

terol-raising saturated fatty acids be interpreted with caution. In 1985 a special committee of the Federation of American Societies for Experimental Biology (FASEB) comprehensively reviewed the health effects of dietary trans fatty acids. Their report concluded that "the *trans* fatty acids as consumed in hydrogenated vegetable oil appear to be the equivalent of oleic acid in their cholesterol-emic properties in humans."<sup>2</sup> Although Mensink and Katan cited this report, they failed to note that the overall conclusions differed completely from theirs.

I point out that Mensink and Katan did not use fat obtained by hydrogenation, as implied. Instead, their fat with high levels of trans fatty acids was catalytically isomerized and not hydrogenated under conditions typical of the manufacture of U.S. margarine and shortening. Although both isomerization and hydrogenation result in the formation of trans and cis positional isomers of monoenes, the distribution of isomers differs substantially. The three most common trans double-bond positions in commercially hydrogenated fats are C10, C11, and C9, in decreasing order of abundance. Also, the distribution of cis monoene isomers was atypical in the study fat. The physiologic effects of the various cis and trans positional isomers are not well understood. The FASEB report noted that "it is essential to consider the effects of *cis* as well as *trans* isomers in interpreting the biologic properties of hydrogenated fats."<sup>2</sup>

The finding of Mensink and Katan that the diet high in trans fatty acids raised total cholesterol levels as compared with the diet high in cis fatty acids is not in agreement with the well-controlled study of Mattson et al.<sup>3</sup> These latter investigators used diets containing cis and trans fats whose fatty-acid compositions were the same except for the presence or absence of trans acids. Furthermore, their study, unlike that of Mensink and Katan, used a fat high in trans fatty acids that was hydrogenated under typical U.S. conditions, and no change was found in total cholesterol levels in the subjects consuming either the diet high in trans fatty acids or the one high in cis fatty acids over a four-week period. These findings are consistent with the FASEB conclusions and other reviews<sup>4,5</sup> that have not found trans fatty acids, as compared with cis fatty acids, to be uniquely hypercholesterolemic in humans.

I also note that the level of trans fatty acids used by Mensink and Katan was about four times higher than that considered typical of the U.S. diet.<sup>2,6</sup> Whether their results are applicable to persons with realistic intakes of trans fatty acids over longer periods remains to be determined. Given the evidence to the contrary,<sup>2</sup> their study does not provide any justification for major changes in U.S. dietary recommendations or in the formulation and labeling of food products.

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4. British Nutrition Foundation Task Force on *Trans* Fatty Acids. *Trans* fatty acids. London: British Nutrition Foundation, 1987.
5. National Research Council, Committee on Diet and Health. Diet and health: implications for reducing chronic disease risk. Washington, D.C.: National Academy Press, 1989.
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*To the Editor:* Recent advances in understanding the effect of nutritional fats on plasma cholesterol\* have called into question the current labeling and promotional practices of companies selling products containing fats. Promotional material now specifies "low

\*Grundy SM. Trans monounsaturated fatty acids and serum cholesterol levels. *N Engl J Med* 1990; 323:480-1.

in saturated fat" as the criterion for acceptable fat composition. But it is now known that not all saturated fatty acids are equally "bad" and not all unsaturated fatty acids are equally "good." Since stearic acid (18:0) is desaturated in the body to oleic acid (18:1), which is neutral with respect to cholesterol levels, and since acids with a chain length of 10 or less have no effect, we need be concerned with only three saturated fatty acids — palmitic acid (16:0), myristic acid (14:0), and (to a lesser extent) lauric acid (12:0). Mensink and Katan have now shown that elaidic acid (trans oleic acid, trans-18:1), which is formed during the hydrogenation of linoleic acid (18:2), has the same effect on serum low-density lipoprotein and high-density lipoprotein cholesterol levels as the cholesterol-raising saturated fatty acids. Given the present level of knowledge, scientifically valid labeling of fats should specify the content of five substances — palmitic, myristic, lauric, and elaidic acids, and cholesterol itself.

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*To the Editor:* The study by Mensink and Katan, in which a diet rich in trans-unsaturated fatty acids was tested for its effect on cholesterolemia, was also (perhaps unintentionally) a comparison of the effects of triglyceride structure.

The authors evaluated the effects of three dietary fats — namely, one rich in oleic acid, one rich in trans-unsaturated fatty acids, and one rich in saturated fatty acids. The methods used in preparing the three fats in this study differed. The oleic acid-rich fat and the saturated fat were both developed by interesterification, whereas the trans fat was not interesterified but mixed. Interesterification randomizes the component fatty acids equally to all three positions of the triglyceride. I and others<sup>1,2</sup> have demonstrated that randomization may have a profound influence on the atherogenic effects of a fat. Mattson et al.<sup>3</sup> found that interesterified trans fat had no hypercholesterolemic effects in humans. Whether the differences in fat preparation in the studies of Mattson et al. and Mensink and Katan could have had any influence on the experimental outcome is not discussed by the latter authors. The influence of the positional distribution of fatty acids on the cholesterolemic effects of dietary fats may be yet another variable that must be addressed in order to understand fully the cholesterol-related effects of fats and oils.

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1. Kritchevsky D, Tepper SA, Vesselinovitch D, Wissler RW. Cholesterol vehicle in experimental atherosclerosis. 13. Randomized peanut oil. *Atherosclerosis* 1973; 17:225-43.
2. Kritchevsky D, Davidson LM, Weight M, Kriek NP, du Plessis JP. Influence of native and randomized peanut oil on lipid metabolism and aortic sudanophilia in the vervet monkey. *Atherosclerosis* 1982; 42:53-8.
3. Mattson FH, Hollenbach EJ, Kligman AM. Effect of hydrogenated fat on the plasma cholesterol and triglyceride levels of man. *Am J Clin Nutr* 1975; 28:726-31.

The above letters were referred to the authors of the article in question, who offer the following reply:

*To the Editor:* We agree with Reeves that the results of a single study can never justify major changes in dietary recommendations or food labeling. Thus, we believe that Garmaise's suggestion that the content of the trans fatty acid elaidic acid be specified on food labels is premature. All the same, for the time being our data do make it appear less desirable for patients with hypercholesterolemia to consume diets high in trans fatty acids.

Reeves mistakenly suggests that our fat high in trans fatty acids was not obtained by hydrogenation. The oil for our study was hydrogenated with a sulfurized-nickel catalyst at a hydrogen pressure of 2 bar (absolute), under conditions that favored the formation of trans rather than saturated fatty acids. The term "isomerized" in our Methods section thus referred to a variety of the usual nickel-hydrogen process through which hydrogenated fats are manufactured in the United States and elsewhere.

Table 1. Distribution of Positional Isomers of Oleic and Elaidic Acid in Five U.S. Margarines and Shortenings and in the Fat High in Trans Fatty Acids in Our Study.\*

POSITION OF DOUBLE BOND	n- $\Delta$	PERCENT TRANS ISOMERS		PERCENT CIS ISOMERS	
		U.S. FATS	STUDY FAT	U.S. FATS	STUDY FAT
12	6	0-1	1	—	—
11	7	1-2	2	—	—
10	8	5-9	10	2-3	27
9	9	9-20†	29†	55-69‡	49‡
8	10	21-25	23	3-8	9
7	11	20-26	21	8-9	8
6	12	11-14	15	9-22	4
5	13	6-14	—	2-3	2
4	14	2-4	—	0-2	1
3	15	1-2	—	0-2	—
2	16	1-2	—	—	—
Total			100		100

\*Data on the five U.S. fats are from Sampugna et al.<sup>1</sup> Values given are the lowest and highest for five samples.

†Elaidic acid.

‡Oleic acid.

Reeves argues that the distribution of positional trans isomers in our fat with high levels of trans fatty acids differed substantially from that in commercial hydrogenated fats. As shown in Table 1, however, the major trans isomers found in U.S. margarines and shortenings<sup>1</sup> were also the major species in our fat. We consider it unlikely that the lowering of serum high-density lipoprotein cholesterol and the elevation of serum low-density lipoprotein cholesterol we found in our subjects would have been caused by our particular mix of isomers only.

As for the study of Mattson et al.,<sup>2</sup> the principal effect of trans fatty acids in our study was on levels of high-density lipoprotein and low-density lipoprotein cholesterol, variables that Mattson et al. did not report. We found an increase in total cholesterol of 10 mg per deciliter (0.26 mmol per liter), whereas Mattson et al. found no effect. Mattson et al. employed a parallel design with groups of 13 and 17 subjects, but did not state the statistical power. Under our conditions such a design would have yielded a 48 percent probability of missing an effect of 10 mg per deciliter through chance fluctuations. Thus, the lack of a significant effect on total cholesterol in the study of Mattson and colleagues may have been due to a lack of statistical power.

Reeves states that the study of Mattson et al., unlike ours, used a fat high in trans fatty acids that was hydrogenated under typical U.S. conditions. In fact, Mattson et al. hydrogenated soybean oil under conditions that maximize the level of trans-monounsaturated fatty acids, and then transesterified nine parts of it randomly with one part safflower-seed oil. This is not a procedure typically used in the production of margarines and shortenings in the United States.

We agree that the intake of trans fatty acids in our study was high. We would expect the response of serum cholesterol to a lower intake of trans fatty acids to be proportionally less, as it is for other fatty acids,<sup>3</sup> but this issue needs further study.

Kritchevsky and coworkers have shown that the atherogenic potential of peanut oil can be decreased by altering its triglyceride structure<sup>4</sup>—i.e., by having fatty acids switch positions on the glycerol backbone of the fat molecules. However, almost all the oleic acid in our diet high in cis fatty acids was derived from nonrandomized sunflower, olive, and rapeseed oils high in oleic acid. Interesterified, fully hydrogenated palm and palm-kernel oil provided only 1.5 percent of the energy in the cis-fatty-acid diet, and none of the energy in the trans-fatty-acid diet. Thus, differences in triglyceride structure cannot explain our findings. Mattson et al. did indeed interesterify their hydrogenated fat with safflower oil, but whether this explains the difference between their results and ours remains to

be established. The evidence that modification of triglyceride structure affects response to dietary fat in humans is not strong, but the issue merits study.

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1. Sampugna J, Pallansch LA, Enig MG, Keeney M. Rapid analysis of *trans* fatty acids on SP-2340 glass capillary columns. *J Chromatogr* 1982; 249:245-55.
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#### DISTAL CORONARY-ARTERY CONSTRICTION IN ANGINA PECTORIS

To the Editor: Pupita et al. (Aug. 23 issue)<sup>1</sup> have sought to explain myocardial ischemia during exercise in patients with stable angina and single coronary-artery occlusion on the basis of a change in the caliber of collateral or distal coronary arteries. They argue against any change in left ventricular load and myocardial oxygen demand on the basis of determinations of the rate-pressure product, using measurements of pressure in the brachial artery. The problem with this approach is that it fails to consider the effects of exercise and vasoactive drugs (nitroglycerin and ergonovine) on other systemic arteries, on wave reflection, and on the amplification of systolic pressure between the central and the peripheral arteries.<sup>2,3</sup> The effects of nitroglycerin may be explained on the basis of this drug's effect on ascending aortic impedance<sup>4,5</sup>—an effect that is underestimated in the measurement of systolic pressure in a peripheral artery.<sup>6</sup> The authors may be correct in their major conclusions, but they are wrong in assuming that systolic pressure is the same in the brachial artery and the ascending aorta under different conditions, and that myocardial oxygen requirements can be determined accurately from recordings of peripheral blood pressure.

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1. Pupita G, Maseri A, Kaski JC, et al. Myocardial ischemia caused by distal coronary-artery constriction in stable angina pectoris. *N Engl J Med* 1990; 323:514-20.
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5. Fitchett DH, Simkus GJ, Beaudry JP, Marpole DGF. Reflected pressure waves in the ascending aorta: effect of glyceryl trinitrate. *Cardiovasc Res* 1988; 22:494-500.
6. Kelly RP, Gibbs HH, O'Rourke MF, et al. Nitroglycerin has more favourable effects on left ventricular afterload than apparent from measurement of pressure in a peripheral artery. *Eur Heart J* 1990; 11:138-44.

The above letter was referred to the authors of the article in question, who offer the following reply:

To the Editor: Dr. O'Rourke argues that aortic pressure may differ from brachial-artery pressure after exercise or the administration of vasoactive drugs. We agree with him. However, we did not attempt