Calcium absorbability

Dear Sir:

The study by Heaney et al (1), "Calcium absorbability from spinach", raises some interesting questions. Dr Heaney is doubtless aware that the Ca-calorie ratio for spinach is 5.4 and for whole milk is 1.94 so that if one were to sort the USDA #72 data base for foods with the highest Ca-calorie ratios, ~10 leafy vegetables (spinach among them) would make the list ahead of milk.

"Calcium absorbability from milk products, an imitation milk, and calcium carbonate" by Recker et al (2) already had reported no difference in absorbability of isotopic Ca added to various liquids, which is not surprising because the absorbability of inorganic Ca could be expected to reflect mainly the pH of its carrier liquid.

Therefore testing the absorption of radiolabelled Ca from spinach grown in the substance relative to the absorption of radiolabeled Ca chloride passively added to milk seems like apples and oranges. Would anyone expect the Ca incorporated into leaf structure and complexed with plant protein to be as readily absorbed as dissociated Ca ions?

One could repeat the experiment in two ways. Radiolabeled $CaCl_2$ could be added to milk and to a homogenate of spinach in which case the differential absorption could be attributed to spinach oxalate binding the Ca. Alternately one could graze the cows on spinach or the fodder of their choice grown in radiolabeled Ca-enriched soil. Milk and spinach would then both be intrinsically labeled and the comparison of Ca absorbability might prove of some value.

One suspects the milk might lose its reported fivefold advantage over spinach.

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Reply to W Harris

Dear Sir:

The radioactive $^{45}CaCl_2$ used as a tracer in absorption experiments is gravimetrically negligible (in the microgram range). Therefore, the chloride cannot accurately be represented as if it were the ionic species in the evaluation of milk calcium absorbability and the pH of its carrier solution does not detectably affect the pH of the labeled product. A Ca tracer is known to exchange very rapidly with the major Ca moieties in the milk (Ca citrate and a Ca phospho-protein complex). So far as we now know, both become uniformly labeled after extrinsic addition of a tracer. This conclusion is supported by extensive experience with absorption studies on mixed-food diets with the traditional balance method. We find that food Ca (most of it derived from milk and cheese) has about the same absorbability as tracer-labeled milk Ca. Thus, by both balance and direct tracer methods, milk calcium absorption ends up being in the range of 25–35% in normal persons. I have little doubt that milk will retain this five- to sixfold advantage over spinach no matter how one looks at it.

I quite agree that green leafy vegetables constitute a better bargain in terms of Ca-calorie ratio. Bok choy is probably the leader here at ~1800 mg Ca/100 kcal. Still, you stack the deck against milk when you use whole milk as the referent. (Skim milk is ~350 mg/100 kcal and whole milk is 194.) Spinach remains a clear exception among the green leafy vegetables. Conventional wisdom attributes the poor absorptive performance of spinach Ca to the oxalate it contains but we are testing this point now and will know more later.

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Reproducibility of individual serum cholesterol response to diet

Dear Sir:

The paper of Grundy and Vega (1) provided a valuable addition to our knowledge about differences between individuals in the response of serum cholesterol to dietary saturated fatty acids. They observed that certain individuals showed only small responses (hyporesponders) whereas others developed high degrees of hypercholesterolemia (hyperresponders). We would, however, like to insert a note of caution. If a subject's response is studied in one trial only—even if it is a trial using control diets and multiple measurements as employed by Grundy and

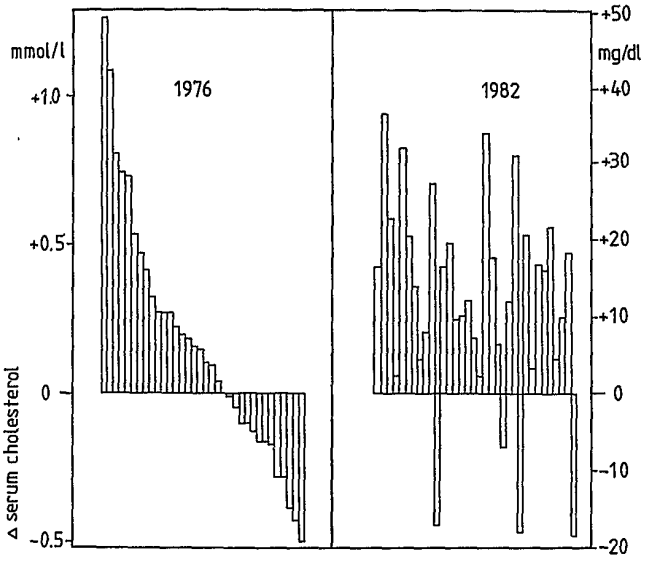

FIG 1. Individual cholesterolemic response to cessation of egg consumption in 32 subjects in a trial in 1976 and in another similar trial in 1982. Positive values indicate a decrease and negative values indicate an increase in serum cholesterol after removal of eggs from the diet. Subjects were ranked by their response in the first trial. Based on data from Beynen and Katan (3).

Vega (1)—then one tends to overestimate the true extent of differences in response between subjects. In the study by Grundy and Vega (1), the reproducibility of the individual cholesterolemic response is not known. In our experience such observed between-person variation could be explained, at least partly, by random within-person fluctuations in the level of serum cholesterol. The variability observed in single short-term experiments by itself does not prove the existence of hyporesponders and hyperresponders.

In three controlled dietary trials that we carried out with the same subjects to address the question whether individuals would exist with a consistently high or low serum cholesterol response to dietary cholesterol (2), the response in each subject was found to be only partly reproducible. Standardized regression coefficients for individual responses in two experiments ranged from 0.34 to 0.53 ($n = 32$). Under less controlled conditions we obtained similar results. The serum cholesterol response to cessation of egg consumption in subjects who habitually consumed at least one egg per day was studied twice in the same subjects, the interval between both studies being 6 y (3). The individual responses, although positively correlated ($r = 0.32$, $n = 34$, $p < 0.05$) were poorly reproducible (**Fig 1**). In the controlled studies (2) the within-person error variance was found to be responsible for ~25% of the apparent variance in response between subjects even if 12 independent blood samples were used to determine each person's response to dietary cholesterol.

A change in the nature of the fat in the diet can influence the serum cholesterol concentration more markedly than a change in the amount of dietary cholesterol can. It could be suggested that within-person variations in the level of serum cholesterol do not greatly inflate the between-person variation in the response of serum cholesterol to substitution of polyunsaturated for saturated fatty acids. However, recent reanalyses of two large series of experiments speak against this suggestion.

Jacobs et al (4) reanalyzed data from some of the classical dietary trials performed between 1963 and 1966 by Keys, Grande, and Anderson in Minnesota. In these experiments the amount of cholesterol and the type of fat in the diet varied and at least two serum cholesterol values per dietary period were known. Quantitative statistical data on the consistency of differences in responsiveness between individuals were not given but it was stressed that consistent differences were small. Most of the men showed a responsiveness within 30% of the value predicted by the formula of Keys and only 2 of 58 men could reliably be labeled nonresponder.

We have reanalyzed another series of experiments (5), performed between 1963 and 1972 by Vergroesen et al (6). Like Grundy and Vega (1) these investigators employed liquid-formula diets differing in fatty acid composition and/or fat content. However, 130 of the subjects (82 men and 48 women) participated not in one but in several experiments—on average, three to four. This allowed us to determine whether subjects who appeared to overrespond or not to respond at all did so consistently. It turned out that they did not. The distribution of individual responses had an SD of 0.39 mmol/L for men and 0.25 mmol/L for women. (In the men studied by Grundy and Vega, these standard deviations ranged from 0.44 to 0.59). However, comparison of responses of the same subject in consecutive experiments showed that most of this variation could be explained by random within-subject fluctuations of the serum cholesterol, which had nothing to do with specific sensitivity to diet. Correction of the observed variation in responses in single experiments for the component actually caused by within-subject fluctuations yielded a distribution of true long-term responses of subjects' cholesterol to dietary fatty acid composition that had an SD of only 0.24 mmol/L for men and 0.14 mmol/L for women, which is much less than the figures of 0.39 and 0.25 derived from single experiments.

We agree with Grundy and Vega (1) that medically significant differences in responsiveness to fat-modified diets do exist in men and, we may add, in women. However, reliance on data from only a single experiment per subject will cause one to overestimate of the extent of this variability. Few if any subjects fail entirely to respond to fat-modified diets provided that they are tested long enough to average out individual fluctuations. In addition, the large within-subject variability of the response makes it next to impossible to reliably identify hyporesponders and hyperresponders in a clinical setting.

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Plasma cholesterol responsiveness to saturated fatty acids

Dear Sir:

In a recent issue Drs Grundy and Vega (1) discussed their data on humans on the plasma cholesterol responsiveness to saturated fatty acids. We fully agree with their conclusions and the need for further investigations that are specifically designed to determine the range of responsiveness to dietary saturated fatty acids and the factors responsible for this variation.

We suggest two factors that should be considered in such specifically designed experiments: *1*) The diets should account for the necessary vitamins, minerals, and lineoleic acid to satisfy essential fatty acid requirements irrespective of the type of fat being studied. *2*) The subgroup for saturated fatty acid glycerides must be recognized so that saturates of medium-chain-length fatty acids, such as the kernel oils, are differentiated from long-chain length fatty acids, such as palm, tallow, and hydrogenated vegetable oils. Our classification table (**Table 1**) is enclosed to illustrate the point.

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TABLE 1
Lipid classification table

Saturates		Monounsaturates	Polyunsaturates		
			ω-6		ω-3
Medium chain	Long chain	ω-9 High oleic	High linoleic	GLA oils	High linolenic
C_6–C_{12}	C_{14}–C_{24}	Olive	Corn	Black currant	Linseed
Kernel Oils	Cocoa butter	Canola	Cotton	Borage	Fish oils
Babassu	Dairy fats	Safflower (Hybrid)	Soya	Primrose	Menhaden
Coconut	Lard	Sunflower (Hybrid)	Safflower (Regular)		Salmon
Cohune	Tallow		Sunflower (Regular)		Mackerel
Palm kernel	Palm				Tuna
Tucum	Stearine				Anchovy
MCT oil					
		← Hydrogenation			
		Stearines Shortenings Margarine Salad oils			
		← Long-chain triglycerides →			