Medium-chain triacylglycerols may not raise cholesterol

Dear Sir:

Although medium-chain triacylglycerols (MCTs; 8:0 and 10:0) historically have been considered nonlipemic for most individuals, the report by Asakura et al (1) suggests that MCTs may be hypercholesterolemic in subjects with hypertriglyceridemia. Although the authors emphasized the hypercholesterolemia induced when MCTs progressively replaced corn oil in the carefully manipulated diet of these subjects, an alternative conclusion would be that the removal of dietary linoleic acid (18:2) was the primary cause of the plasma cholesterol elevation. Patients were adapted to a low-fat diet (containing 22% of energy as fat) to a low-fat diet (containing 22% of energy as fat) in which 100% corn oil represented about one-half (12%/22%) of the total fat energy, including ≈8% of energy from 18:2. Progressive replacement of corn oil with MCTs resulted in <2% of energy from 18:2 in the final diet period (estimated as 20% of the intrinsic dietary fat) when 100% MCT was the added fat. This exchange progressively increased total cholesterol and triacylglycerol, with MCTs contributing equally to the elevation in total cholesterol, even though the increase in triacylglycerol was not significant. Thus, MCTs increased cholesterol in apolipoprotein B–rich lipoproteins as dietary 18:2 was reduced from 8% of energy to <2% of energy, the rise in total cholesterol being significant only when all the corn oil was removed. The background carbohydrate and other intrinsic fatty acids were constant and tended not to complicate interpretation here, which was a nice aspect of the study design.

The failure to alter plasma triacylglycerol values in this study likely reflects the fact that high-carbohydrate diets (22% of energy as fat in this case) are hypertriglyceridemic in their own right. Had the total fat provided 30–40% of energy, MCTs might have had a more favorable effect on triacylglycerol. More important is the fact that 18:2 is the principle dietary fatty acid responsible for reducing hepatic fatty acid and triacylglycerol synthesis as well as VLDL secretion induced by carbohydrate, and presumably, induced by MCTs acting like carbohydrate (2). It is well appreciated that 18:2 also can enhance impaired LDL receptor activity (3), and carefully controlled fatty acid exchanges showed that progressive decreases in 18:2 per se raise total cholesterol when diet saturated fatty acids (SFAs) are high but stable, ie, when 18:1 replaces 18:2 (4). In the relative absence of dietary cholesterol, the resulting increase in LDL reflects an overproduction of LDL more than impaired clearance (5). We described these fatty acid interrelations previously in terms of the 18:2 threshold, wherein a specific amount of 18:2 is required to protect against total cholesterol elevation during consumption of SFAs and cholesterol (6).

Examples of these fatty acid interrelations specifically involving MCTs were shown in normolipemic women (7) and hamsters (8). In fact, even when women were fed a low-18:2 diet (3% of energy), MCTs proved less cholesterolemic than a source of longer-chain SFAs (trilaurin). Furthermore, the hamster study found MCTs to be as cholesterol lowering as safflower oil in a cholesterol-free diet when 18:2 intake was adequate at 5% of energy.

Although the current data support the 18:2 threshold concept, they are not definitive because, as is often the case in such experiments, 2 important variables (MCTs and 18:2) were altered simultaneously in opposite directions. Thus, it is not clear which is to blame, rising MCTs or declining 18:2. But substantial evidence would argue the latter is most critical (6). A more definitive design would have kept 18:2 constant at 5–6% of energy and exchanged MCTs for 18:1 or carbohydrate, which are considered neutral. Furthermore, the clinical data cited in support of the cholesterolemic nature of MCTs (9, 10), like the comparison in normolipemic women (7), suffer the same shortcoming as the present study, ie, 18:2 was lower (and below threshold) in the MCT diet period than in the control diet period. The clinically relevant point is that an adequate source of 18:2 needs to be supplied when MCTs, or even carbohydrate, replace other long-chain SFAs and monounsaturated fatty acids (5).

In summary, MCTs should not be considered as SFAs that raise total cholesterol and LDL. Nor do they represent a substitute for 18:2 that will effectively reduce circulating apolipoprotein B–rich lipoproteins in the absence of 18:2.

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REFERENCES


Reply to KC Hayes

Dear Sir:

In our study of medium-chain triacylglycerols (MCTs) in hypertriglyceridemic individuals (1), we were disappointed to find that provision of MCTs as the major source of dietary fat did not lower plasma triacylglycerol concentrations, which was the major objective of the study, and in addition, had the inconvenience of raising plasma cholesterol. Hayes raises the possibility that a low-fat diet (carbohydrate- or MCT-rich) may correct the hypertriglyceridemia provided that an ideal proportion of 18:2 is added to the diet. This is an interesting suggestion that should be tested experimentally in humans no matter how convincing the animal data. Whatever answers one draws from future experiments on these proposed dietary modifications, the bottom line is that MCTs seem useless for the treatment of hyperlipidemia. In contrast, carbohydrate-induced hyperlipidemia, which is a well-known phenomenon that occurs in both healthy persons and in several cases of moderate hypertriglyceridemia, may benefit from Hayes’s interesting proposal because it would likely be circumvented by adding the right amount of 18:2 to a fat-free diet without raising, and probably lowering, plasma cholesterol.

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Hunter-gatherer diets—a shore-based perspective

Dear Sir:

Cordain et al (1) estimated that Paleolithic hunter-gatherers would have consumed as much animal food as possible. I support the inclusion of fish and shellfish in Cordain et al’s estimate of animal food intake because I believe that fish, shellfish, and other shore-based foods were crucial for human brain evolution (2–4). I have 2 comments about the reference values Cordain et al used for plant and animal macronutrient composition.

First, their reference macronutrient values for plant foods were 62% carbohydrate, 24% fat, and 14% protein. The list of food types for which this reference macronutrient profile was obtained did not include vegetables (see Table 3 of reference 1). In commonly available databases of the macronutrient contents of plant foods other than nuts and seeds, the fat content rarely seems to exceed 1% by weight. Does this imply that Cordain et al’s macronutrient database does not really represent most plant foods or, alternatively, that nuts and seeds are interpreted to represent most plant foods consumed? Even if plant foods in the Paleolithic period did contain an average of 24% of energy as fat by proximate analysis, this value needs to be corrected downward by ≈30% to yield the content of actual fatty acids that are available for energy from plant material other than nuts. Was this correction made?

Second, Cordain et al emphasized the risk of protein toxicity by referring extensively to the outcome of the consumption of large amounts of meat containing <5% fat by weight. Lean muscle tissue is 2–3% fat, but animal organs other than muscle, which tend to be 5–10% fat, would also have been consumed. Body fat itself would also have been eaten. Furthermore, hominids would have faced fierce competition from carnivores for the copious amounts of meat needed to be eaten to induce protein toxicity; therefore, protein toxicity probably did not occur often, and certainly not for extended periods.

As Milton’s (5) editorial points out, it makes empirical sense that foods of relatively high nutrient and energy densities would be consumed when available. However, Milton states that “Hunter-gatherers were not free to determine their diets, rather it was their predetermined biological requirements for particular nutrients that constrained their evolution. At the same time, these dietary needs apparently allowed for selection to favor increased brain size in the human lineage and the concomitant development of technologic, social, and other abilities directed at securing these nutrients” (5). Modern humans in a totally free-choice situation ultimately choose a diet that is complete in energy and nutrients. Those who cannot choose freely often develop malnutrition or specific nutrient deficiencies. Many factors, including climate, competition, and food availability would have been constraints affecting the daily or seasonal diet of hunter-gatherers; in that sense they may not have been totally free to determine their diets. However, in my view, it was the discovery of and adaptation to a high-quality shore-based diet that was a major determinant of the rate and extent of human brain evolution, not the other way around as implied by Milton (5).

We argue that the shore-based ecologic niche was uniquely able to stimulate expansion of the primate brain because, in addition to being a plentiful supply of dietary energy and protein, it