between the treatment groups was attributable to the pharmacologic effect of orlistat on the absorption of dietary fat rather than to an aversive effect that drove the dietary fat intake of the orlistat-treated patients below that of the placebo group. However, it is possible that avoidance of gastrointestinal side effects could play a role in controlling consumption of dietary fat in excess of the recommended 30%.

We agree that weight loss without the use of medication would be optimal. In clinical practice, however, some patients cannot achieve and most patients cannot sustain long-term weight loss. Orlistat is intended for use as an adjunct to a program of diet and exercise. It is not meant to take the place of a program of lifestyle and behavioral changes. Whereas the difference in weight loss maintained between the placebo and orlistat groups appears modest, previously published studies of orlistat use showed that small weight losses can be clinically significant in preventing relapse of obesity-related complications (4, 5). Furthermore, categorical analysis of the percentage of patients who lost >10% of initial body weight with orlistat shows that, as with many drugs, some patients do extremely well, whereas others may not (5). In clinical practice, for example, we do not continue to give an antihypertensive agent that does not lower blood pressure; additional or alternative treatment options are considered. We suspect the same will be true of antiobesity agents, including orlistat; patients who are successful will continue to use them, and those who are not may require additional counseling, dietary advice, or therapies. Last, although there is great value in identifying factors related to successful weight management, one should cautiously compare the 30-kg weight loss sustained over 5 y in the cohort of patients enrolled in the National Weight Control Registry (6) with other obesity treatments because the former is a self-selected population whose experience may not be typical of that of most obese adults.

Obesity is a disorder of overnutrition. There are no data that we are aware of to support the suggestion that consuming a diet containing 30% fat coupled with lipase inhibition to block the absorption of one-third of dietary fat energy is different from simply consuming a diet that is ≈20–25% fat with respect to the micronutrient content or fat-soluble vitamin contents. Diets containing similar amounts of dietary fat have not been shown to produce micronutrient or vitamin deficiencies (7).

Finally, we concur with McCarthy that there is a need for further research regarding satiety. We also agree that there are many areas of future research that could potentially improve the long-term efficacy of obesity treatment, including the extent to which orlistat therapy may act as a deterrent to dietary fat consumption in some patients, interactions between dietary intake and exercise, and existing and future pharmacologic options.

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References


Protein, fat, and ischemic heart disease

Dear Sir:

Hu et al (1) write that “a high dietary protein intake is often accompanied by increases in saturated fat and cholesterol intakes.” The statement has an interesting logic. Either it is correct, and their finding that a high protein intake correlates with reduced risk of ischemic heart disease contradicts the connection of dietary saturated fat to this disease, or it is not correct. This puzzle has a simple solution: the connection between dietary saturated fat and ischemic heart disease does not exist (2).

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References


Reply to OH Holmqvist

As shown in Table 1 of our article (1), protein intake, especially animal protein, is positively associated with saturated fat because major sources of protein such as red meat also contain high amounts of saturated fat. Therefore, our multivariate analyses
controlled for saturated fat intake. We previously published results on saturated fat intake and risk of coronary heart disease in the Nurses’ Health Study (2). In this study, 5% of energy from saturated fat, compared with an equivalent amount of energy from carbohydrates, was associated with a nonsignificant 17% greater risk of coronary disease (relative risk: 1.17; 95% CI: 0.97, 1.41; \( P = 0.10 \)). In metabolic studies, replacing carbohydrates with saturated fat increases not only plasma LDL cholesterol, but also HDL cholesterol (3). The weak effect observed in prospective studies is consistent with the possibility that the proportional increase in plasma HDL-cholesterol concentrations produced by saturated fatty acids largely compensates for the adverse effects of these fatty acids on LDL concentrations.

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REFERENCES

Animal protein and ischemic heart disease

Dear Sir:

The important paper by Hu et al (1) on findings from the Nurses’ Health Study (NHS) deserves comment, especially now that these findings have been publicized in the popular media (2). In my opinion, several highly questionable interpretations of the data have been made. The study by Hu et al purports to show, in contrast with previous evidence, that increased consumption of animal protein is associated with decreased risk of ischemic heart disease (IHD), although this observation is only marginally significant.

The importance of this paper can hardly be overemphasized. It not only reports evidence mostly contrary to the existing literature, but also reveals an important shortcoming of this widely reported study, both in the experimental design and in the method of analysis. Dietary protein (as quintile means) ranged from 14.7% to 24.0% of energy and an overwhelming 80% of this protein was from animal sources; these findings suggest the consumption of a virtually carnivorous diet. This becomes even more evident in view of the relatively high intake of total fat (36–41% of energy, as quintile means) and the very low intake of fruit and vegetables and dietary fiber of the study cohort. Even the intake of protein in the lowest quintile was \( \approx 50\% \) more than recommended (3), perhaps close to 90–100% more than the requirement when the unusually high concentration of high-efficiency animal protein and the statistical construction of the recommended dietary allowances are taken into account.

This dietary experience contrasts sharply with the findings of the original international correlation studies (4, 5) that showed impressive associations between selected dietary factors and chronic degenerative diseases. The contrast between the diets of the cohorts in the international correlation studies and in the NHS can be illustrated by comparing the respective protein-fat associations in these cohorts. The correlation of total fat with animal protein in the international correlation study diets was \( \approx 90–95\% \), whereas in the NHS dietary range, the correlation was small and nonsignificant (\( \approx 15\% \)). Furthermore, both animal fat and animal protein, but not plant fat, were found to be tightly associated with breast cancer in the international correlation studies.

These earlier findings from the international correlation studies suggest that the incidence of chronic degenerative disease was associated with animal-based food consumption over a broad range of intakes—from very low amounts—at the expense of plant-based food consumption, and not necessarily with the consumption of any particular nutrient or nutrient group. The NHS dietary experience, in contrast, differs because of the uniformly high consumption of animal-based foods, thus severely limiting a meaningful investigation of the comprehensive effects either of this food group or of individual foods and related nutrients within this group. As for virtually every other study of Western subjects, the NHS does not permit a discriminating analysis of the diet-disease associations originally observed in the international correlation studies; the necessary range of intake of these foods and their respective nutrients is missing. Not only is the detection of meaningful disease-related associations for individual foods and their indicator nutrients compromised, but the prospect of making paradoxical observations is increased and the investigation of the more comprehensive dietary effects is ignored.

Although the statistical method used in this study is popular and well accepted, it is also based on the highly unlikely assumption that the independent effects of individual nutrients are primarily and comprehensively responsible for the multiplicity of disease outcomes. This method originally was meant for testing the safety and efficacy of pharmaceuticals, not for evaluating the comprehensive effects of multiple dietary and nutritional components. In the study by Hu et al, for example, inclusion of various “known” risk factors in the analytic model cannot eliminate the problem of residual confounding, as is often implied. Also, as shown in Table 4 of the article, the group in the highest quintile of protein intake and at lowest risk for IHD also paradoxically smoked less, consumed less alcohol, exercised more, had lower body mass, and consumed more fruit, vegetables, dark bread, dietary fiber, folate, and polyunsaturated fat but less white bread, sweets, and desserts than the groups who consumed less protein—factors for which significant trends among quintiles of protein intake were seen and which are thought to be protective of IHD. In contrast, the high-protein consumers also had a longer history of hypertension and more family history of IHD, with each factor presumably contributing to increased IHD risk.

Within a dietary range in which one food group so predomi- nates, it makes no sense to me that it is possible to reliably...