Letters to the Editor must not exceed 400 words in length and may be subject to editing or abridgment. Letters must be limited to three authors and five references. They should not have tables or figures and should relate solely to an article published in Circulation within the preceding 12 weeks. Only some letters will be published. Authors of those selected for publication will receive prepublication proofs, and authors of the article cited in the letter will be invited to reply. Replies must be signed by all authors listed in the original publication.

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 outstanding 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 protocol2 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 discovered3 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,4 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,4 especially compared with more conventional cardiovascular treatments.

Not only did Ernst omit important information, he also listed an inaccurate reference for the meta-analysis5 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 performed 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
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John Wilson
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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”)6 and Wilson state, chelation therapy is not based on good science.7

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-
Initially, a study may prove that the method is ineffective. Proponents now claim that the research was flawed, did not adhere to their protocol, or was wrongly analyzed. The press coverage yet again brings financial gain. This pattern repeats itself with depressing regularity, eg, when laetrile or Di Bella’s cancer cure were promoted. I wonder whether chelation therapists are trying to play a similar game.

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Assessment of LV Mass by Echocardiography
To the Editor:

The data presented by Vasan et al1 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 from cardiomyopathy.

The general utility of the data, however, would be enhanced by displaying it as shown here in the Figure, which illustrates the relations between LV mass, LV end-diastolic internal dimension (ID), and combined LV wall thickness, superimposed on the relation between LV mass, LV end-diastolic internal dimension and combined LV wall thicknesses [septum plus posterior wall], respectively, using the Penn corrected American Society of Echocardiography LVM2. For the Figure, the lower set of symbols (o) represents the 95th percentile values of LV mass in men (height, 0–61") and the upper set (□) represents the 95th percentile values of LV mass in men (height, 61–78") reported in Tables 2 and 3 of the article by Vasan et al. 1

In this way, it is readily seen, for example, that an individual with an LV ID of 5.0 cm who has a combined LV wall thickness of 2.0 cm has an LV mass beyond the 95th percentile range of 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.

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Response

We thank Drs Nidorf and McQuillan for their insightful comments on our work. 1 We have developed a figure to display the relations between LV mass, LVIDed, and LVWT (left ventricular mass, left ventricular internal diameter end diastole, and sum of the left ventricular wall thicknesses [septum plus posterior wall], respectively, using the Penn corrected American Society of Echocardiography LVM2) for the Figure. The lower set of symbols (o) represents the 95th percentile values of LV mass in women (height, 0–72") and the upper set (□) represents the 95th percentile values of LV mass in men (height, 61–78"). To use this figure correctly, it is necessary to locate the intersection of LVIDed with a specific LVWT line (or interpolate); the ordinate is the calculated LV mass. Then it is necessary to compare the calculated LV mass with a sex-specific LVM class.

In this way, it is readily seen, for example, that an individual with an LV ID of 5.0 cm who has a combined LV wall thickness of 2.0 cm has an LV mass beyond the 95th percentile range of 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.

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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.

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Evolution, Cholesterol, and Low-Fat Diets

To the Editor:

Steinberg et al.1 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 standard 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. 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

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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.

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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), or sometimes geographic (for example, Silk Route 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.2

The Council of Biology Editors’ manual3 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
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.

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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.

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