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EDITORIAL

The Cholesterol hypothesis: Time for the obituary?

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Abstract

The cholesterol hypothesis links cholesterol intake and blood levels to cardiovascular disease. It has had enormous impact on health care and society during decades, but has little or no scientific backing that is relevant for the human species. Apparently, the hypothesis is false and should be buried.

The historical background to the hypothesis of a causal relationship between the level of serum cholesterol and the development of atherosclerosis began with Rudolf Virchow's description (1856) of the atherosclerotic plaque with its cholesterol deposits. Nikolai Anitchkov's experiment with rabbits in St Petersburg (1913) was a key publication. He fed rabbits with cholesterol from egg yolks and found that they developed atherosclerotic plaques containing cholesterol. When he tried with other animals – carnivores – it was not possible to reproduce the results. They didn't get atherosclerosis.

Two publications by Ancel Keys had a tremendous impact on the general belief of the cholesterol hypothesis. In 1953 he reported that the dietary intake of fat was significantly correlated to the serum cholesterol level and the incidence of cardiovascular death in six countries (1). It appeared very convincing but the problem was that these six countries were selected from all together 22 countries. There was no correlation whatsoever if all the countries were included. The study was obviously a falsification. The other publication came 1986 – the Seven-countries study (2). Keys followed 12000 middle-aged men and recorded their diet and cholesterol values for many years. With statistical maneuvers he “showed” that saturated fat was the culprit.

The idea that cholesterol is dangerous took root with the well-known Framingham study (3). It was found that the cholesterol level had been slightly increased after a heart attack in previously healthy

men. Therefore, it was claimed that high cholesterol was a risk factor for myocardial infarction. Amazingly, very little attention was taken when the 30 years follow-up of the Framingham project was published (4). It turned out that high cholesterol was not a risk factor for men older than 47 years and not for women at all. Further, it was found that more men had died of a heart attack among those whose cholesterol had decreased over the years. The authors wrote:

“For every milligram percent cholesterol had decreased, cardiovascular mortality and total mortality increased by fourteen and eleven percent”.

Other studies have strongly supported this conclusion. Sachdeva and coworkers (5) found that the cholesterol level in patients with acute myocardial infarction was substantially lower than in normal controls at the same age. Al-Mallah and coworkers (6) found lower LDL values in patients with acute myocardial infarction and also that the mortality rate was twice as high among patients with the lowest LDL values.

These studies showed clearly that there is no causal relationship between the cholesterol level in blood and the risk of dying from a myocardial infarction but the so-called cholesterol hypothesis is still alive.

The most momentous arguments for keeping the idea alive are the reported beneficial effects of cholesterol-lowering drugs – the statins. But how valid are the arguments? To answer that question, one must consider the pivotal role powerful drug

companies have increasingly played in relevant research and publications. It has become a “modus operandi” for statin manufactures to plan, carry out, analyze the results of clinical trials and then use professionals to write the articles under the name of well-known academics, so called Key Opinion Leaders (KOLs). As pointed out in the newly published books, *White Coat, Black Hat* (Carl Elliot) and *Medical Research for Hire* (Jill Fisher) many of these trials are accomplished by Contract Research Organizations (CROs). Ghostwriting and Ghost management have been important instruments for marketing drugs.

In an excellent and unmasking article Michel de Lorgeril and Patricia Salen (7) reviewed and discussed the cholesterol-lowering drug trials published before and after the Vioxx affair was disclosed in 2005 (which resulted in new clinical research regulations). Before the Vioxx scandal the dominating part of the published statin trials were highly positive, especially in the secondary prevention trials. After 2005 most studies have been either negative or obviously biased.

A Cochrane study including 14 primary prevention trials with statins was recently published (8). The authors concluded:

“Caution should be taken in prevention with statins for primary prevention among people at low cardiovascular risk”

A population based investigation in Sweden (9) including almost 2 million men and 2 million women found that despite a widespread and increasing utilization of statins during the years 1998 to 2002 there was no correlation to the incidence or mortality of acute myocardial infarction. This is in harmony with the meta-analysis of Ray et al (10) showing no prolongation of life by use of statins in randomized controlled trials involving 65 229 participants.

In summary, we have now an overwhelming amount of scientific data that falsify the cholesterol myth. So, it is time to say goodbye to this old, ill-founded and fallacious lipid hypothesis.

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