Lipid Energy Model

A large body of evidence supports the use of very-low-carbohydrate ketogenic diets for weight loss, reversing <u>metabolic syndrome</u>, putting <u>type 2 diabetes into remission</u>, and improving a long list of other issues. And while most individuals who adopt this way of eating experience a decrease in total cholesterol and LDL-C, in some people this increase, and in a small subset they increase dramatically. Concern about the implications of this change with regard to risk for cardiovascular problems is one of the main reasons physicians and nutritionists may be hesitant to recommend a dietary therapy that is otherwise <u>noted for numerous health benefits</u>.

<u>A recent paper</u> presents a new hypothesis that provides mechanistic explanations for the rise in cholesterol seen in some people on very low-carb diets, and also raises the possibility that this increase may not automatically be cause for concern, but rather, is a logical phenomenon explained by lipoprotein dynamics and body energy demands in the context of carbohydrate restriction. (It has long been known that serum cholesterol <u>may increase during weight loss</u>, but it typically returns to a lower level when weight has stabilized. The new paper seeks to explain why, among some people following very low-carb diets, cholesterol remains markedly elevated even in the absence of weight loss.)

The paper builds upon research published earlier this year covering <u>a "lean mass hyper-responder" phenotype</u>, which was something we discussed in a <u>previous Research Forum</u>. With more and more people following ketogenic diets, evidence has emerged for a triad of signs among a subset of individuals on very low-carb diets. These people tend to be very lean (relatively low BMI), physically active, and they had total cholesterol and LDL-C levels considered "normal" prior to adopting a very low-carb diet. The triad observed in these individuals *after* switching to a low-carb diet is HDL-C \geq 80 mg/dL, LDL-C \geq 200 mg/dL, and triglycerides \leq 70 mg/dL.

Despite such elevated LDL-C, many of these individuals are found to have <u>coronary artery</u> <u>calcium scores of zero</u>, suggesting no atherosclerosis. The long-term ramifications of elevated LDL-C in the presence of no other signs of compromised health are not yet known, but <u>research</u> <u>is currently underway</u> to study these "lean mass hyper-responders" to see if they experience an inordinate incidence of cardiovascular disease and/or events.

It's critical to answer these contentious questions because low-carb diets are well known to improve blood sugar control and insulin sensitivity, <u>decrease triglycerides</u>, lower blood pressure, <u>reverse non-alcoholic fatty liver disease</u>, help normalize hormone levels in PCOS, and more. In many people, an increase in LDL-C is the *only* potentially adverse change from adopting a low-carb diet. When <u>so many other indicators of health get better</u>, research like this can get us closer to understanding whether a rise in LDL-C is always—and independently—pathogenic, or whether it may be a harmless physiological adaptation among exceptionally lean people following very low-carb diets.

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