

## Trans Fatty Acids and Plasma Lipoproteins

*Editorial Note: Information released on November 17, 1999, stated that the United States Food and Drug Administration (FDA) has proposed new rules for trans fatty acids in nutrition labeling, nutrient content claims, and health claims. A comment period was established to allow interested parties to make clear their concerns and observations regarding the proposed rule. This comment period was extended to April 17, 2000, owing to the number of people interested in submitting comments and the amount of time they require to do so. The new rule proposes to require including trans fatty acids in the Nutrition Facts panel of foods containing greater than 0.5 grams trans fat per serving. On the Nutrition Facts panel, after the heading "Saturated fat," a symbol such as an asterisk will alert consumers to a footnote stating that the product "\*Includes \_\_\_ g trans fat." If a food contains less than 0.5 grams trans fat, such labeling will be optional because analytical methods cannot reliably measure lower levels. The FDA has also proposed specific limits as to the nutrient content or health claims that can be made on food items that contain trans fat.*

Perceptions of the health effects of trans fatty acids, particularly in the form of margarine, have undergone several changes during the past 10 years. What was once heralded as the healthy alternative to butter now assumes the role of co-conspirator. A new study finds that consumption of trans fatty acids, such as those found in stick margarine and shortening, have negative effects on lipoprotein profiles that are comparable to those of saturated fatty acids. In the prevention and treatment of cardiovascular diseases, therefore, it is recommended that consumers reduce intakes of both saturated and trans fatty acids.

In 10 years trans fatty acids went from a fat generally regarded as safe and possibly beneficial to one considered unfavorable for coronary heart disease risk. Until 1990, conventional wisdom was that trans fatty acids were innocuous, although a few scientists did worry about possible harm.<sup>1,2</sup> However, studies in the 1960s and 1970s by Anderson et al.<sup>3</sup> and Vergroesen (Unilever research laboratory),<sup>4</sup> respectively, showed only a modest cholesterol-elevating effect of partially hydrogenated fats, which are rich in trans, on total serum cholesterol levels, and a study from Mattson et al. (Procter and Gamble)<sup>5</sup> showed no effect at all. Because total cholesterol was considered the major intermediary between dietary fats and coronary heart disease, this seemed to give trans fatty acids a clean bill.

Two papers were instrumental in challenging this view.

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The first one, by Mensink and Katan,<sup>6</sup> showed that the modest rise in cholesterol induced by trans fatty acids concealed a large rise in low-density lipoprotein (LDL) cholesterol combined with a lowering in high-density lipoprotein (HDL) cholesterol. The authors therefore concluded that the effect of trans fatty acids on the serum lipoprotein profile was at least as unfavorable as that of cholesterol-raising saturated fatty acids. The second paper, by Willett and coworkers,<sup>7</sup> reported a positive association between trans fatty acid intake and subsequent coronary heart disease in a large cohort of women and suggested that partially hydrogenating vegetable oils contributed to the occurrence of coronary heart disease.

In 1994, Willett and Ascherio<sup>8</sup> stated the message more forcefully regarding the adverse effects of trans fatty acids by calculating that greater than 30,000 deaths/year in the United States might be due to consumption of partially hydrogenated vegetable fat. This statement caused much controversy even though the calculation was straightforward, and indeed fairly conservative. The only debatable assumption was that the association between low HDL levels and coronary heart disease is causal and that a fall in HDL caused by consumption of trans fatty acids will therefore increase coronary heart disease mortality. Although the evidence for this is less complete than that for changes in LDL, the assumption is plausible: The association between low HDL levels and coronary heart disease is consistent and strong, and drugs that raise HDL lower the incidence of coronary heart disease in randomized clinical trials.<sup>9</sup>

Apart from the dramatic presentation in terms of the number of deaths, the controversy stemmed mostly from the fact that in the United States margarines had long been considered the healthy alternative to butter owing to their lower saturated fat content. Because most U.S. margarines contained a high proportion of trans fatty ac-

ids, however, scientists and health educators—to say nothing of industry—would encounter an about-face if the adverse effects of *trans* were to prove true.

The situation in Europe and elsewhere was somewhat easier. Soft margarines high in polyunsaturated fatty acids had been positioned as heart-healthy in Europe since the late 1960s, but these margarines contained little or no *trans* fatty acids, not because of health concerns but for purely technical reasons. The regular brands of margarine in Europe, however, were often high in *trans* fatty acids derived from partially hydrogenated vegetable and fish oil; these margarines would be affected if consumers rejected foods high in *trans* fatty acids.

Partially hydrogenated edible oils are a major worldwide commodity, and the controversy regarding their health effects spawned a large number of studies. The latest of these is a careful trial by Lichtenstein et al.,<sup>10</sup> who studied the effects of diets with a broad range of *trans* fatty acid content on serum lipoprotein cholesterol levels in 18 women and 18 men. The diets contained 30% of calories from fat, two-thirds of which was either unhydrogenated soybean oil, semiliquid “squeeze” margarine, soft margarine in a tub, stick margarine, or shortening. A diet containing butter served as a reference. The *trans* fatty acid content of the diets ranged from approximately 1% of daily caloric intake in the diets enriched with soybean oil or semiliquid margarine to almost 7% in the stick margarine diet, with intermediate values for the diets containing soft margarine or shortening. The increase in *trans* was balanced by a decrease in polyunsaturated fatty acids, whereas total, saturated, and monounsaturated fats were similar between diets.

The diets were fed in random order for periods of 5 weeks each. This duration was well chosen because although the effects of most fats on blood lipoprotein levels reach a steady state within 2–3 weeks, effects of *trans* fatty acids may require 4 weeks or longer to reach a steady state.

The unhardened soybean oil, margarines, and shortening all decreased total cholesterol levels compared with butter. These decreases, however, included falls in both HDL and LDL. There is increasing evidence that modification of HDL levels will modify the risk of coronary heart disease,<sup>9</sup> such that a fall in cholesterol owing to HDL is likely to increase rather than decrease heart disease risk. The authors<sup>10</sup> therefore calculated the ratio of total cholesterol to HDL cholesterol, which is a more specific predictor of coronary heart disease risk than either total cholesterol or HDL cholesterol alone. This ratio of total cholesterol to HDL cholesterol was unfavorably high for both the butter diet and the stick margarine diet, which was rich in *trans* fatty acids. The lowest values were seen for the soybean oil and semiliquid squeeze margarine diets, with intermediate values for diets containing soft margarine

and shortening. *Trans* fatty acids also caused a small elevation of lipoprotein(a) and an increase in fasting serum triglycerides, which is in line with observations from other studies.<sup>11</sup>

The effects of *trans* fatty acids on blood lipids and lipoproteins form “a sound basis on which to make a strong recommendation to the general public and to food manufacturers to emphasize the use of vegetable oils in their natural state and after minimal hydrogenation,” to quote Lichtenstein et al.<sup>10</sup> This statement forms part of a broadening consensus on the adverse effects of *trans* fatty acids. In turn, the United States Food and Drug Administration has recently been prompted to consider including the amount of *trans* fatty acids in a food on the Nutrition Facts panel of food labels as part of the saturated fat content.<sup>12</sup>

Food manufacturers in Europe, Canada, and elsewhere removed *trans* fatty acids from most of their retail margarines and other retail fats 4–5 years ago when the deleterious effects of *trans* fatty acids first became clear.<sup>13</sup> *Trans*-free margarines are now also available in the United States. Margarines, however, were never the major source of *trans* fatty acids. Perhaps the reason so much attention focused on margarines was that the *trans* findings were in such stark contrast with health claims made earlier on for margarines. The largest dietary source of *trans* fatty acids both in the United States and elsewhere is shortenings.

In 1997, U.S. per capita consumption of fat from margarines was 9.9 lb/year (12 g/day) compared with 20.9 lb/year (26 g/day) from vegetable shortenings.<sup>14</sup> The rapid growth of away-from-home eating will make the difference even larger because shortenings are typically added to the foods that consumers eat “on the go,” such as baked goods and sweets. Vegetable shortenings are also used extensively for deep fat frying in the food service industry. Such shortenings are made from partially hydrogenated vegetable oils, and they contain 11–34% *trans* fatty acids.<sup>15</sup> As a result, a medium-size helping of French fries contains 5–6 grams, a doughnut contains 2 grams, and an ounce of crackers contains 2 grams of *trans* fatty acids.<sup>15</sup> Incidentally, the *trans* fatty acid content of commercial vegetable shortenings is considerably higher than the 9.9% *trans* in the shortening studied by Lichtenstein et al.;<sup>10</sup> a typical commercial shortening would therefore have produced a higher ratio of total cholesterol to HDL cholesterol, similar to that seen with the stick margarine.

Can manufacturers replace these high-*trans* fatty acid shortenings with better fats? Lichtenstein et al.<sup>10</sup> recommended that food manufacturers emphasize the use of vegetable oils in their natural state, but substitution of unhydrogenated for partially hydrogenated oils in cookies, crackers, pastries, and other baked goods degrades mouthfeel and shelf life, and unhydrogenated oils are less stable upon deep fat frying. Technology could probably

overcome these problems, but the investment required is huge. In addition to cost, manufacturers might be reluctant to invest in fast foods with less *trans* fatty acids because, unlike retail margarine, food eaten away from home usually does not carry a nutrition label. Costly efforts to reduce *trans* fatty acid content and improve the health value of fast foods therefore might go unnoticed by consumers and bring no profit to the producer.

Thus there is still a long way to go in replacing *trans* fatty acids with more healthy fats. However, the enterprise is worthwhile because it can have a marked impact on coronary heart disease risk. This is because it requires no effort from the consumer (although a major effort from the producer) and because the largest consumers of foods rich in *trans* fatty acids are often the poor, the young, and the less educated, who have the least healthy lifestyles and are difficult to reach through nutrition education efforts.

What happened in the field of *trans* fatty acids during the past 10 years has implications that go beyond margarines and shortenings. First, it confirmed the strength of the scientific approach to public health controversies. In a plea for the application of rational science to complicated health issues, Borst<sup>16</sup> said, "The greatest strength of the scientific approach is always that it can yield compelling data that are highly counter-intuitive." Ten years ago it seemed highly counterintuitive that partially hydro-

genated soybean oil could be as bad as butter for the lipoprotein risk profile, but compelling data have forced us to rethink the issue, to the benefit of consumer health.

Second, the agreement between findings from scientists around the globe has been remarkable. A Sounding Board paper<sup>17</sup> that accompanied the Lichtenstein et al.<sup>10</sup> paper reviewed the effects of *trans* fatty acids on the LDL:HDL ratio and on the risk of coronary heart disease. As shown in Figure 1, which has been adapted from that paper,<sup>17</sup> the outcomes of studies performed around the world during the past 10 years<sup>6,10,18-24</sup> lie closely around a straight line that relates the intake of *trans* to the elevation of the LDL:HDL ratio. Thus, this type of empirical study can yield results of general validity even though the mechanism through which fatty acids affect blood lipoprotein levels remains unclear.

Finally, entire populations can evidently eat food components that increase disease risk without that being noticed for many years. Foodstuffs are often considered safe and wholesome if large populations have eaten them for a long time without apparent harm, but the validity of this approach has never been critically evaluated. Outcrops of rare diseases will soon catch the eye of an attentive doctor: AIDS was quickly recognized as a new disease because it caused Kaposi's sarcoma, which, until then, was a highly uncommon disease. Factors that increase the occurrence of more common diseases, however, can go

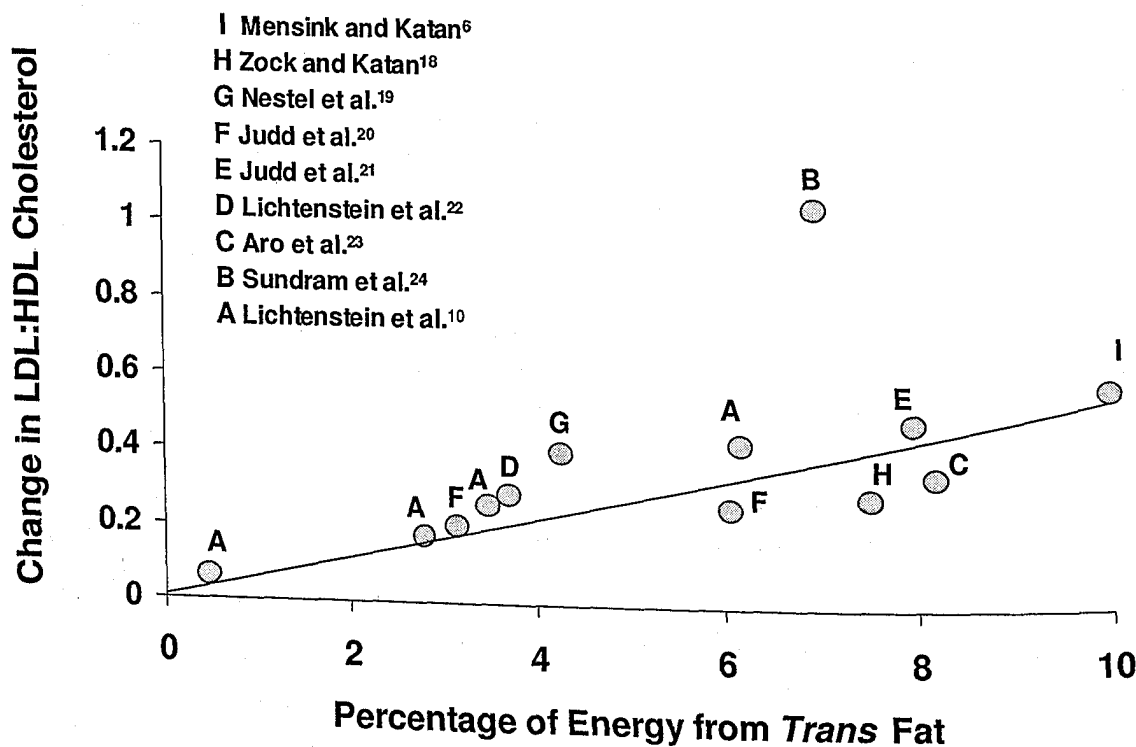


Figure 1. Results of randomized studies of the effects of a diet high in *trans* fatty acids on the ratio of low-density lipoprotein (LDL) cholesterol to high-density lipoprotein (HDL) cholesterol. (In the absence of marked changes in very low-density lipoprotein cholesterol, changes in the LDL:HDL ratio are numerically similar to changes in the ratio of total cholesterol to HDL cholesterol.) The line indicates the best-fit regression, after exclusion of the outlying value of Sundram et al.<sup>24</sup> From reference 17, with permission. Copyright ©1999 Massachusetts Medical Society. All rights reserved.

unrecognized for a long time. The cholesterol-raising factor in coffee beans is an example.<sup>25</sup> Scandinavian populations have long consumed large amounts of boiled coffee rich in cafestol, which markedly raises cholesterol and the risk of coronary heart disease. However, nobody noticed the association between this particular technique of brewing coffee and the risk of coronary heart disease in Finland and Norway until systematic epidemiologic and experimental studies made the conclusion inevitable.<sup>25</sup> The same process happened with partially hydrogenated fats, which have been a major food ingredient for most of the past century.

Only painstaking quantitative research can show us whether a food is healthy. Hard data are also indispensable in order to convince the food industry to change its products, because the investments required are huge and cannot be made frivolously. In the case of *trans* fatty acids, the system has worked, yet there is much to be done.

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