

TRANS-FATS AUGMENTS CORONARY HEART DISEASE---FIND THE RELATION**Dr. Anil Batta***

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ABSTRACT

A large body of data from epidemiologic, clinical trial, animal, and in vitro studies demonstrate adverse consequences of industrially synthesized Trans fatty acids (TFAs) on the risk of coronary heart disease (CHD). A growing database of more recent research from virtually all experimental models demonstrates evidence of detrimental consequences of TFAs on the risk of MI & Diabetes. Evidence is accumulating about the physiological and cellular mechanisms of action that account for the many adverse effects TFAs have on CHD and diabetes. In a relatively short period of time (i.e., from around the early 1990s to the present time, or almost 20 years), we have gained a good understanding of the health effects of TFAs. Trans-fatty acid intake is associated with coronary heart disease (CHD), but the atherogenic potential of individual *trans*-fatty acids (FA) from partially hydrogenated oils (18:1 and 18:2) of dairy products (16:1 and 18:1) is unclear. Incident cases ($n = 48$) of a first nonfatal myocardial infarction (MI) were matched with population controls ($n = 48$) for age, gender and area of residence. Odds ratios (OR) and 95% confidence intervals were calculated from conditional logistic regression models. Total adipose tissue *trans*-fat was positively associated with risk of MI. After adjusting for established risk factors and other confounders, the OR by quintiles of total *trans*-fat were 1.00, 1.34, 2.05, 2.22 and 2.94 (P -test for trend < 0.01). This association was attributed mainly to 18:2 *trans*-FA that were abundant in both adipose tissue and in partially hydrogenated soybean oil, margarines and baked products used by this population; OR = 1.00, 0.96, 2.09, 3.51 and 5.05 (P -test for trend < 0.001). Adipose tissue 16:1 *trans*-FA were also associated with MI; OR = 1.00, 1.57, 1.39, 1.34 and 2.58 (P -test for trend < 0.05). An association with 18:1 *trans*-FA was not detected. High 18:2 *trans*-FA in adipose tissue are associated with increased risk of MI. Because the use of hydrogenated oils is increasing worldwide, the research on TFAs is a good example of how an evidence base has been built and translated into public policy that targets improved health. It is impressive that the TFA research has been coupled to public policy actions to decrease TFAs in the food supply so quickly.

KEY WORDS: Trans fatty acids, MI, CHD, Diabetes.**INTRODUCTION****What are Trans fatty acids?**

Trans unsaturated fatty acids, or *trans* fats, are solid fats produced artificially by heating liquid vegetable oils in the presence of metal catalysts and hydrogen.^[1] This process, partial hydrogenation, causes carbon atoms to bond in a straight configuration and remain in a solid state at room temperature. Naturally-occurring unsaturated fatty acids have carbon atoms that line up in a bent shape, resulting in a liquid state at room temperature.

Which foods contain *trans* fatty acids?

Trans fats are produced commercially in large quantities to harden vegetable oils into shortening and margarine. Food manufacturers also use partial hydrogenation of vegetable oil to destroy some fatty acids, such as linolenic and linoleic acid, which tend to oxidize, causing fat to become rancid with time. The oils used to

cook French fries and other fast food are usually this kind of partially hydrogenated oil, containing *trans* fats. Commercial baked goods frequently include *trans* fats to protect against spoilage. A small amount of *trans* fat is also produced in the gastrointestinal tract of cattle, so that low levels of these isomers are found in dairy and beef fat. Commercial production of partially hydrogenated fats began in the early 20th century and increased steadily until about the 1960s as processed vegetable fats displaced animal fats in the diets of the U.S. and other Western countries. Lower cost was the initial motivation, but health benefits were later claimed for margarine as a replacement for butter. Although the average level of *trans* fat in margarines has declined with the advent of softer versions, per capita consumption of *trans* fatty acids has not changed greatly since the 1960s because of the increased use in commercially-baked products and fast foods.

What are the health effects of *trans* fats?

Concerns have been raised for several decades that consumption of *trans* fatty acids might have contributed to the 20th century epidemic of coronary heart disease.^[2] Metabolic studies have shown that *trans* fats have adverse effects on blood lipid levels--increasing LDL ("bad") cholesterol while decreasing HDL ("good") cholesterol. This combined effect on the ratio of LDL to HDL cholesterol is double that of saturated fatty acids.^[3] *Trans* fats have also been associated with an increased risk of coronary heart disease in epidemiologic studies.^[4] Based on the available metabolic studies, we estimated in a 1994 report that approximately 30,000 premature coronary heart disease deaths annually could be attributable to consumption of *trans* fatty acids.^[4] In response to these reports, a 1995 review sponsored by the food industry concluded that the evidence was insufficient to take action and that further research was needed.^[5] Since that time many more metabolic studies have been conducted and additional prospective epidemiologic studies have been reported. Because of the weight of the evidence, the FDA has recently issued a proposal for including *trans* fatty acid content on the food label. One important issue is whether to list *Trans* fat as a separate constituent or to combine it with saturated fat.

Review

A seminal paper published by Mensink & Katan in 1990 reported that a diet with 10% of energy from TFAs versus a diet with 10% of energy from oleic acid significantly ($P < 0.001$) increased LDL cholesterol (LDL-C) (14 mg/dL) and significantly lowered ($P < 0.001$) HDL cholesterol (HDL-C) (7 mg/dL). Saturated fat (10% of energy) also increased LDL-C (18 mg/dL), but had no effect on HDL-C compared with oleic acid. The authors concluded that the effect of TFAs on the serum lipoprotein profile is at least as unfavorable as that of the cholesterol-raising saturated fatty acids (SFAs) because of their similar LDL-C raising effects. Moreover, TFAs may be more detrimental because they also lower HDL-C versus SFAs. Soon after Willett and colleagues in 1993 published the results from the Nurses' Health Study of 85,095 women without diagnosed CHD, stroke, diabetes, or hypercholesterolemia at the start of the study, and reported that the intake of TFA isomers was related to the risk of CHD after 8 years of follow-up. Using the Willett food frequency questionnaire, the authors reported that TFAs increased relative risk (highest versus lowest quintile was 1.50 [95% confidence interval: 1.12–2.00], P for trend = 0.001). The authors concluded that the consumption of partially hydrogenated vegetable oils may contribute to occurrence of CHD. In an early review evaluating the scientific evidence on TFAs and CHD (Alison et al 1993), data supporting a relation between TFA intake and CHD risk were considered equivocal on the basis of results reported from observational studies. In a position paper on TFAs published by the American society of clinical nutrition in 1996, the authors noted, based on the

state of the science to date, that it cannot be concluded that the intake of TFAs is a risk factor for CHD. Before making any new dietary recommendations or changes in nutrition policy concerning TFAs, the position paper concluded that data were needed, comparable to that available for SFAs, about the intake of TFAs, their biological effects and associated mechanisms of action, and their relation to disease. Based on the current database available at the time of its publication, the ASCN/AIN position paper on TFAs concluded that it was premature to make new dietary recommendations for the population at large or to change nutrition policy with respect to TFA labeling. The "early" consensus was that the "debate" about TFAs should not detract from the role that SFAs played in CHD risk. Over the next decade, additional epidemiologic studies were published that showed a consistent adverse association of TFAs with increased CHD risk (reviewed by Mojaffarian et al in 1996). In addition, well-controlled, clinical studies were conducted that showed a dose-response relationship between dietary TFAs and LDL-C (Judd et al 2002). Collectively, the clinical studies demonstrated a dose-response relationship between TFA intake and TC/HDL-C (reviewed by Ascherio et al 1996). Meta-analyses evaluated the effects of substituting TFAs for carbohydrate calories and demonstrated an LDL-C raising effect that was similar to SFAs; however, unlike SFAs, TFAs did not raise HDL-C (Mensink et al 2004), resulting in the conclusion that TFAs lower HDL-C compared to SFAs and consequently increase the LDL-C/HDL-C ratio, which is a strong independent risk factor for CVD.

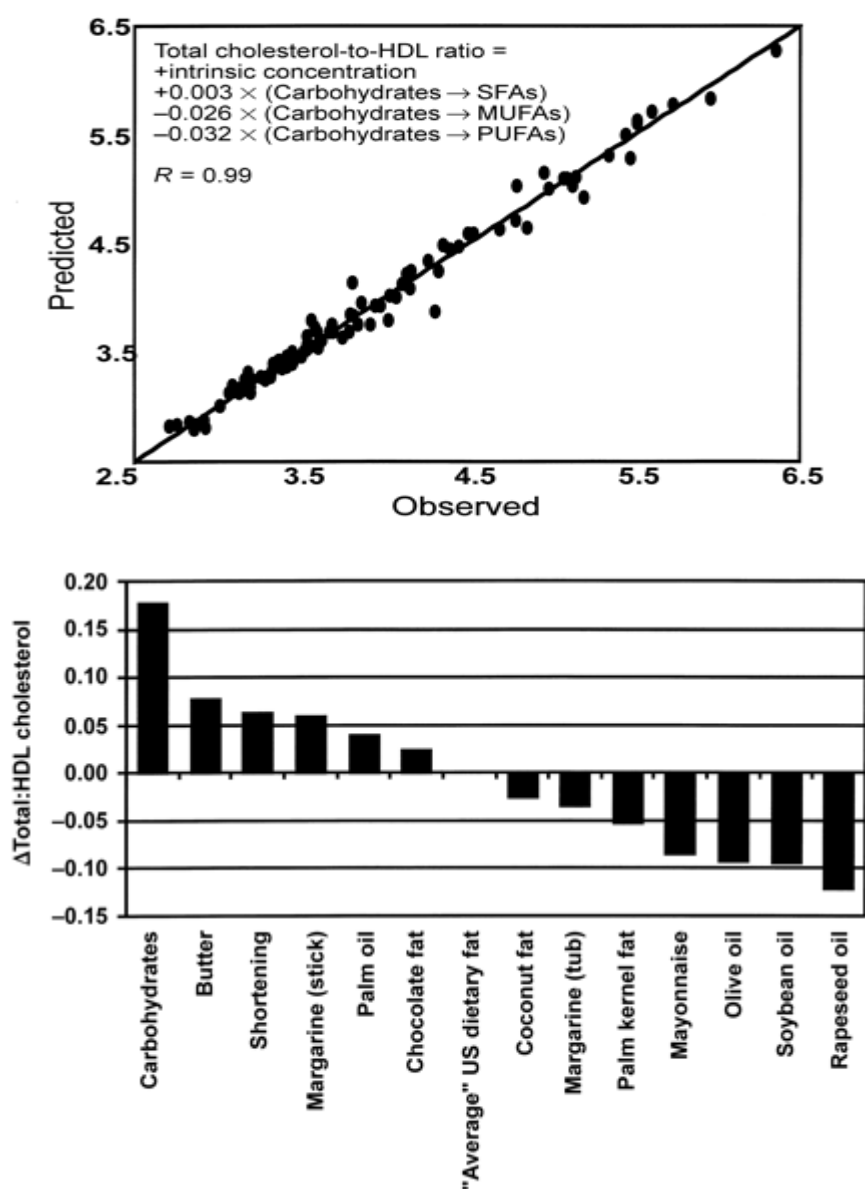
MATERIAL AND METHODS

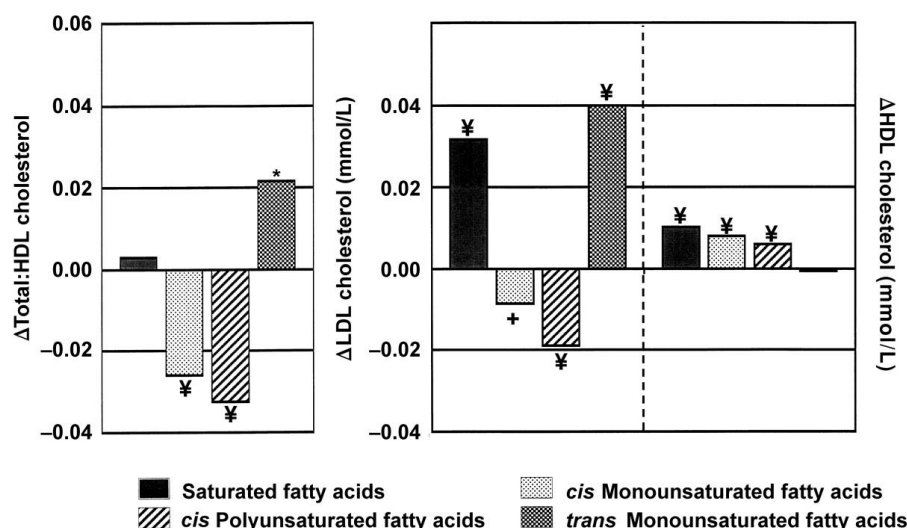
Subjects provided information on socioeconomic, demographic and health characteristics during an interview. The samples were stored at -80°C in deep freezer of Reasearch Lab. Energy and nutrient intakes were assessed with an FFQ developed and validated specifically for use among Faridkot.^[2, 5] Dietary information obtained by the FFQ was used for validation purposes and to assess confounding by dietary factors that do not have good biomarkers of intake such as saturated fat intake. The fatty acid composition of all major types of fat used for cooking in Punjab was determined (Campos, H., unpublished data, 1999–2001) and incorporated into the nutrient calculation. The catchment area for this study was patients coming to GGS Medical College and Hospital that compose patients coming to OPD and IDP of Punjab & their relatives as control. Eligible case subjects were men and women who were diagnosed as survivors of a first acute MI by two independent cardiologists. They were ≥ 55 y old on the day of their first MI, were physically or mentally unable to answer the questionnaire, and had a previous hospital admission related to CVD. Enrollment was carried out while cases were in the hospital's step-down unit. To achieve 100% ascertainment, fieldworkers carried out daily visits to the hospitals. Cases ($n = 53$) were matched by age (± 5 y), sex and area of residence to

population controls ($n = 53$) randomly identified. Therefore, control subjects came from the source population that gave rise to the cases and were unlikely to have undiagnosed CVD due to poor access to medical care. Control subjects were ineligible if they had ever had an MI. All cases and controls were visited in their homes for the collection of dietary and health information, anthropometric measurements and biological specimens. Participation was 97% for cases and 90% for controls. All subjects gave informed consent on documents approved by the ethical Committee.

OBSERVATION

In a relatively short period of time, there has been an impressive evolution of the evidence base demonstrating an adverse relationship between TFA intake and CHD risk. The epidemiologic studies were instrumental in establishing the rationale for conducting well-controlled clinical studies that definitively demonstrated the role that TFA intake played in CHD risk. The proliferation of the evidence base was key for the current actions/policies that have been implemented to decrease TFAs in the food supply. The emerging data on TFA intake and diabetes incidence (Risesus et al 2006) insulin resistance and adiposity (Teegala et al 2009) could reinforce the importance of decreasing TFAs in the diet.





TABLE

Estimated regression coefficients for mean changes (Δ) in serum lipids and lipoproteins when carbohydrates constituting 1% of dietary energy are replaced isoenergetically with saturated fatty acids (SFAs) (Carbohydrates \rightarrow SFAs), *cis* monounsaturated fatty acids (MUFAs) (Carbohydrates \rightarrow MUFAs), or *cis* polyunsaturated fatty acids (PUFAs) (Carbohydrates \rightarrow PUFAs) *I*

Lipid or lipoprotein	No. of diets; no. of studies	Carbohydrates \rightarrow SFAs	Carbohydrates \rightarrow MUFAs	Carbohydrates \rightarrow PUFAs
<i>I</i> 95% CI in parentheses. Apo, apolipoprotein.				
Δ Total:HDL cholesterol	99; 42	0.003 (-0.008, 0.013)	-0.026 (-0.035, -0.017)	-0.032 (-0.042, -0.022)
<i>P</i>		0.613	<0.001	<0.001
Δ Total cholesterol (mmol/L)	114; 47	0.036 (0.029, 0.043)	-0.006 (-0.012, 0.000)	-0.021 (-0.027, -0.015)
<i>P</i>		<0.001	0.061	<0.001
Δ LDL cholesterol (mmol/L)	102; 43	0.032 (0.025, 0.039)	-0.009 (-0.014, -0.003)	-0.019 (-0.025, -0.013)
<i>P</i>		<0.001	0.004	<0.001
Δ HDL cholesterol (mmol/L)	102; 43	0.010 (0.007, 0.013)	0.008 (0.005, 0.011)	0.006 (0.003, 0.009)
<i>P</i>		<0.001	<0.001	<0.001
Δ Triacylglycerol (mmol/L)	110; 45	-0.021 (-0.027, -0.015)	-0.019 (-0.024, -0.014)	-0.026 (-0.031, -0.020)
<i>P</i>		<0.001	<0.001	<0.001
Δ Apo B (mg/L)	57; 23	2.6 (-1.4, 6.5)	-4.8 (-8.1, -1.5)	-7.7 (-11.3, -4.2)
<i>P</i>		0.195	0.006	<0.001
Δ Apo A-I (mg/L)	55; 22	5.7 (2.3, 9.1)	5.2 (2.3, 8.1)	2.2 (-0.9, 5.3)
<i>P</i>		0.002	0.001	0.165

DISCUSSION

We assessed the relationship between adipose tissue *trans*-FA and the risk of MI. We detected a positive association between *trans*-FA and MI. This association was attributed mainly to 18:2 *trans*-FA, which were abundant in both adipose tissue and in partially hydrogenated soybean oil. We did not detect an association between 18:1 *trans*-FA and MI. The association between total adipose tissue *trans*-fat and MI found in our study is consistent with findings from prospective studies that examined this association using intake data from industrialized nations.^[8, 10, and 14] In developed countries *trans*-fat derives mainly from margarines, baked products, fast foods and processed foods.^[9] In contrast, the main source of *trans*-FA in our study was partially hydrogenated soybean oil consumed in homemade meals. Our data suggest a potential positive association between 16:1 *trans*-FA and MI. These data are consistent with previous studies but these early studies did not control for important confounders.^[12, 2, and 3] Only the fifth quintile was associated with MI and the trend was weak. Therefore, it is possible that although we adjusted for confounders, some confounding may have remained because the main sources of 16:1 *trans*-FA are also important sources of saturated fat. More studies are required to confirm this result. Other studies using biomarkers of intake have not found an association between *trans*-FA and CHD,^[12, 13] probably because of small sample sizes.^[6, 8] In studies of diet and CHD, a small sample size limits the ability to adjust for dietary confounders such as *cis*-polyunsaturated FA that tend to be highly correlated with *trans*-FA but have opposite effects on MI. This association remained non significant. Our finding of distinct associations between types of *trans*-FA and MI offers some insight into these apparent discrepancies. It has been postulated that the adverse effects of *trans*-FA may be confined to specific isomers^[13], and some experimental studies suggest that elaidic acid (18:1n-9*t*) may be more harmful than *trans*-vaccenic acid (18:1n-11*t*)^[11]. Consistent with our data, epidemiologic studies have also found that increased RBC 18:2, but not 18:1*trans*-FA is associated with increased risk of primary cardiac arrest^[19]. These differences in risk are difficult to explain because most intervention studies have focused on total or 18:1 *trans*-FA and data on the effects of 18:2 *trans*-FA on plasma lipids are scarce. Interestingly, the MI risk associated with intake of total *trans*-fat observed in epidemiologic studies is substantially higher than what is predicted from its effects on plasma lipoproteins^[9], suggesting that other factors may account for this association, such as lipoprotein[a]^[3-9]. *Trans*-FA can also impair Δ^6 desaturase activity and decrease eicosanoid production.^[1, 9] It is also possible that dietary *trans*-FA may include other isomers with more potent effects than those studied in intervention trials. We compared the levels of adipose tissue 18:1 and 18:2 *trans*-FA in several populations. Adipose tissue *trans*-FA levels varied widely across populations. The highest levels (18:1 and 18:2 *trans*-FA) and higher

variability were found where three prospective studies found an association between total *trans*-fat intake and MI.^[10-13]

CONCLUSION

Five years ago evidence was strong that *trans* fat had deleterious impacts on blood lipids; ensuing studies have confirmed these metabolic findings and strengthened epidemiologic support for an important adverse effect on risk of coronary heart disease. These data highlight the need for rapid implementation of labeling requirements that include fast foods. Because partially hydrogenated fats can be eliminated from the food supply by changes in processing that do not require major efforts in education and behavioral modification, these changes would be an extremely efficient and rapid method for substantially reducing rates of coronary disease.

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