

Trans Fats Judged Major Villain in Cardiovascular Disease

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BOSTON, April 13 - Consumption of trans fatty acids raised lipid levels and increases the risk of coronary heart disease, sudden death from cardiac causes, and possibly diabetes, according to a review article.

The risk of coronary heart disease increased 23%, said the review in the April 13 issue of *New England Journal of Medicine*. Sudden death from a cardiac event was up 47% and tripled when evaluated for certain trans-fat isomers.

In fact, the adverse health effects of trans fatty acids, still dangerously high in the U.S., are far stronger on average than those of food contaminants or pesticide residues, which have received considerably more attention, said Dariush Mozaffarian, M.D., at the Harvard School of Public Health, and colleagues including Walter Willett, M.D., and Meir Stampfer, M.D.

Trans fats, unsaturated fatty acids with at least one double bond in the trans configuration, are formed during the partial hydrogenation of vegetable oils, a process that converts these oils into the semisolid fats found in deep-fried foods, bakery products, packaged snack food, margarines, and crackers, the researchers said.

Findings in the review are as follows:

- **Lipid Levels:** Trans fatty acids have markedly adverse effects on serum lipids. Their consumption raises levels of low-density lipoprotein (LDL) cholesterol, reduces high-density lipoprotein (HDL) cholesterol, and increases the ratio of total cholesterol to HDL cholesterol, a powerful predictor of coronary heart disease risk. Trans fats also increase triglyceride levels, compared with the intake of other fats.
- **Potential Molecular Mechanisms:** Fatty acids are powerful modulators of cell function, altering membrane fluidity and responses of membrane receptors. They appear to affect lipid metabolism, although these mechanisms are not well established. A review of the pathways in which trans fats affect lipid and nonlipid risk factors for coronary heart disease warrants additional investigation.

- **Cardiovascular Disease:** On a per-calorie basis, trans fats appear to increase coronary heart disease risk more than any other micronutrient, conferring a substantially increased risk at levels as low as 1% to 3% of total energy intake. In a meta-analysis of four prospective cohort studies of nearly 140,000 participants, a 2% increase in energy intake from trans fats was linked to a 23% increase in the incidence of coronary heart disease (pooled relative risk 1.23; 95% CI, 1.11 to 1.37; $P < 0.001$).

- **Sudden Death:** A large community-based, case-control study found that levels of trans fats in erythrocyte membranes were associated with an increased risk of sudden cardiac death (odds ratio for interquintile range, 1.47, 95% CI, 1.01 to 2.13, after adjustment for other risk factors).

Further adjustment for levels of other membrane fatty acids found that high trans-18:2 levels (fatty acids with two double bonds in the trans position) were associated with a tripling of sudden death from cardiac causes (interquintile OR 3.95; 95% CI, 1.71 to 5.44).

- **Diabetes:** Here the findings are equivocal. Two of three studies found trans fatty acids were not implicated in diabetes (male health professionals and women in Iowa). However, a third study of 84,941 female nurses followed for 16 years found a positive association ($P < 0.001$ for trend), with a risk 39 percentage points greater in the highest quintile.

Molecular mechanisms that might account for a trans-fat effect in diabetes are not well established, but evidence of trans-fat effects on metabolism in adipocytes and on systemic inflammation suggest plausible pathways, the researchers concluded.

Given the adverse effects of trans fatty acids, the potential for harm is clear, the researchers wrote. On the basis of the reported relationship between trans fat intake and coronary heart disease 10% to 19% of coronary heart disease events in the U.S. could be averted by reducing the intake of trans fats. Given the 1.2 million annual myocardial infarctions and deaths from coronary heart disease in the U.S., near-elimination of trans fats might avert between 72,000 (6%) and 228,000 (19%) of coronary heart disease events each year, Dr. Mozaffarian and his team wrote.

Turning to the issue of consumer food choices and industry's role in producing the dangerous fats, Dr. Mozaffarian noted that the FDA's mandatory specifications for trans-fat content on food labels required

since January 2006 could be helpful but only if consumers read the labels.

What's more, he said, the labels can be misleading. For example, producers of foods that contain less than 500 mg of fatty acids per serving are allowed to list the content as zero on the packaging. But in multiple servings -- several pats of margarine or several cookies a day -- consumers might unwittingly exceed substantial amounts of the trans fats. Furthermore, food labels are rarely seen in restaurants, bakeries, and other retail food outlets.

Overall adverse effects are seen even at low levels of intake: 1% to 3% of total energy intake, or approximately 20 to 60 calories (2g to 7 g) for a person consuming 2,000 calories per day, according to the investigators. "Thus complete or near-complete avoidance of industrially produced trans fats may be necessary to avoid adverse effects and would be prudent to minimize health risks," they said.

Trans-fat intake could also be reduced if food manufacturers and restaurants chose alternatives to partially hydrogenated oils, the team said. Partially hydrogenated vegetable oils are attractive to the food industry because of their long shelf life, stability during deep-frying, and their potential palatability in baked goods and sweets.

Despite concerns that decreasing the use of partially hydrogenated oils would increase the cost of certain foods and reduce their palatability, recent experience in Europe suggests otherwise, the researchers wrote.

For example, in 2004, Denmark mandated that all oils and fats used in locally made or imported products must contain less than 2% industrially produced trans fatty acids. By contrast, the same foods in the U.S. contain 5g to 10 g of trans fatty acids.

In Denmark, the trans fats were replaced with cis unsaturated fatty acids and some saturated fatty acids from tropical oils or fully hydrogenated vegetable oils in certain cookie and bakery products. This move essentially eliminated the use of trans fats in Denmark. Both government and industry representatives agree that the change did not affect the quality, cost, or availability of food, the researchers reported. On the basis of European experience, these fats can be replaced by cis unsaturated fats without increasing the cost or the quality of food, the researchers said.

In Norway, Finland, and The Netherlands, similar cooperative efforts have resulted in substantial

reductions in trans-fat use, they said.

Although the FDA acknowledges the potential harm from consumption of industrially produced trans fats, the agency nevertheless maintains that partially hydrogenated oils are basically safe, Dr. Mozaffarian's team wrote. A petition to the FDA, they said, called for removal of partially hydrogenated oils from the "generally regarded as safe" category. Doing so would effectively eliminate the consumption of industrially produced trans fatty acids in the U.S., the team wrote. Substantial reduction in these oils appears feasible and could be effected through legislation or voluntary efforts by food manufacturers.

The researchers also asked health care providers to advise consumers about how to eliminate these risks by reading labels and making wise food choices, and they suggest that food manufacturers choose to use other fats in food production and preparation.

In summing up, the investigators said, "These steps should help reduce the consumption of trans fatty acids, possibly resulting in substantial health benefits such as averting thousands of coronary heart disease events each year in the United States."

Action Points

When talking with patients about food choices, remind them to read labels looking for trans fatty acids amounts but also to heed the serving amounts stated on the label.

Remind patients that the unhealthy trans fats are found in deep-fried foods, bakery products, packaged snack food, margarines, and crackers, and to try to avoid these foods.

Primary source: New England Journal of Medicine

Source reference:

Dariush Mozaffarian, et al, "[Trans Fatty Acids and Cardiovascular Disease](#)," *New England Journal of Medicine* 2006; 354:1601-1613.