Four papers in this issue\textsuperscript{1–4} report the analyses of the associations between dietary and other variables and plasma lipids and lipoproteins in the Lipid Research Clinics (LRC) populations. One paper\textsuperscript{4} reports on the associations between changes in dietary intake and changes in plasma lipids during a modest intervention within these populations. From this set of observations, with varying statistical approaches, a pattern of associations consistent with earlier experimental evidence emerges. These observations reinforce the suggestion of McGill et al.\textsuperscript{5} that, although clear proof of causative relationships among dietary composition, serum lipids, and ischemic heart disease has not been established in free-living human populations, the weight of suggestive evidence in such populations, together with experimental evidence concerning the relationship between change in diet and subsequent change in serum lipids, prevents us from discounting or discarding the lipid hypothesis.

Liu et al.\textsuperscript{6} and later Beaton et al.\textsuperscript{7} have demonstrated the danger of the false negative conclusion with regard to studies of diet-serum lipid relationships. Because there is a wide variation in intake from day to day within the same individual (intraindividual variation) it follows that a 1-day observation, although potentially quite accurate, provides a poor description of that individual's usual intake. It is the usual intake, rather than a particular day's intake, that we expect to influence serum lipids or other biological parameters. When 1-day intake data are used in population analyses, it is to be expected that correlations and regression slopes will be greatly diminished.\textsuperscript{6,7} The absence of a statistically significant relationship may then be interpreted, potentially incorrectly, as implying the absence of biologically significant relationships between the variables.\textsuperscript{5}

In the studies by Beaton et al.,\textsuperscript{7} a further point emerges. The greater the magnitude of the within-individual variation in relation to the between-individual variation, the more likely will it be that these relationships are missed. Phrasing this differently, the greater the ratio of variances, the greater is the ratio of the true relationship to the observed relationship.

Seen in this perspective, the present studies are important and informative. Nevertheless, they must continue to be interpreted with caution.

In data bases such as those collected in the LRC Prevalence Study, involving as they do cross-sectional observations, it is quite possible that the observed relationships are spurious. It is interesting then that both T. Gordon et al.\textsuperscript{1} and Schwartz et al.\textsuperscript{2} observed significant inverse associations between low density lipoprotein cholesterol (LDL-C) and total energy and total carbohydrate intakes among these adults. Since the two papers adopted quite different approaches to data analyses, the likelihood of spurious associations is greatly reduced. It should not be surprising that D. Gordon et al.\textsuperscript{3} failed to see such relationships among individuals seen at the original visit of the Coronary Primary Prevention Trial (CPPT). This cross-sectional data base is appreciably smaller in size, thereby reducing the likelihood of demonstrating relationships. Further, and perhaps more important, the subjects have been preselected on the basis of high plasma cholesterol level; the range of this variable would be greatly reduced in comparison to the Prevalence population, thereby greatly diminishing the likelihood of detecting correlations.

Conversely, D. Gordon et al.\textsuperscript{3} did see relationships between the changes in dietary intake (total fat, total dietary cholesterol, and dietary polyunsaturated fatty acids), and the changes in plasma cholesterol (mainly LDL-C) during a modest
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These relationships were not seen in the cross-sectional analyses of the Prevalence data \(^1\) or the initial visit data of the CPPT. \(^2\) The relationships between LDL-C and total energy and carbohydrate intakes \(^1\), \(^2\) were not seen in the intervention analyses. \(^3\)

Does this imply contradiction? No. The study of Beaton et al., \(^7\) based on similar adult subjects, demonstrated that among the dietary variables included in the present series of papers, the lowest variance ratios existed in total energy, total carbohydrate, total protein, and total fat. The highest ratios existed for variables such as dietary cholesterol (mg/day and mg/1000 kcal) and polyunsaturated to saturated fat (P/S) ratio. In cross-sectional studies it would be particularly difficult to demonstrate relationships with the dietary cholesterol or the P/S ratios. With the more powerful design of a before and after intervention, such relationships might be seen. Because the paper by D. Gordon et al. \(^3\) took into account weight change, the effects of total energy and total carbohydrate (here changes in energy and carbohydrate) might well be lost as a part of the weight effect.

The study of diet-plasma lipid associations in children by Glueck et al. \(^4\) is again suggestive of true biological relationships; although it is somewhat more difficult to interpret this, inconsistencies across age and sex may simply reflect small group sizes or perhaps, also, true age-dependent biological changes in relationships between diet and plasma lipids. It is interesting to note that these authors did see statistically significant relationships for two of the variables with the highest variance ratios (most difficult situation), dietary cholesterol and P/S ratio.

Together, these papers are consistent with the hypothesis that plasma cholesterol, particularly the LDL-C fraction, is influenced by diet. Clearly they do not prove the hypothesis. The reader is cautioned to avoid making any inference about the relative strengths of the associations with individual dietary variables without first recognizing that the ratio of within-individual to between-individual variances differs among the nutrient variables. The same caution is expressed in comparing the apparent strengths of associations with variables such as weight and Quetelet Index (weight/height\(^2\)) and those with dietary variables. The former might be expected to have much more favorable variance ratios. As concluded by Schwarz et al. \(^2\) it is a recognition of the problems of the dietary methodology, and their expected effect on statistical relationships, that makes the demonstration of even the low order relationships in these papers particularly noteworthy.

References


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Diet-plasma lipid relationships within a free-living population.

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