Scandinavian Cardiovascular Journal
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713683216

The fallacies of the lipid hypothesis

Uffe Ravnskov

First Published on: 10 July 2008

To cite this Article: Ravnskov, Uffe (2008) 'The fallacies of the lipid hypothesis', Scandinavian Cardiovascular Journal,

To link to this article: DOI: 10.1080/14017430801983082
URL: http://dx.doi.org/10.1080/14017430801983082

Scandinavian Cardiovascular Journal
2008, 1–4, iFirst article

informa
healthcare

REVIEW ARTICLE

The fallacies of the lipid hypothesis

UFFE RAVNSKOV

Magle Stora Kyrkogata 9, 22350 Lund, Sweden

Abstract
Most researchers to-day consider that a high intake of saturated fat and elevated LDL cholesterol are the most important causes of atherosclerosis and coronary heart disease. The lipid hypothesis has dominated cardiovascular research and prevention for almost half a century although the number of contradictory studies may exceed those that are supportive. The harmful influence of a campaign that ignores much of the science extends to medical research, health care, food production and human life. There is an urgent need to draw attention to the most striking contradictions, many of which may be unknown to most doctors and researchers.

Key words: *Cholesterol, saturated fat, cardiovascular disease*

The lipid hypothesis consists of two main postulates. The first says that a high intake of saturated fat raises blood cholesterol and the second that high cholesterol leads to atherosclerosis and cardiovascular disease. The philosopher Karl Popper is usually cited as codifying the principle of falsifiability that scientific theories must meet. The lipid hypothesis conforms to this requirement: if saturated fat promotes cardiovascular disease by raising cholesterol, a high intake should be followed by high total and/or low-density-lipoprotein (LDL) cholesterol and should be associated with an increased risk of achieving cardiovascular disease; a decreased intake should reduce that risk. If high total or LDL cholesterol causes atherosclerosis, people with high cholesterol should be more atherosclerotic and run a greater risk of achieving cardiovascular disease than people with low cholesterol, and a lowering of total and/or LDL cholesterol should lead to regress, or at least to a slower progress of atherosclerosis and to a lower risk of cardiovascular disease. If these outcomes are not found, that is, if saturated fat does not reliably increase cholesterol, if cholesterol does not reliably predict atherosclerosis and cardiovascular disease, the theory must be accepted as false. In the following I shall demonstrate that the postulates have been falsified effectively in many studies.

Saturated fat

According to all official guidelines a diet rich in carbohydrates and poor in fat, in particular saturated fat, is said to be the best non-pharmaceutical way to prevent cardiovascular disease. The main argument against saturated fat is that a high intake raises blood cholesterol. A strong contradiction of this statement is that the lowest cholesterol concentrations ever seen have been measured in African tribes whose diet consists almost entirely of animal food (1). Even if this is considered an exception – in such a complex system, the standards of falsifiability are not absolute – the cholesterol-raising effect cannot be considered highly predictable, because in at least ten recent controlled low-carbohydrate trials, where intakes of saturated fat were 3–7 times higher than the recommended upper limit, total or LDL cholesterol remained unchanged. As the concentration of small dense LDL particles is a stronger risk factor for cardiovascular disease than LDL cholesterol itself it is also a contradiction to the theory that LDL size is inversely associated with intake of saturated fat (2).

Even if a high intake of saturated fat raised cholesterol to any extent in more balanced diets, this is surrogate outcome. The crucial question is whether a high intake leads to cardiovascular disease, but few studies support that notion. At least

Correspondence: Uffe Ravnskov, Magle Stora Kyrkogata 9, S 22350 Lund, Sweden. Tel and Fax: +46 46145022. E-mail: ravnskov@tele2.se

(Received 8 February 2008; accepted 12 February 2008)

ISSN 1401-7431 print/ISSN 1651-2006 online
DOI: 10.1080/14017430801983082

30 cohort and case-control studies including more than 300 000 individuals have found that coronary patients have not eaten more saturated fat before their first heart attack than others (1). More at odds is that in at least seven cohort studies stroke patients had eaten significantly less. There is no support from autopsy studies either: low-consumers are just as atherosclerotic as high-consumers (1), and a meta-analysis of the controlled, randomised dietary clinical trials found no effect of reducing saturated fat, either on coronary morbidity, coronary mortality, or total mortality (1).

High cholesterol

Contrary to the widely held belief among doctors and researchers, there is little evidence that high cholesterol leads to cardiovascular disease. Autopsy studies of individuals who have died from non-medical causes have confirmed Landé and Sperry's observation from 1936 of an absence of an association between total or LDL cholesterol and degree of atherosclerosis, measured before death or immediately after (Figure 1) (2). A few autopsy studies of patients with cardiovascular disease have found a weak association, probably because such studies always include proportionally more patients with familial hypercholesterolaemia. As the latter on average always are more atherosclerotic than others, and as their cholesterol is higher, their inclusion automatically creates an association between cholesterol and atherosclerosis, although, as explained below, their higher degree of atherosclerosis may not be due to their high cholesterol (Figure 2) (3).

Some studies of young and middle-aged men have found high cholesterol to be a risk factor for coronary disease, whereas others have not (4). On

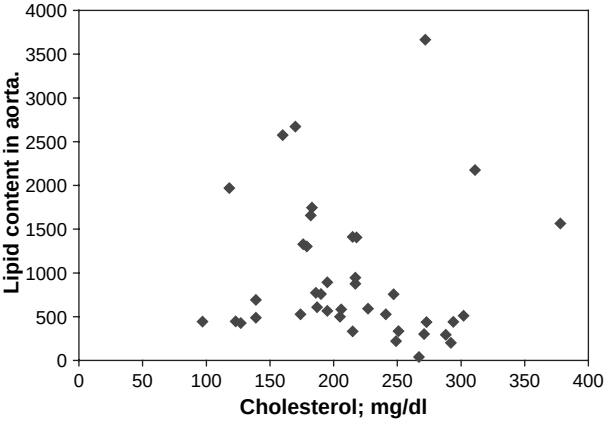

Figure 1. Association between degree of atherosclerosis and total cholesterol concentration in the blood in 40 men and women between 50–69 years, who had died violently without preceding disease. The figure is constructed using data from Landé and Sperry (see ref. 7).

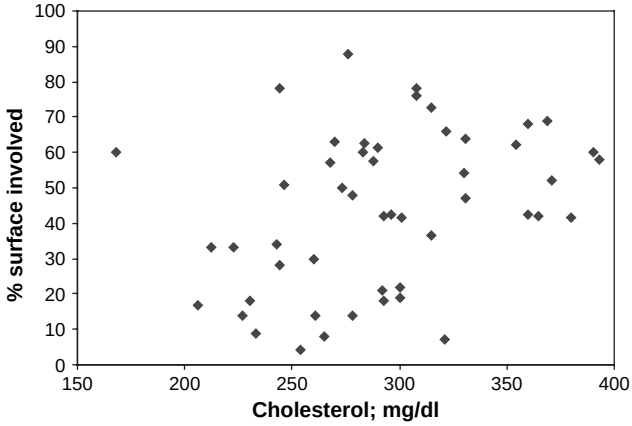

Figure 2. Association between degree of atherosclerosis and total cholesterol at autopsy. It is obvious that the weak association disappears after exclusion of individuals with cholesterol above 350 mg/dl. (9 mmol/l). Redrawn from Solberg et al. (see ref. 7).

the other hand, high cholesterol has not been found to be a risk factor in patients with diabetes (4), patients with established heart disease (3), patients with terminal renal failure, (5) or in women (3), and, most surprising, rarely in old people (6), although at least in Sweden more than 90% of all coronary deaths occur in people above age 65. Also contradictory is that neither the concentration of LDL nor total cholesterol predict the degree of progress of angiographic changes (7), and neither are associated with peripheral atherosclerosis or intermittent claudication (8). In cohorts of people with familial hypercholesterolaemia, LDL or total cholesterol do not predict future coronary heart disease or peripheral atherosclerosis; those with moderately elevated cholesterol run the same risk as those whose cholesterol is 2–3 times higher than the mean value in normal people (9–12). Indeed, in one study those with the highest cholesterol had the lowest risk of heart disease (12). Even Brown and Goldstein were aware of the lack of an association between cholesterol and cardiovascular disease among these people. Thus, in a 1983 paper they wrote: "Among FH patients (both heterozygous and homozygous), there is considerable variation in the rate of progression of atherosclerosis, despite uniformly elevated LDL levels."(13). The explanation may be that other hereditary abnormalities are seen in some of these people, for instance a predisposition to abnormalities of the coagulation system, which is a strong risk factor for coronary heart disease in familial hypercholesterolaemia (14).

Cholesterol lowering does not prevent cardiovascular disease

Meta-analyses of the cholesterol lowering trials before the introduction of the statins found no effect

of cholesterol lowering on heart mortality; indeed, total mortality increased (15). Statin treatment is able to lower heart mortality, but the effect is trivial, it is only present in high-risk, young and middle-age male patients, and the small effect achieved is probably due to the statins′ pleiotropic effects, not to cholesterol lowering, because there is no association between initial cholesterol, or degree of cholesterol lowering, and the clinical or angiographic outcome (3,6).

Unfortunately, the statins have many side effects, such as muscular problems, liver damage, renal failure, depression, amnesia and nerve damage, as well as impotence, abortion and severe birth defects (16–19). According to the reports from the statin trials, all of which have been sponsored by the drug companies, side effects are mild and rare, but underreporting is prevalent. Muscular symptoms for instance are said to occur in less than one percent, but researchers independent on the drug companies have found the frequency to be 64% (20) and 75% (21). This side effect may not only be painful, it also hampers exercising, the most important, the cheapest and the least harmful measure in the prevention of heart disease.

High cholesterol may be beneficial

By 1992, a meta-analysis of 19 cohort studies including more than 600 000 men and women from many countries had found that cholesterol was inversely associated with mortality from respiratory and digestive diseases (22), most of which were of an infectious origin. The observation was in line with a large number of epidemiological, laboratory and experimental studies showing that high cholesterol protects against infections (6). The main effect seems to be exerted by the LDL molecule. For instance, mice with FH challenged with bacterial endotoxin by injection with Gram-negative bacteria, had an 8-fold increased LD50, and a significantly delayed and overall lower mortality than control mice. Also, pharmacologically induced hypocholesterolaemia led to a markedly increased endotoxin mortality that was returned to normal after injection of exogenous lipoproteins; and the haemolytic effects of *Staphylococcus aureus* α-toxin was prevented by adding purified LDL to the test tube (6). In agreement with this idea, individuals with familiar hypercholesterolaemia had a longer life expectancy than others before year 1900, where the main cause of mortality was infectious diseases (23). A recent, large follow-up study found that their average lifespan was normal because the increased coronary mortality was balanced by a decreased mortality from other diseases (24). Older people with high cholesterol live longer than older people with low cholesterol, and this author has tabulated the many clinical studies that have confirmed the benefits of high cholesterol in various types of infectious diseases (6).

Conclusions

The cholesterol hypothesis has failed to stand up to the standard of falsifiability. In a medical theory, it takes more than one counter-example, but this review has pointed to the numerous studies that contradict basic predictions. Although I have followed the literature in this field meticulously for almost 18 years I may have overlooked supportive studies. However, a few supportive studies cannot outweigh the large number of contradictory ones. But the cholesterol campaign continues, inappropriate studies are funded and controversial studies are either ignored or cited as if they were supportive (15,26). There is, however, increasing awareness that the diet-heart hypothesis is sustained by a number of social, political and financial factors, most of which have little to do with science or any established success in public health.

References

1. Ravnskov U. The questionable role of saturated and polyunsaturated fatty acids in cardiovascular disease. J Clin Epidemiol. 1998;51:443–60.
2. Krauss RM, Blanche PJ, Rawlings RS, Fernstrom HS, Williams PT. Separate effects of reduced carbohydrate intake and weight loss on atherogenic dyslipidemia. Am J Clin Nutr. 2006;83:1025–31.
3. Ravnskov U. The Cholesterol Myths. Washington: New Trends Publishing; 2000.
4. Roselli della Rovere G, Lapolla A, Sartore G, Rossetti C, Zambon S, Minicuci N, et al. Plasma lipoproteins, apoproteins and cardiovascular disease in type 2 diabetic patients. A nine-year follow-up study. Nutr Metab Cardiovasc Dis. 2003; 13:46–51.
5. Bellomo G, Lippi G, Saronio P, Reboldi G, Verdura C, Timio F, et al. Inflammation, infection and cardiovascular events in chronic hemodialysis patients: a prospective study. J Nephrol. 2003;16:245–51.
6. Ravnskov U. High cholesterol may protect against infections and atherosclerosis. Q J Med. 2003;96:927–34.
7. Ravnskov U. Is atherosclerosis caused by high cholesterol. Q J Med. 2002;95:397–403.
8. Mölgaard J, von Schenk H, Kuusi T, Holme I, Lassvik C, Taskinen MR, et al. Plasma lipoprotein abnormalities and apolipoptotein E phenotypes in intermittent claudication. A multivariate analysis of randomly selected subjects. Nutr Metab Cardiovasc Dis. 1996;6:114–23.
9. Miettinen TA, Gylling H. Mortality and cholesterol metabolism in familial hypercholesterolemia. Arteriosclerosis. 1988; 8:163–7.
10. Neil HAW, Seagroatt V, Betteridge DJ, Cooper MP, Durrington PN, Miller JP, et al. Established and emerging

coronary risk factors in patients with heterozygous familial. hypercholesterolaemia. Heart. 2004;90:1431–7.
11. Rodriguez G, Bertolini S, Nobili F, Arrigo A, Masturzo P, Elicio N, et al. Regional cerebral blood flow in familial hypercholesterolaemia. Stroke. 1994;25:831–6.
12. Hopkins PN, Stephenson S, Wu LL, Riley WA, Xin Y, Hunt SC. Evaluation of coronary risk factors in patients with heterozygous familial hypercholesterolemia. Am J Cardiol. 2001;87:547–53.
13. Brown MS, Goldstein JL. Lipoprotein metabolism in the macrophage: Implications for cholesterol deposition in atherosclerosis. Ann Rev Biochem. 1983;52:223–61.
14. Jansen AC, van Aalst-Cohen ES, Tanck MW, Cheng S, Fontecha MR, Li J, et al. Genetic determinants of cardiovascular disease risk in familial hypercholesterolemia. Arterioscler Thromb Vasc Biol. 2005;25:1475–81.
15. Ravnskov U. Cholesterol lowering trials in coronary heart disease: frequency of citation and outcome. BMJ. 1992;305: 15–9.
16. Ravnskov U, Rosch PJ, Sutter MC, Houston MC. Should we lower cholesterol as much as possible? BMJ. 2006;332: 1330–2.
17. Solomon H, Samarasinghe YP, Feher MD, Man J, Rivas-Toro H, Lumb PJ, et al. Erectile dysfunction and statin treatment in high cardiovascular risk patients. Int J Clin Pract. 2006;60: 141–5.
18. Kenis I, Tartakover-Matalon S, Cherepnin N, Drucker L, Fishman A, Pomeranz M, et al. Simvastatin has deleterious effects on human first trimester placental explants. Hum Reprod. 2005;20:2866–72.
19. Edison RJ, Muenke M. Central nervous system and limb anomalies in case reports of first-trimester statin exposure. N Engl J Med. 2004;350:1579–82.
20. Marzoa-Rivas R, Crespo-Leiro MG, Paniagua-Marin MJ, Llinares-Garcia D, Muniz-Garcia J, Aldama-Lopez G, et al. Safety of statins when response is carefully monitored: a study of 336 heart recipients. Transplant Proc. 2005;37: 4071–3.
21. Langsjoen PH, Langsjoen JO, Langsjoen AM, Lucas LA. Treatment of statin adverse effects with supplemental Coenzyme Q10 and statin drug discontinuation. Biofactors. 2005; 25:147–52.
22. Sinzinger H, O'Grady J. Professional athletes suffering from familial hypercholesterolaemia rarely tolerate statin treatment because of muscular problems. Br J Clin Pharmacol. 2004;57: 525–8.
23. Jacobs D, Blackburn H, Higgins M, Reed D, Iso H, McMillan G, Neaton J, et al. Report of the Conference on Low Blood Cholesterol: Mortality Associations. Circulation. 1992;86: 1046–60.
24. Sijbrands EJG, Westendorp RGJ, Defesche JD, de Meier PHEM, Smelt AHM, Kastelein JJP. Mortality over two centuries in large pedigree with familial hypercholesterolaemia: family tree mortality study. Br Med J. 2001;322: 1019–23.
25. Neil HAW, Hawkins MM, Durrington PN, Betteridge DJ, Capps NE, Humphries SE; Simon Broome Familial Hyperlipidaemia Register Group and Scientific Steering Committee. Non-coronary heart disease mortality and risk of fatal cancer in patients with treated heterozygous familial hypercholesterolaemia: a prospective registry study. Atherosclerosis. 2005;179:293–7.
26. Ravnskov U. Quotation bias in reviews of the diet-heart idea. J Clin Epidemiol. 1995;48:713–9.