direction failed to dissuade the individual who edited our manuscript from following common, if incorrect, practice.
Chelation Therapy for Vascular Disease
L. Terry Chappell and John Wilson

_Circulation_. 1999;99:164-167
doi: 10.1161/01.CIR.99.1.164

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/99/1/164

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located,
click Request Permissions in the middle column of the Web page under Services. Further information about
this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/