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Bioidentical Hormones Natural Thyroid

Cholesterol Levels and Atherosclerosis: Autopsy Studies Show No Correlation

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Cholesterol Levels and Atherosclerosis: Autopsy Studies Show No Correlation

By Jeffrey Dach MD

Drs William Ware (25) and Uffe Ravnskov(1) have both pointed out an inconvenient truth. Many autopsy studies dating back to 1936 all show the same finding: cholesterol levels **do not** correlate with the amount of atherosclerosis found on autopsy

studies.(1)(25) If accepted as true, this would indeed disprove the cholesterol theory of atherosclerotic heart disease. *Left Image: CAT scan of atherosclerotic disease in coronary artery (white arrow). Courtesy of [Pathology Outlines.com](#)*

Drs Landé and Sperry conducted an autopsy study published in the 1936 Archives of Pathology. They say:

*“In fresh autopsy material in 123 cases of violent death they compared the serum cholesterol content with the lipid content of the aorta. **No relationship was present in any age group. It is concluded that the incidence and severity of atherosclerosis in man is not directly correlated with the blood serum cholesterol content.**”(2)*

Dr KS Mathur did another autopsy study published in 1962 in Circulation.



*... 7al autopsies for a study of int and severity of atherosclerosis in the aorta and the coronary and cerebral arteries... **No correlation could be observed between the serum cholesterol level and the amount and severity of atherosclerosis in the arteries.**(3)*

A more recent study of 51 autopsies, by Dr Braz in the 2007 J Med Biol Res showed:

*“that in patients with severe atherosclerosis blood cholesterol and triglyceride levels **seem to have little influence on coronary lipid content, indicating that other factors may contribute to arterial lipid deposition and plaque formation.**”(4)*

Dr Paterson published two studies in 1960 and 1963 (Circulation) evaluating “Serum lipid levels and the severity of coronary and cerebral atherosclerosis in adequately nourished men, 60 to 69 years of age.” He says:

*“No significant relationships, nor any trend toward such relationships, were found in 18 individual analyses concerning the coronary arteries. Furthermore, the mean serum lipid levels were consistently (but not significantly) higher in persons who did not have demonstrable sequelae of coronary sclerosis at autopsy than in persons who had sequelae. **We conclude from these results that the validity of the “lipid theory” of atherosclerosis remains unproved, as far as the coronary arteries are concerned.**”(5-6)*

Many other have reported similar findings (7,8)

Mainstream Cardiology Has Rejected This Information

Of course, as Dr William Ware has pointed out, mainstream cardiology has ignored and rejected the information that autopsy studies showing no correlation between serum cholesterol and extent and severity of coronary artery disease.(25) Another inconvenient fact ignored by conventional cardiology is that modern imaging studies with Calcium Scoring have falsified the cholesterol theory of heart disease.(25) This was discussed in my previous [article](#).

My Neighbor Bill

Last week I was having a beer in the back yard with my neighbor, Bill who is recovering from a triple bypass operation. Bill said:

“It was my darn cholesterol that caused it....I’m taking Lipitor (statin drug) and my cholesterol is a lot lower now.”

I said “that’s great, Bill”. People believe that cholesterol causes heart disease thanks to drug company television advertising. I didn’t have the heart to tell Bill the theory cholesterol causes heart disease has been disproved by numerous autopsy studies. I knew that Bill believed in the cholesterol theory of heart disease, and any information to the contrary would induce a state of shock and disbelief. The benefit from statin drugs is not solely from reduction of LDL cholesterol. Rather, the benefit of statin drugs, if any, arises from the pleiotropic effects as anti-inflammatory drugs.(17-18)

Pleiotropic Effects Explain Clinical Benefit of Statins (if any)

This is a quote from Dr Kavalipati(17):

*“Over the years, analyses of several clinical studies, including the landmark HPS and ASCOT-LLA trial, reported **findings with statins that were inexplicable with the lipid-lowering mechanism alone.**”(17)*

At the same time the statin drug reduces serum cholesterol, there is a simultaneous pleiotropic effect (anti-inflammatory) which is completely independent from the cholesterol lowering effect. How much clinical benefit is due to cholesterol lowering, and how much benefit is due to pleiotropic effects is a matter of debate. According to Dr Oesterle in Circulation Research 2017:

*“Statins may exert cardiovascular protective effects that are independent of LDL-cholesterol lowering called pleiotropic effects.....The relative contributions of statin pleiotropy to clinical outcomes, however, **remain a matter of debate and are hard to quantify** because the degree of isoprenoid inhibition by statins correlates to some extent with the amount of LDL-cholesterol reduction.”(18)*

All the Benefits of Statin Drugs Are Due to Pleiotropic Effects

My best guess is that **all the benefits** of statins are due to pleiotropic effects. This is supported by the fact that other lipid lowering drugs using a different mechanism from statins failed to prevent heart attacks or strokes. (23,24) A perfect example is the new drug, **evacetrapib**, which lowers LDL and increases HDL cholesterol using a different mechanism from statins. After the evacetrapib failed to prevent heart attacks or strokes in a huge randomized placebo controlled trial

published in 2017 NEJM, the drug was abandoned. (23,24) The drugs lowered cholesterol, but had no clinical benefit in preventing cardiac events.

Statin Drug Studies Before and After 2005

Dr Michel de Lorgeril in his two articles from 2015 and 2016 reveals an unpleasant fact.(22,23) Because of the Vioxx Scandal, Congress tightened rules for clinical drug trials in 2005. Statin drug studies before 2005 are of questionable validity, and after 2005 are more “transparent”, “honest” and of greater validity.(22,23) This is Dr Michel de Lorgeril’s conclusion:

*“In conclusion, this review strongly suggests that **statins are not effective for cardiovascular prevention**. The studies published before 2005/2006 were probably flawed, and this concerned in particular the safety issue. A complete reassessment is mandatory. Until then, physicians should be aware that the **present claims about the efficacy and safety of statins are not evidence based.**”(22)*

Statins Not Beneficial In Primary Prevention

Regarding primary prevention of heart disease by statin drugs in healthy patients with only elevated cholesterol and no known underlying heart disease, Dr Michel de Lorgeril says that **Statin drugs have no benefit, and their discontinuation might even save lives:**

*“We conclude that (1) despite the recent hype raised by HOPE-3, the cholesterol-lowering rosuvastatin is likely **not beneficial** in intermediate-risk individuals without cardiovascular disease (primary prevention). This trial may even represent a typical example of how evidence-based medicine has been flawed in commercial studies. (2) Statin discontinuation does not lead to increased (Ischemic Heart Disease) IHD and overall mortality, at least in the months following interruption of treatment. On the contrary, **one might even conclude that statin discontinuation could save lives.**”(23)*

Conclusion: Many autopsy studies dating back to 1936 show no correlation between cholesterol level and severity of atherosclerotic disease. The clinical benefit of statin drugs, if any, is entirely due to the pleiotrophic effects. Reduction of cholesterol with non-statin drugs do not prevent heart attacks or strokes. (19-25) For more information on what really causes heart disease and how to prevent it see my [previous article](#) on this topic.

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[Statin Choir Boy Turns Disbeliever](#)

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[Statin Drugs for Women, Just Say No](#)

Links and References

Serum lipid levels and atherosclerosis

1) [Is atherosclerosis caused by high cholesterol?](#)

U. Ravnskov QJM: An International Journal of Medicine, Volume 95, Issue 6, 1 June 2002, Pages 397–403,

1936

2) Landé, K. E., and W. M. Sperry. "[Human atherosclerosis in relation to the cholesterol content of the blood serum.](#)" Arch. Pathol. 22 (1936): 301-312.

Abstract : The authors accepted the finding of previous workers that a correlation exists between the degree of arteriosclerosis in man and the lipid content of the aorta. In fresh autopsy material in 123 cases of violent death they compared the serum cholesterol content with the lipid content of the aorta. **No relationship was present in any age group. It is concluded that the incidence and severity of atherosclerosis in man is not directly correlated with the blood serum cholesterol content.**-A. Lyall.

3) Mathur, K. S., et al. "[Serum cholesterol and atherosclerosis in man.](#)" Circulation 23.6 (1961): 847-852.

Two hundred cases were selected from medicolegal autopsies for a study of the relationship of serum cholesterol to the amount and severity of atherosclerosis in the aorta and the coronary and cerebral arteries. A preliminary study of cholesterol before and after death in 20 cases showed a close parallel between the two when

the sample of blood was taken within 16 hours of death.

The mean serum total cholesterol showed a tendency to rise from 122 mg. per cent ± 16 in the first decade to 176 mg. per cent ± 28 in the fifth decade. A statistically significant correlation was found between serum total cholesterol levels and age up to the fifth decade.

No correlation could be observed between the serum cholesterol level and the amount and severity of atherosclerosis in the arteries. When all the cases were divided into arbitrary groups according to the amount of atherosclerosis, a rise in the levels of mean serum total cholesterol was seen in the first six successive groups of aortic atherosclerosis. But when age was excluded from the correlation between atherosclerosis and serum cholesterol, the interrelationship between the two was found to be statistically insignificant.

4) Braz J Med Biol Res. 2007 Apr;40(4):467-73.

Coronary fat content evaluated by morphometry in patients with severe atherosclerosis has no relation with serum lipid levels.

Braz DJ Jr1, Gutierrez PS, da Luz PL.

The relationship between **lipid serum levels and coronary atherosclerotic plaque fat content was studied in 51 necropsy patients.** Serum lipids were measured by standard techniques, during life, in the absence of lipid-lowering drugs. Intima, intimal fat and media areas were measured using a computerized system in cryosections of the odd segments of the right, anterior descending and circumflex coronary arteries stained with Sudan-IV. Mean intimal and lipid areas were 5.74 ± 1.98 and 1.22 ± 0.55 mm² ($22.12 \pm 8.48\%$) in 26 cases with high cholesterol (≥ 200 mg/dL) and 4.98 ± 1.94 and 1.16 ± 0.66 mm² ($22.75 \pm 9.06\%$) in 25 cases with normal cholesterol (< 200 mg/dL; $P > 0.05$). Patients with high levels of low-density lipoprotein (≥ 130 mg/dL, $N = 15$) had a higher intima/media area ratio than those with normal levels of low-density lipoprotein (< 130 mg/dL, $N = 13$, $P < 0.01$). No significant difference in the morphometrical variables was found in groups with high or low serum levels of triglycerides (≥ 200 mg/dL, $N = 13$ vs < 200 mg/dL, $N = 36$) or high-density lipoprotein (≥ 35 mg/dL, $N = 11$ vs < 35 mg/dL, $N = 17$). The association between the morphological measurements and serum levels of cholesterol, its fractions, and triglycerides was also tested and the correlation coefficients were low. Although high cholesterol is a risk factor, **we show here that in patients with severe atherosclerosis blood cholesterol and triglyceride levels seem to have little influence on coronary lipid content, indicating that other factors may contribute to arterial lipid deposition and plaque formation.**

Paterson

5) Paterson, J. C., Lucy Dyer, and E. C. Armstrong. "Serum cholesterol levels in human atherosclerosis." Canadian Medical Association Journal 82.1 (1960): 6.

The results lend little support to the contention that the severity of atherosclerosis is related to the level of serum cholesterol, except perhaps when it exceeds 300 mg. %. In 58 cases in the age group 60-69 years, significant relationships between the level of serum cholesterol and the severity of disease were found only once in 40 statistical analyses, and the complications of atherosclerosis were just as frequent in cases with low serum cholesterol levels (150-199 mg. %) as in cases with moderately high ones (250-299mg.%).

6) Paterson, J. C., Rosemary Armstrong, and E. C. Armstrong. "Serum lipid levels and the severity of coronary and cerebral atherosclerosis in adequately nourished men, 60 to 69 years of age." *Circulation* 27.2 (1963): 229-236.

No significant relationships, nor any trend toward such relationships, were found in 18 individual analyses concerning the coronary arteries. **Furthermore, the mean serum lipid levels were consistently (but not significantly) higher in persons who did not have demonstrable sequelae of coronary sclerosis at autopsy than in persons who had sequelae. We conclude from these results that the validity of the lipid theory" of atherosclerosis remains unproved, as far as the coronary arteries are concerned.**

7) *Am J Med.* 1982 Aug;73(2):227-34. Cabin HS, Roberts WC.

Relation of serum total cholesterol and triglyceride levels to the amount and extent of coronary arterial narrowing by atherosclerotic plaque in coronary heart disease. Quantitative analysis of 2,037 five mm segments of 160 major epicardial coronary arteries in 40 necropsy patients.

The amount of cross-sectional area narrowing by atherosclerotic plaques was determined histologically in each 5 mm segment of the entire lengths of the right, left main, left anterior descending, and left circumflex coronary arteries in 40 patients with fatal coronary heart disease and known fasting serum total cholesterol and triglyceride levels. The patients were divided into four groups based upon the serum total cholesterol and triglyceride levels: group I, total cholesterol of 250 mg/dl or less, triglyceride of 170 mg/dl or less; group II, total cholesterol of 250 or less, triglyceride of more than 170; group III, total cholesterol of more than 250, triglyceride of 170 or less; group IV, total cholesterol of more than 250, triglyceride of more than 170. The number of 5 mm segments of coronary artery narrowed severely (76 to 100 percent in cross-sectional area) by atherosclerotic plaques in each group was as follows: 172 of 505 (34 percent) 5 mm segments from group I; 242 of 353 (69 percent) segments from group II; 120 of 295 (41 percent) from group III and 425 of 884 (48 percent) segments from group IV. The mean percentage of 5 mm segments narrowed severely was significantly greater in group II than in group I (p less than 0.005) or group III (p less than 0.01). Additionally, the mean number of four coronary arteries per subject severely narrowed and the number of subjects with severe narrowing of the left main coronary artery were significantly greater in groups II and III than in group I. **The percentages of 5 mm segments narrowed severely correlated significantly with the serum triglyceride level (p less than 0.03).** Although it

correlated with the number of severely narrowed coronary arteries per subject, **the serum total cholesterol level did not correlate with the percentage of 5 mm segments of coronary artery with severe narrowing.**

8) MÉNDEZ, JOSÉ, and CARLOS TEJADA. "Relationship between serum lipids and aortic atherosclerotic lesions in sudden accidental deaths in Guatemala City." The American journal of clinical nutrition 20.10 (1967): 1113-1117.

Postmortem blood samples were collected from 43 individuals, who died suddenly in accidents in Guatemala City, within 2-5 hr after death. Aortas and coronary arteries were obtained for staining and grading.

No significant correlation was found between the extent of the lipid streak or fibrous plaque lesions in the aorta and either serum cholesterol or lipid phosphorus concentration, or serum cholesterol-to-lipid phosphorus ratio.

Correlation with the coronary lesions could not be calculated due to the small number of cases presenting such lesions. Although there was no correlation between serum lipid levels at death and aortic atherosclerotic lesions, it is recognized that the lipid levels of an earlier period in the subject's life might have had a more significant influence.

The postmortem serum cholesterol levels of nine patients dying in the hospital were abnormally low in some cases, because of the specific cause of death, time of prior hospitalization and, in particular, of the agonal period suffered before death. These cases need to be eliminated from any study of the relationship between serum lipid levels and atherosclerosis.

9) Solberg, Lars A., and Jack P. Strong. "Risk factors and atherosclerotic lesions. A review of autopsy studies." Arteriosclerosis, Thrombosis, and Vascular Biology 3.3 (1983): 187-198.

angiography

pdf

10) Nitter-Hauge, Sigurd, and Ivar Enge. "Relation between blood lipid levels and angiographically evaluated obstructions in coronary arteries." British heart journal 35.8 (1973): 791.

We were unable to find any significant correlation between the serum lipids and the severity of the obstructive disease.

11) Johnson, K. M., D. A. Dowe, and J. A. Brink. "Traditional clinical risk assessment tools do not accurately predict coronary atherosclerotic plaque burden: a CT angiography study." AJR. American journal of roentgenology 192.1 (2009): 235. OBJECTIVE: The objective of our study was to determine the degree

to which Framingham risk estimates and the National Cholesterol Education Program (NCEP) Adult Treatment Panel III core risk categories correlate with total coronary atherosclerotic plaque burden (calcified and noncalcified) as estimated on coronary CT angiograms.

MATERIALS AND METHODS: Coronary CT angiography was performed in 1,653 patients (1,089 men, 564 women) without a history of coronary heart disease (mean age \pm -SD: men, 51.6 \pm -9.7 years; women, 56.9 \pm -10.5 years). The most common reasons for the examination were hypercholesterolemia, family history, hypertension, smoking, and atypical chest pain. The coronary tree was divided into 16 segments; four different methods were used to quantify the amount of atherosclerotic plaque or the degree of stenosis in each segment, and segment scores were combined to give total scores. Framingham risk estimates and NCEP risk categories were calculated for each patient.

RESULTS: Correlation of plaque scores with the Framingham 10-year risk estimates were modest: Spearman's rho was 0.49–0.55. For all comparisons of NCEP risk categories to plaque score categories, the proportion of raw agreement, $p(0)$, was less than 0.50. Cohen's kappa ranged from 0.18 to 0.20. **Overall, 21% of the patients would have their perceived need for statins changed by using the coronary CTA plaque estimates in place of the NCEP core risk categories; 26% of the patients on statins had no detectable plaque.**

CONCLUSION: Coronary risk stratification using a risk factor only-based scheme is a **weak discriminator of the overall atherosclerotic plaque burden in individual patients**. Patients with little or no plaque might be subjected to lifelong drug therapy, whereas many others with substantial plaque might be undertreated or not treated at all.

12) Circulation. 1985 May;71(5):881-8.

[Lipoprotein predictors of the severity of coronary artery disease in men and women.](#) Reardon MF, Nestel PJ, Craig IH, Harper RW.

In this study we examined the relationships between levels of several components of plasma lipoproteins and severity of coronary artery disease in 65 men and 42 women who underwent coronary arteriography for suspected coronary disease. Severity of coronary atherosclerosis was scored as the extent of disease seen at arteriography. Univariate analyses of the relationships between the plasma lipoprotein parameters and score for severity of atherosclerosis revealed a marked difference between men and women. **In men, the score for severity of atherosclerosis was strongly related to the low-density lipoprotein (LDL) cholesterol and apolipoprotein B concentrations, whereas in women it was related to the triglyceride concentrations in plasma intermediate-density lipoprotein (IDL) and LDL and to the cholesterol and apolipoprotein B concentrations in IDL.** The significance of these correlations was not negated by possible confounding factors such as alcohol intake, diabetes, and treatment with thiazides and beta-adrenergic blockers. Stepwise regression analyses of data adjusted for weight and age indicated that 22% of the variation in the score for **severity of atherosclerosis could be accounted for by levels of LDL cholesterol in**

men. No other lipoprotein parameter could account for any further variation. **In contrast, cholesterol did not account for any variation in the score for severity of atherosclerosis in women,** whereas plasma triglyceride accounted for 16% of the observed variation in this group. No relationships were found between score for severity of atherosclerosis and high-density lipoprotein cholesterol or plasma apolipoprotein A-I concentrations in either group.(ABSTRACT TRUNCATED AT 250 WORDS).

13) Am J Cardiol. 1991 Mar 1;67(6):479-83.

Relation of serum lipoprotein cholesterol levels to presence and severity of angiographic coronary artery disease. Romm PA1, Green CE, Reagan K, Rackley CE.

To assess the relation of lipid levels to angiographic coronary artery disease (CAD), lipid profiles were obtained on **125 men and 72 women** undergoing **diagnostic coronary angiography**. CAD, defined as greater than or equal to 25% diameter narrowing in a major coronary artery, was present in 106 men (85%) and 54 women (75%). Multiple regression analyses revealed that **only high-density lipoprotein (HDL) cholesterol level in men, and age and total/HDL cholesterol ratio in women, were independently associated with the presence of CAD** after adjustment for other risk factors. HDL cholesterol level and age were significantly correlated with both extent (number of diseased vessels) and severity (percent maximum stenosis) of CAD in men. In women, age was the only independent variable related to severity, whereas age and total/HDL cholesterol ratio were related to extent. **Of 71 patients with total cholesterol less than 200 mg/dl, 79% had CAD. With multiple regression analyses, HDL cholesterol was the only variable independently related to the presence and severity of CAD in these patients** after adjustment for age and gender; **extent was significantly associated with age and male gender, and was unrelated to any of the lipid parameters.** With use of multiple logistic and linear regression analyses of the group of 197 patients, HDL cholesterol was the most powerful independent variable associated with the presence and severity of CAD after adjustment for age and gender. HDL cholesterol was also an independent predictor of extent. Age was independently associated with each of the end points examined, and was the variable most significantly related to extent. These data add to the growing body of information demonstrating an important association between HDL and CAD.

14) Am J Epidemiol. 1981 Apr;113(4):396-403.

Community pathology of atherosclerosis and coronary heart disease: post mortem serum cholesterol and extent of coronary atherosclerosis.

Oalman MC, Malcom GT, Toca VT, Guzmán MA, Strong JP.

Abstract

Little is known about the direct relationship between serum cholesterol and the extent of coronary atherosclerosis in human populations even though the association of serum cholesterol levels with risk of developing coronary heart

disease (CHD) is well documented. **The results of this study of men 25-44 years of age, residents of Orleans Parish, Louisiana, show a significant relationship between post mortem serum cholesterol levels and extent of more advanced lesions (raised lesions) in the coronary arteries in 110 autopsied white men, but not in the cases of 221 autopsied black men.** When disease categories comprising CHD cases and non-CHD cases (basal group) were evaluated, the racial difference in the cholesterol-lesion associations persisted. **The reason for the racial difference in the observed cholesterol-lesion association is not clear.** Additional research, where younger age groups are included, and considering earlier lesions and other risk factors in different environments may help in clearing this question.

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intravascular ultrasound

Statin Pleomorphic effect?

15) [Relation Between Progression and Regression of Atherosclerotic Left Main Coronary Artery Disease and Serum Cholesterol Levels as Assessed With Serial Long-Term \(\$\geq 12\$ Months\) Follow-Up Intravascular Ultrasound](#) Clemens von Birgelen, Marc Hartmann, Gary S. Mintz, Dietrich Baumgart, Axel Schmermund, Raimund Erbel
Circulation. 2003;108:2757-2762

Background— The relation between serum lipids and risk of coronary events has been established, but there are no data demonstrating directly the relation between serum low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol versus **serial changes in coronary plaque dimensions.**

Methods and Results— We performed standard analyses of **serial intravascular ultrasound (IVUS) studies of 60 left main coronary arteries obtained 18.3 \pm 9.4 months apart to evaluate progression and regression of mild atherosclerotic plaques in relation to serum cholesterol levels.** Overall, there was (1) a positive linear relation between LDL cholesterol and the annual changes in plaque plus media (P&M) cross-sectional area (CSA) ($r=0.41$, $P<0.0001$) with (2) an LDL value of 75 mg/dL as the cutoff when regression analysis predicted on average no annual P&M CSA increase; (3) an inverse relation between HDL cholesterol and annual changes in P&M CSA ($r=-0.30$, $P<0.02$); (4) an inverse relation between LDL cholesterol and annual changes in lumen CSA ($r=-0.32$, $P<0.01$); and (5) no relation between LDL and HDL cholesterol and the annual changes in total arterial CSA (remodeling). Despite similar baseline IVUS characteristics, patients with an LDL cholesterol level ≥ 120 mg/dL showed more annual P&M CSA progression and lumen reduction than patients with lower LDL cholesterol.

Conclusions— There is a **positive linear relation between LDL cholesterol and**

annual changes in plaque size, with an LDL value of 75 mg/dL predicting, on average, no plaque progression. HDL cholesterol shows an inverse relation with annual changes in plaque size.

16) Noakes, T. D. "The 2012 University of Cape Town Faculty of Health Sciences centenary debate: "Cholesterol is not an important risk factor for heart disease, and the current dietary recommendations do more harm than good"." South African Journal of Clinical Nutrition 28.1 (2015): 19-33.

<https://www.ncbi.nlm.nih.gov/pubmed/11263954>

Exp Mol Pathol. 2001 Apr;70(2):103-19.

Coronary heart disease, hypercholesterolemia, and atherosclerosis. I. False premises.

Stehbens WE1. Department of Pathology and Molecular Medicine, Wellington School of Medicine, Wellington, New Zealand.

Lipid-rich caseous debris of advanced lesions stimulated interest in the role of cholesterol and lipids in atherosclerosis. Lipid-containing arterial lesions in cholesterol-overfed animals (cholesterolosis) and xanthomatous vascular lesions in subjects with familial hypercholesterolemia were then misrepresented as being atherosclerotic and led to the development of the hypercholesterolemic/lipid hypothesis. It is untenable that cholesterol, an essential multifunctional metabolite, is pathogenic at all blood levels and hypercholesterolemia is not prerequisite for human or experimental atherosclerosis. Serum cholesterol levels display a poor correlation with atherosclerosis at autopsy and with unreliable national coronary heart disease (CHD) mortality in each sex. Atherosclerosis topography and its iatrogenic production in humans and experimentally in herbivores by hemodynamic means both support a biomechanical causation and preclude causality by any circulating humoral factor. CHD, not a specific disease, is a nonspecific complication of many diseases including atherosclerosis and cannot be equated with coronary atherosclerosis due to differences in pathology and pathogenesis. Thus, extrapolations from CHD risk factors or correlations with fallacious vital statistics to atherosclerosis are invalid. It follows that the hypercholesterolemic/lipid hypothesis evolving from false premises, misuse of CHD, scientific misrepresentation, and fallacious data has no legitimate basis.

17) Kavalipati, Narasaraju, et al. "[Pleiotropic effects of statins.](#)" Indian journal of endocrinology and metabolism 19.5 (2015): 554.

18) Oesterle, Adam, Ulrich Laufs, and James K. Liao. "[Pleiotropic Effects of Statins on the Cardiovascular System.](#)" Circulation Research (2017).

The statins have been used for 30 years to prevent coronary artery disease and stroke. Their primary mechanism of action is the lowering of serum cholesterol through inhibiting hepatic cholesterol biosynthesis thereby upregulating the hepatic low-density lipoprotein (LDL) receptors and increasing the clearance of LDL-cholesterol. **Statins may exert cardiovascular protective effects that are**

independent of LDL-cholesterol lowering called pleiotropic effects. Because statins inhibit the production of isoprenoid intermediates in the cholesterol biosynthetic pathway, the post-translational prenylation of small GTP-binding proteins such as Rho and Rac, and their downstream effectors such as Rho kinase and nicotinamide adenine dinucleotide phosphate oxidases are also inhibited. In cell culture and animal studies, these effects alter the expression of endothelial nitric oxide synthase, the stability of atherosclerotic plaques, the production of proinflammatory cytokines and reactive oxygen species, the reactivity of platelets, and the development of cardiac hypertrophy and fibrosis. The relative contributions of statin pleiotropy to clinical outcomes, however, remain a matter of debate and are hard to quantify because the degree of isoprenoid inhibition by statins correlates to some extent with the amount of LDL-cholesterol reduction. This review examines some of the currently proposed molecular mechanisms for statin pleiotropy and discusses whether they could have any clinical relevance in cardiovascular disease.

19) DuBroff, Robert, and Michel de Lorgeril. "Cholesterol confusion and statin controversy." World journal of cardiology 7.7 (2015): 404.

The role of blood cholesterol levels in coronary heart disease (CHD) and the true effect of cholesterol-lowering statin drugs are debatable. In particular, **whether statins actually decrease cardiac mortality and increase life expectancy is controversial.** Concurrently, the Mediterranean diet model has been shown to prolong life and reduce the risk of diabetes, cancer, and CHD. We herein review current data related to both statins and the Mediterranean diet. **We conclude that the expectation that CHD could be prevented or eliminated by simply reducing cholesterol appears unfounded.** On the contrary, we should acknowledge the inconsistencies of the cholesterol theory and recognize the proven benefits of a healthy lifestyle incorporating a Mediterranean diet to prevent CHD.

Core tip: Traditional efforts to prevent cardiovascular disease have emphasized the benefits of cholesterol lowering and statin drugs. Often overlooked is the fact that numerous studies of cholesterol lowering have failed to demonstrate a mortality benefit and the benefits of statins may have been overstated. The Mediterranean diet has consistently lowered cardiovascular events and mortality in numerous studies and does not typically lower cholesterol levels. Alternative theories of atherosclerosis are independent of cholesterol metabolism and may provide the key to future preventive strategies.

Nearly twenty years ago two landmark randomized clinical trials appeared in The Lancet which forever changed the course of medicine for patients with coronary heart disease (CHD). The 4S study employed a cholesterol-lowering statin drug and reported a 30% mortality reduction[1]. The Lyon Diet Heart Study utilized the Mediterranean diet and reported a 70% mortality reduction[2]. Subsequent studies of the Mediterranean diet have confirmed these findings and also shown a reduced risk of cancer, diabetes, and Alzheimer's disease[3-6]. Subsequent statin studies have led the United States Food and Drug Administration to issue warnings

regarding the increased risk of diabetes and decreased cognition with statin drugs. Paradoxically, statins have gone on to become a multi-billion dollar industry and the foundation of many cardiovascular disease prevention guidelines while the Mediterranean diet has often been ignored. We believe this statin-centric cholesterol-lowering approach to preventing CHD may be misguided.

20) Okuyama, Harumi, et al. "Statins stimulate atherosclerosis and heart failure: pharmacological mechanisms." *Expert review of clinical pharmacology* 8.2 (2015): 189-199. [Statins stimulate atherosclerosis and heart failure Okuyama Harumi Expert review clin pharm 2015](#)

In contrast to the current belief that cholesterol reduction with statins decreases atherosclerosis, we present a perspective that **statins may be causative in coronary artery calcification and can function as mitochondrial toxins** that impair muscle function in the heart and blood vessels through the **depletion of coenzyme Q10 and 'heme A'**, and thereby **ATP generation. Statins inhibit the synthesis of vitamin K2**, the cofactor for matrix Gla-protein activation, which in turn protects arteries from calcification. Statins inhibit the biosynthesis of selenium containing proteins, one of which is glutathione peroxidase serving to suppress peroxidative stress. **An impairment of selenoprotein biosynthesis** may be a factor in congestive heart failure, reminiscent of the **dilated cardiomyopathies seen with selenium deficiency. Thus, the epidemic of heart failure and atherosclerosis that plagues the modern world may paradoxically be aggravated by the pervasive use of statin drugs.** We propose that current statin treatment guidelines be critically reevaluated.

21) de Lorgeril, Michel, and Mikael Rabaeus. "[Beyond confusion and controversy, Can we evaluate the real efficacy and safety of cholesterol-lowering with statins?.](#)" *Journal of Controversies in Biomedical Research* 1.1 (2016): 67-92.

A strong controversy has emerged about the reality of safety and efficacy of statins as stated by company-sponsored reports. However, physicians need credible data to make medical decisions, in particular about the benefit/harm balance of any prescription. This study aimed to test the validity of data on the company-sponsored statin trial by comparing them over time and then comparing statins with each other. **Around the years 2005/2006, new stricter Regulations were introduced in the conduct and publication of randomized controlled trials (RCTs).** This would imply that RCTs were less reliable before 2006 than they were later on. To evaluate this, we first reviewed RCTs testing the efficacy of statins versus placebo in preventing cardiovascular complications and published after 2006. Our systematic review thereby identified four major RCTs, all testing rosuvastatin. **They unambiguously showed that rosuvastatin is not effective in secondary prevention, while the results are highly debatable in primary prevention.** Because of the striking clinical heterogeneity and the inconsistency of the published data in certain RCTs, meta-analysis was not feasible. We then examined the most recent RCTs comparing statins to each other: all showed that

no statin is more effective than any other, including rosuvastatin. Furthermore, **recent RCTs clearly indicate that intense cholesterol-lowering (including those with statins) does not protect high-risk patients any better than less-intense statin regimens.** As for specific patient subgroups, **statins appear ineffective in chronic heart failure and chronic kidney failure patients.** We also conducted a MEDLINE search to identify all the RCTs testing a statin against a placebo in diabetic patients, and we found that once secondary analyses and subgroup analyses are excluded, **statins do not appear to protect diabetics.** As for the safety of statin treatment – a major issue for medical doctors – it is quite worrisome to realize that **it took 30 years to bring to light the triggering effect of statins on new-onset diabetes, manifestly reflecting a high level of bias in reporting harmful outcomes in commercial trials,** as has been admitted by the recent confession of prominent experts in statin treatment. **In conclusion, this review strongly suggests that statins are not effective for cardiovascular prevention. The studies published before 2005/2006 were probably flawed,** and this concerned in particular the safety issue. A complete reassessment is mandatory. Until then, **physicians should be aware that the present claims about the efficacy and safety of statins are not evidence based.**

22) Rabaeus, Mikael, Paul V. Nguyen, and Michel de Lorgeril. “Recent flaws in Evidence Based Medicine: statin effects in primary prevention and consequences of suspending the treatment.” *Journal of Controversies in Biomedical Research* 3.1 (2017): 1-10.

Statin therapy is presented as a protection against ischemic heart disease (IHD) complications. As IHD is often a fatal disease, statins are thereby supposed to decrease cardiovascular mortality and increase life expectancy. However, these benefits are increasingly challenged in the medical community, the controversy being particularly intense when discussing the effects of statins in **primary prevention** and the consequences of statin discontinuation. Both primary prevention and treatment discontinuation have been recently used by investigators linked to the pharmaceutical industry to justify and boost prescription and consumption of statins and other cholesterol-lowering medications. We herein review some recent commercial data related to primary prevention with rosuvastatin and statin discontinuation and their respective effects on IHD and overall mortality rate. We conclude that (1) **despite the recent hype raised by HOPE-3, the cholesterol-lowering rosuvastatin is likely not beneficial in intermediate-risk individuals without cardiovascular disease (primary prevention).** This trial may even represent a typical example of how evidence-based medicine has been flawed in commercial studies. (2) **Statin discontinuation does not lead to increased IHD and overall mortality, at least in the months following interruption of treatment.** On the contrary, **one might even conclude that statin discontinuation could save lives.** One possible explanation of this apparently paradoxical finding is that statin discontinuers, in the same time they stop statin therapy, likely try to adopt a healthy lifestyle. Further studies are needed to confirm the real effects of statin discontinuation in various clinical

conditions. In the meantime, it is not evidence based to claim that statin discontinuation increases mortality or saves lives.

Non-Statins Lipid Lowering Drug Fails

23) Lincoff, A. Michael, et al. "Evacetrapib and cardiovascular outcomes in high-risk vascular disease." *New England Journal of Medicine* 376.20 (2017): 1933-1942.

Abstract **BACKGROUND:** The cholesteryl ester transfer protein inhibitor evacetrapib substantially raises the high-density lipoprotein (HDL) cholesterol level, reduces the low-density lipoprotein (LDL) cholesterol level, and enhances cellular cholesterol efflux capacity. We sought to determine the effect of evacetrapib on major adverse cardiovascular outcomes in patients with high-risk vascular disease.

METHODS:

In a multicenter, randomized, double-blind, placebo-controlled phase 3 trial, we enrolled 12,092 patients who had at least one of the following conditions: an acute coronary syndrome within the previous 30 to 365 days, cerebrovascular atherosclerotic disease, peripheral vascular arterial disease, or diabetes mellitus with coronary artery disease. Patients were randomly assigned to receive either evacetrapib at a dose of 130 mg or matching placebo, administered daily, in addition to standard medical therapy. The primary efficacy end point was the first occurrence of any component of the composite of death from cardiovascular causes, myocardial infarction, stroke, coronary revascularization, or hospitalization for unstable angina.

RESULTS:

At 3 months, a 31.1% decrease in the mean LDL cholesterol level was observed with evacetrapib versus a 6.0% increase with placebo, and a 133.2% increase in the mean HDL cholesterol level was seen with evacetrapib versus a 1.6% increase with placebo. After 1363 of the planned 1670 primary end-point events had occurred, the data and safety monitoring board recommended that the trial be terminated early because of a lack of efficacy. After a median of 26 months of evacetrapib or placebo, a primary end-point event occurred in 12.9% of the patients in the evacetrapib group and in 12.8% of those in the placebo group (hazard ratio, 1.01; 95% confidence interval, 0.91 to 1.11; $P=0.91$).

CONCLUSIONS:

Although the cholesteryl ester transfer protein inhibitor evacetrapib had favorable effects on established lipid biomarkers, treatment with evacetrapib did not result in a lower rate of cardiovascular events than placebo among patients with high-risk vascular disease.

24) [Dashing Hopes, Study Shows a Cholesterol Drug Had No Effect on Heart Health](#)
By GINA KOLATA/APRIL 3, 2016 *New York Times*

25) cholesterol atherosclerosis falsified coronary artery plaque Ware Medical Hypotheses 2009 Ware, William R. "The mainstream hypothesis that LDL cholesterol drives atherosclerosis may have been falsified by non-invasive imaging of coronary artery plaque burden and progression." *Medical hypotheses* 73.4 (2009): 596-600.

Summary



Article Name

Cholesterol Levels and Atherosclerosis: Autopsy Studies Show No Correlation

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«A día de hoy, ¡el método más eficaz para tratar problemas articulares y de espalda! ¡No existe otro tratamiento similar!»

Fotografía: El profesor Park recibe el premio Nobel por su descubrimiento: una nueva vía para el tratamiento del sistema musculoesquelético.

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My reply: The weak and unpredictable correlations probably reflect bias, because most of the studies were performed on selected individuals.

Dr Ravnskov replies to this comment here:

<https://academic.oup.com/qj...>

Is atherosclerosis caused by high cholesterol? U. Ravnskov
QJM: An International Journal of Medicine, Volume 95, Issue 6, 1 June 2002, Pages 397–403,

Quote Dr Ravnskov,

"More recent autopsy studies have found weak or inconsistent correlations between LDL-cholesterol or total cholesterol and various measures of atherosclerosis.9 For instance, the most severe degree of atherosclerosis was found mainly in individuals with extremely high cholesterol, whereas small

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charles grashow → jeffrey_dach_md

7 months ago



"Therefore, to prove that the concentration of LDL-cholesterol has

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