of their relevant pharmacokinetic and pharmacodynamic properties. Furthermore, consideration of factors such as biological variability and dose-response, which express therapeutic action in terms of efficacy as well as toxicity, are in large part poorly defined within the AREDS study design. Characterization of the pharmacologic response to various high-dose vitamin and nutrient administration requires stringent assessment of population-, disease-, and formulation-specific variables that may influence the occurrence of adverse effects in ways not described in the AREDS.

For example, changes in drug disposition with age are characterized by alterations in lean body mass, which influences the volume of distribution and partition coefficients pertinent to fat-soluble vitamins, particularly α-tocopherol. Furthermore, individuals who use vitamin A₁ as a source of beta-carotene should be advised that absorption of vitamin A₁ (retinol) varies considerably depending on the formulation of the preparation as well as the amount of dietary fat an individual typically ingests.² In addition, febrile infections and stress may markedly decrease serum retinol, whereas chronic renal disease may result in significantly elevated serum retinol, requiring the need for an alteration in intake.³

Moreover, the AREDS neglects to discuss assignment of causality, as well as the temporal relationship and outcome of reported adverse events, particularly those noted as “circulatory.” Furthermore, discussion of additive or synergistic effects, either observed or potential, of the AREDS therapy with various prescription and nonprescription products is lacking. The AREDS also does not address the need for continuing surveillance of the safety of vitamin and nutrient therapy for AMD in terms of elucidation of unexpected idiosyncratic reactions, an important yet complex task because of the ease of accessibility of such agents. Additionally, and perhaps of greater significance, it is unknown how the results of ongoing prospective trials of vitamin and nutrient therapy for disorders other than AMD will affect those currently following AREDS recommendations.⁴

Vitamins and nutrients are not only ubiquitous in nature and easily obtained from nourishing diets, they are also aggressively marketed by pharmaceutical companies eager to promote perceived as well as validated claims of health benefit. In addition, the clever marketing strategies of pharmaceutical companies, such as those promoting doses that “exceed AREDS recommendations,” demonstrate the need for clinicians to closely monitor vitamin and nutrient intake. I believe that the AREDS findings are inadequate in the elucidation of clear and concise safety guidelines for entities that are largely unregulated and widely promoted with an array of ingredients, formulations, and equivalency provided for public interpretation.

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**Correction**

Author Name Omitted. In the Clinicopathologic Reports, Case Reports, and Small Case Series article titled “Photodynamic Therapy in Adult-Onset Vitelliform Macular Dystrophy Misdiagnosed as Choroidal Neovascularization,” published in the December issue of the ARCHIVES (2002;120:1761-1763), Gianni Virgili, MD, was omitted and should have been listed in the signature block as the last author.