intake or plasma levels of lutein in our study, although this could be undertaken.

A number of epidemiologic studies have now demonstrated an association between dietary intake or plasma levels of antioxidant vitamins and the risk of atherosclerotic vascular disease. However, large-scale randomized trials to test further for a causal relationship between antioxidant intake and ischemic heart disease have provided conflicting results (2). Although there is plausible biological evidence to suggest antioxidants may prevent the early stages of atherosclerosis, it is unknown as to whether they alter the later processes that produce clinical events. To determine the role of antioxidant vitamins in atherosclerosis, it may be more appropriate to examine the relationship between dietary intake or plasma levels of these vitamins and measures of early atherosclerosis rather than clinical cardiovascular events (3).

Although we remain very interested in investigating antioxidant defenses against lipid peroxidation and novel risk factors for atherosclerosis, we would support the concept that this essential ongoing research should not distract us from efforts to implement more proven preventive strategies (4).

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REFERENCES


Controlling the Effectiveness of Digoxin

In a recent issue of the Journal, Adams, et al. (1) correctly stated that: “taking digoxin did significantly better than those not taking the drug, but the serum concentration did not correlate with outcome.” Nevertheless, they concluded: “These results support the possibility that a lower therapeutic goal for serum digoxin concentration is warranted in patients with heart failure.”

This conclusion is flawed because in individual patients the concentration of digoxin in the serum does not accurately represent the amount of digoxin in the tissues where it works. The digoxin in the serum is only a tiny fraction of the total amount of digoxin in the body. The total amount of digoxin in the body is easy to calculate from the doses administered, and it does correlate with outcome (2–4). Guiding dosage this way allowed high doses of digoxin (15 to 19 μg/kg of lean body weight) to be given to patients after cardiac operations, and the patients recovered rapidly (5,6).

Because serum digoxin concentrations poorly guide dosage and results, contradictions between serum levels and results have been seen by many doctors. Low serum concentrations of digoxin appeared in patients who received therapeutic benefits. In contrast, high serum concentrations of 2.5 ng/ml have been seen in patients who had no signs or symptoms of toxicity.

Dr. Jelliffe published a method for calculating the milligrams of digoxin needed to produce a specific peak total body load of digoxin and to engender a desired therapeutic result (2–4). A safe, effective mean of peak total body digoxin to treat heart failure is 8 to 10 μg/kg of lean body weight. This program is used at the University of Southern California/Los Angeles County Medical Center and at several other hospitals.

Studying the effects of digoxin requires knowing the total amount of digoxin in the body, which controls the amount of digoxin in the tissues where digoxin works.

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REFERENCES


REPLY

We appreciate Dr. Krohn’s interest and comments concerning our analysis. We believe our conclusions as stated in the study are correct. While it is true that the serum digoxin concentration (SDC) is significantly higher than the tissue concentration during the distributive phase of digoxin dosing (6 to 12 h), both the SDC and the amount of drug in the body decline in parallel and are directly related 12 to 24 h post-dose (1). This is the rationale for the recommendation to always draw the SDC as a trough during 6 to 12 h post-dose (1). This was mandated in both the PROVED and RADIANCE protocols.

We agree with Dr. Krohn’s statement that total body stores of digoxin are easy to calculate. Unfortunately, we are unable to do this for each individual patient in these studies. However, the dosing guidelines cited by Dr. Krohn are incorporated into the dosing table that is currently included in the Lanoxin package.