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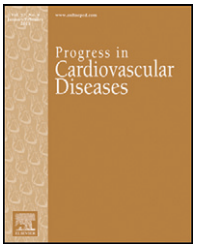

The Evidence for Saturated Fat and for Sugar Related to Coronary Heart Disease

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ABSTRACT

Dietary guidelines continue to recommend restricting intake of saturated fats. This recommendation follows largely from the observation that saturated fats can raise levels of total serum cholesterol (TC), thereby putatively increasing the risk of atherosclerotic coronary heart disease (CHD). However, TC is only modestly associated with CHD, and more important than the total level of cholesterol in the blood may be the number and size of low-density lipoprotein (LDL) particles that contain it. As for saturated fats, these fats are a diverse class of compounds; different fats may have different effects on LDL and on broader CHD risk based on the specific saturated fatty acids (SFAs) they contain. Importantly, though, people eat foods, not isolated fatty acids. Some food sources of SFAs may pose no risk for CHD or possibly even be *protective*. Advice to reduce saturated fat in the diet without regard to nuances about LDL, SFAs, or dietary sources could actually *increase* people's risk of CHD. When saturated fats are replaced with refined carbohydrates, and specifically with added sugars (like sucrose or high fructose corn syrup), the end result is not favorable for heart health. Such replacement leads to changes in LDL, high-density lipoprotein (HDL), and triglycerides that may increase the risk of CHD. Additionally, diets high in sugar may induce many other abnormalities associated with elevated CHD risk, including elevated levels of glucose, insulin, and uric acid, impaired glucose tolerance, insulin and leptin resistance, non-alcoholic fatty liver disease, and altered platelet function. A diet high in added sugars has been found to cause a 3-fold increased risk of death due to cardiovascular disease, but sugars, like saturated fats, are a diverse class of compounds. The monosaccharide, fructose, and fructose-containing sweeteners (e.g., sucrose) produce greater degrees of metabolic abnormalities than does glucose (either isolated as a monomer, or in chains as starch) and may present greater risk of CHD. This paper reviews the evidence linking saturated fats and sugars to CHD, and concludes that the latter is more of a problem than the former. Dietary guidelines should shift focus away from reducing saturated fat, and from replacing saturated fat with carbohydrates, specifically when these carbohydrates are refined. To reduce the burden of CHD, guidelines should focus particularly on reducing intake of concentrated sugars, specifically the fructose-containing sugars like sucrose and high-fructose corn syrup in the form of ultra-processed foods and beverages.

Statement of Conflict of Interest: see page 468.

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Abbreviations and Acronyms

CAD = coronary artery disease

CHD = coronary heart disease

CV = cardiovascular

HDL = high-density lipoprotein

HFCS = high fructose corn syrup

LDL = low-density lipoprotein

MI = myocardial infarction

NAFLD = non-alcoholic fatty liver disease

oxLDL = oxidized low-density lipoprotein

SFA = saturated fatty acids

TC = total serum cholesterol

TG = triglyceride

US = United States

CVD = cardiovascular disease

Background and history

Atherosclerotic coronary heart disease (CHD) is responsible for one in every six deaths in the United States (US).[1] Almost 1 million myocardial infarctions (MIs) occur each year,[1] and approximately 15% of patients die as a result of their event.[1] CHD is also a leading cause of morbidity throughout the developed world, and a substantial driver of health-care related costs.[2]

In trying to limit the global burden of CHD, prevention is a key strategy. Historically, dietary approaches to CHD prevention focused on cholesterol.

The presence of cholesterol in atherosclerotic plaque was first reported in 1843.[3] Subsequent studies in the early part of the 20th century showed that feeding rabbits cholesterol produced atherosclerosis.[4–6] The fact that rabbits are naturally herbivores (never eating cholesterol in their usual diet) made the significance of these experiments uncertain, and while dietary cholesterol intake may exert some effects on serum cholesterol and ultimately atherosclerotic plaques in humans, dietary cholesterol has increasingly become less of a concern for CHD.[7] Other dietary culprits may be of greater concern.

During the 1950s, American scientist Ancel Keys developed a theory of dietary saturated fat as the principal promoter of elevated serum cholesterol and heart disease. Keys' theory was embraced by the American Heart Association (AHA), who in 1961 officially recommended that Americans lower their intake of saturated fat.[8] The theory was also embraced by the US federal government as outlined in its 1977 Dietary Goals.[9]

A competing theory gained less traction than Keys' but nonetheless had its proponents. Around the same time Key's made his case against saturated fat, a British physiologist, John Yudkin, argued that sugar was actually more closely related to CHD incidence and mortality.[10]

In truth, both Yudkin and Keys could find support for their theories in observational studies, partly because people eat foods, not isolated food constituents. Dietary sources of saturated fat are also often dietary sources of sugar and people who eat large amounts of sugar often also eat large amounts of saturated fat.

Today, with more than a half-century of science since Yudkin and Keys developed their theories, there are now ample data to better assess the potential contributions of saturated fat and sugar to CHD. This paper will review the evidence to date, considering basic science, epidemiology, and clinical-trial data pertaining to CHD risk, CHD events, and CHD mortality.

Saturated fat and CHD risk factors

Although the magnitude of the effect likely varies by specific dietary intake and individual susceptibility,[11,12] it is well-accepted that saturated fats can raise blood levels of total cholesterol (TC).[13–15] Since the majority of blood cholesterol is packaged in low-density lipoproteins (LDL), elevations in TC reflect elevations in LDL.[16] LDL is thought to raise the risk of CHD, and LDL is often referred to as "bad cholesterol."

However, LDL is actually a heterogeneous group of particles, and the sum total of all LDL particles considered together is only modestly associated with cardiovascular (CV) risk.[17,18] For instance, the Framingham Heart Study showed that in men over 50 and in women there was no association between elevated TC (which would mostly be packaged in LDL) and CHD.[19]

A consideration with LDL and CHD risk may be particle size and density. Small, dense LDL particles may behave differently than large buoyant ones. Small-dense LDL is more susceptible to oxidation and is pro-atherogenic,[20–22] pro-thrombotic,[23–26] and pro-inflammatory.[27] Conversely large buoyant LDL may be resistant to oxidation and may even be anti-atherogenic.[28] Although the role in particle size in predicting CV events remains controversial, it may not be the total serum level of LDL that matters as much as the relative proportion of small to large particles.

A high concentration of small-dense LDL and a low concentration of large buoyant LDL has been associated with greater CHD risk.[29] In the Quebec Cardiovascular Study, there was a 3-fold increase in CHD risk in individuals with small-dense LDL after adjustment for total LDL concentration, and other lipid fractions.[30]

Randomized trial data suggest that eating saturated fats can decrease small-dense LDL and increase large buoyant LDL.[31] In other words, consumption of saturated fat may favorably shift LDL proportions to be *protective* against CHD—although, admittedly, not all literature supports the benign or protective nature of large buoyant LDL.[32,33]

Regardless, just as LDL is not a single type of particle, saturated fat is not single kind of fat. Saturated fats are a heterogeneous group of compounds; their effects differ based on the specific fatty acids they contain. For example, while the saturated fatty acid (SFA), palmitate, seems to raise levels of LDL, the SFA, stearate, does not.[34]

The metabolic aspects of SFAs are complex and non-uniform but existing evidence suggests that certain SFAs may confer measurable benefits for lipid profiles and CHD risk. For instance, several SFAs enhance the metabolism of high-density lipoprotein (HDL).[34] HDL is often referred to as "good cholesterol" as this cholesterol-containing lipoprotein is associated with lower risk of CHD. In general, the higher the HDL level, and lower the level of non-HDL cholesterol or the TC/HDL ratio, the better.[35–38] In fact, the TC/HDL ratio is a better predictor of CHD risk than TC, LDL alone, or various other lipid makers (e.g., apolipoproteins A-I, A-II and B).[39,40]