HIGH LDL CHOLESTEROL IS NOT AN INDEPENDENT RISK FACTOR FOR HEART ATTACKS AND STROKES

A study published in the British Medical Journal shows that not only is high LDL cholesterol not a risk factor for all-caused mortality nor for cardiovascular mortality, but just the reverse is true. There is a perfect inverse relationship between LDL cholesterol and all-caused mortality and cardiovascular mortality. In fact, cardiovascular mortality was highest in those with the lowest LDL cholesterol.

Ravinskov U, et al. Lack of an association or an inverse association between low-density-lipoprotein cholesterol and mortality in the elderly. BMJ Open, 2016. ----- This study states, "it is well known that total cholesterol becomes less of a risk factor or not a risk factor at all for all-caused and for cardiovascular disease mortality with increasing age. We decided to investigate this issue …"

In people over age 60 there is an inverse association between all-caused mortality and LDL, and cardiovascular mortality was highest in the lowest LDL cholesterol quartile. In conclusion: High LDL cholesterol is inversely associated with mortality in people over 60 years. This finding is inconsistent with the cholesterol hypothesis (i.e., that cholesterol, and particularly LDL cholesterol, is inherently atherogenic). Since elderly people with high LDL live as long or longer with those with low LDL, our analysis provides reason to question the validity of the cholesterol hypothesis.

Lindberg O, et al. Inverse association of serum cholesterol with plasma insulin in the elderly. Aging, 1998. ----- This study shows in the 70-year-old age group that it is low LDL cholesterol that is associated with elevated plasma insulin (as found in insulin resistance, leading to Metabolic Syndrome and Type 2 Diabetes). LDL cholesterol, HDL cholesterol and total cholesterol were lowest in those with the highest plasma insulin.

VonMuhlen D, et al. Sex and time differences in the associations of non-high-density lipoprotein cholesterol versus other lipid and lipoprotein factors in the prediction of cardiovascular death. Am J Cardiol, 2003. ----- This study (the Rancho Bernardo Study) showed that in woman, there was absolutely no correlation between high total cholesterol or high LDL cholesterol and the incidence of coronary heart disease and cardiovascular disease deaths. The only predictive indicator of cardiovascular disease in women was low HDL

relative to total cholesterol. In men, low HDL relative to total cholesterol as well as elevated LDL and elevated triglycerides predicted significantly increased risks of coronary heart disease and cardiovascular disease --- but none of these associations were independent risk factors when allowance was made for smoking, elevated systolic blood pressure, fasting plasma glucose, body mass index, and physical activity. In women, that predictive power of deficient HDL to total cholesterol ratio was an independent risk factor --- independent of estrogen use and all the risk factors listed above for men.

HDL cholesterol is inversely correlated with coronary heart disease, and that relationship of HDL cholesterol to coronary heart disease is independent of LDL cholesterol. That conclusion is drawn from a systemic re-examination of the Frammingham Heart Study, the Lipid Research Clinics Prevalence Mortality Follow-up Study, the Lipid Research Clinics-Coronary Primary Prevention Trial, and the Multiple Risk Factor Intervention Trial --- comparing the results of these fours studies with an earlier report from the British Regional Heart Study that (erroneously) suggested that low HDL cholesterol was not a significant risk factor for coronary heart disease.

The Munster Heart Study (prospective cardiovascular Munster Study, PROCAM) clearly identified all the usual suspects that are correlated with myocardial infarction and sudden cardiac death --- including age, LDL cholesterol, deficient HDL cholesterol, systolic blood pressure, cigarette smoking, diabetes, angina, and family history. However, only serum triglycerides (and perhaps lipoprotein(a)) was determined to be an independent risk factor.

Tyrolerha. Serum Lipoproteins and risk factors: Recent epidemiological studies in individuals with and without prevalent cardiovascular disease. Eur Heart J, 1999.

Thomopoulos C, et al. Effect of low-density lipoprotein cholesterol lowering by statins on outcome incidents. Clin Cardiol, 2015. ----- This study showed that a Cochrane meta-analysis revealed that for every 1,000 patients taking statins for 5 years there would be 5 fewer strokes and 10 fewer coronary heart disease events. --- But --- even the small number of patients who are (statistically speaking) protected from cardiovascular events, the small risk reduction was not proportional to or even related to the degree to which the statins lowered LDL cholesterol. To quote the study, “risk ratios were not associated with LDL

cholesterol lowering … raising the hypothesis that the extent of LDL lowering might not be accompanied by incremental critical event reduction."

----- How do we interpret that study? It shows that the entire model of risk prevention by driving down LDL is fallacious. This confirms the many other studies we have presented showing that elevated cholesterol is not an independent risk factor for heart attacks and strokes. If, statistically speaking, a small number of people on statins were protected from a cardiovascular event, it must therefore have been (if indeed there was a cause-and-effect relationship) by the statins doing something other than lowering cholesterol. What might that something be? We know that the number one risk factor for heart attacks and strokes is an elevated triglyceride to HDL ratio. Any protective effects from statins, therefore, must derive from their ability to lower triglycerides --- and have nothing whatsoever to do with decreasing cholesterol.

The most comprehensive Cochrane database reviews of studies purporting to show the benefits of statins in primary prevention of cardiovascular disease reveal major problems with data reliability. Evaluating statins for primary prevention means that administering statins to those with high cholesterol prevents cardiovascular events in those with no history of cardiovascular disease. But the meta-analyses show that the data includes:

- Failure to report adverse events.
- Inclusion of people who already have cardiovascular disease.
- Extreme heterogeneity of data (--- wildly inconsistent findings from one database to the next).

Once such Cochrane database review concludes: "Caution should be taken in prescribing statins for primary prevention among people at low cardiovascular risk."

Taylor F. Statins for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev, 2001.

A similar study looked at statins, not in primary prevention in those with low CVD risk, but in those with high CVD risk. That study concludes: "This meta-analysis did not find evidence for the benefit of statin therapy on all-caused mortality in a high-risk primary prevention set up."

Ray K. Statins and all-caused mortality in high-risk primary prevention: A meta-analysis of eleven randomized controlled trials involving 65,229 participants. Arch Intern Med, 2010.

HDL Cholesterol is a complex molecule with antioxidant, anti-inflammatory, anti-thrombotic, anti-platelet, and vasodilatory properties --- including protection of LDL from oxidation. Driving LDL cholesterol down with statins does nothing to prevent oxidation of the LDL. Also important is that non-HDL cholesterol --- i.e., the sum of LDL plus VLDL --- reflects that cholesterol in all atherogenic particles containing apolipoprotein B as a far better predictor of cardiovascular risk and future mortality than is LDL alone. Considering the significance of oxidized LDL rather than total LDL, and the contribution of VLDL being greater than LDL --- explains "success" at driving LDL down to below 100 (even according to the most optimistic medical-pharmaceutical propaganda) only reduces the risk of cardiovascular events by 31%, leaving a residual risk of 69%.

The most effective way to comprehensively address cardiovascular disease risk is by considering the primary and independent risk factors --- including low HDL cholesterol, elevated triglycerides, as well as inflammatory cytokines and prostaglandins that increase the oxidation of LDL.

Alagona P. Beyond LDL cholesterol: the role of elevated triglycerides and low HDL cholesterol in residual CVD risk remaining after statin therapy. Am J Manag Care, 2009.

Tryptophan catabolism through the kynurenine pathway (measured by the kynurenine/tryptophan ratio) is induced by the Th1 inflammatory cytokine Interferon-gamma. The elevated kynurenine/tryptophan ratio is a marker of cell-mediated immune activation. The inflammation indicated by an elevated ratio is predictive of acute coronary events. Inflammation associated with tryptophan catabolism increases the odds of an acute coronary event in older adults by 57%. (This Interferon-gamma-mediated inflammation also increases the risk of hip fractures and cancer.)

Sulog, et al. Neopterin and kynurenine/tryptophan ratio as predictors of coronary events in older adults. Int J Cardiol, 2013.

C-reactive protein (CRP) is an independent risk factor of coronary heart disease. The Frammingham Risk Score (FRS) has long been the basis of the cardiovascular disease model that places total cholesterol and LDL cholesterol at the top of the risk factor list. Yet CRP is shown not only to be an independent risk factor of cardiovascular disease, but is also entirely independent of the FRS.

Koenig W, et al. C-reactive protein modulates risk prediction based on the Frammingham Score: Implications for future risk assessment. Circulation, 2004.

The original Framingham model for cardiovascular disease that placed a high emphasis on cholesterol as a risk factor had major problems that invalidated the data as independent risk factors for CVD. Most particularly, the FRS data was drawn from a patient population that did not exclude diabetics. Diabetes, of course, is significantly related to cardiovascular risk, and any risk model for CVD must separate diabetics into a separate cohort. [See the Article, "STATINS ARE DANGEROUS DRUGS" for more on the connection between diabetes and CVD, and how statin drugs cause diabetes and cause CVD the lower they drive the LDL Cholesterol.]

Mathenym, et al. Systemic review of cardiovascular disease risk assessment tools. Agency for healthcare research and quality, 2011 May.

Ravinskov. The retreat of the diet heart hypothesis. Journal of American Physicians and Surgeons 8, No 3 (2003), 94-95.

Ravinskov. Is atherosclerosis caused by high cholesterol? O J Med 95, (2002) 397-403.