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Common Dietary Fat and Intestinal Microbes Linked to Heart Disease

A new pathway has been discovered that links a common dietary lipid and intestinal microflora with an increased risk of heart disease, according to a Cleveland Clinic study published in the latest issue of Nature.

The study shows that people who eat a diet containing a common nutrient found in animal products (such as eggs, liver and other meats, cheese and other dairy products, fish, shellfish) are not predisposed to cardiovascular disease solely on their genetic make-up, but rather, how the micro-organisms that live in our digestive tracts metabolize a specific lipid -- phosphatidyl choline (also called lecithin). Lecithin and its metabolite, choline, are also found in many commercial baked goods, dietary supplements, and even children's vitamins.

The study examined clinical data from 1,875 patients who were referred for cardiac evaluation, as well as plasma samples from mice. When fed to mice, lecithin and choline were converted to a heart disease-forming product by the intestinal microbes, which promoted fatty plaque deposits to form within arteries (atherosclerosis); in humans, higher blood levels of choline and the heart disease forming microorganism products are strongly associated with increased cardiovascular disease risk.

"When two people both eat a similar diet but one gets heart disease and the other doesn't, we currently think the cardiac disease develops because of their genetic differences; but our studies show that is only a part of the equation," said Stanley Hazen, M.D., Ph.D., Staff in Lerner Research Institute's Department of Cell Biology and the Heart and Vascular Institute's Department of Cardiovascular Medicine and Section Head of Preventive Cardiology & Rehabilitation at Cleveland Clinic, and senior author of the study. "Actually, differences in gut flora metabolism of the diet from one person to another appear to have a big effect on whether one develops heart disease. Gut flora is a filter for our largest environmental exposure -- what we eat."

Dr. Hazen added, "Another remarkable finding is that choline -- a natural semi-essential vitamin -- when taken in excess, promoted atherosclerotic heart disease. Over the past few years we have seen a huge increase in the addition of choline into multi-vitamins -- even in those marketed to our children -- yet it is this same substance that our study shows the gut flora can convert into

something that has a direct, negative impact on heart disease risk by forming an atherosclerosis-causing by-product."

In studies of more than 2,000 subjects altogether, blood levels of three metabolites of the dietary lipid lecithin were shown to strongly predict risk for cardiovascular disease: choline (a B-complex vitamin), trimethylamine N-oxide (TMAO, a product that requires gut flora to be produced and is derived from the choline group of the lipid) and betaine (a metabolite of choline).

"The studies identify TMAO as a blood test that can be used in subjects to see who is especially at risk for cardiac disease, and in need of more strict dietary intervention to lower their cardiac risk," Dr. Hazen said.

Healthy amounts of choline, betaine and TMAO are found in many fruits, vegetables and fish. These three metabolites are commonly marketed as direct-to-consumer supplements, supposedly offering increased brain health, weight loss and/or muscle growth.

These compounds also are commonly used as feed additives for cattle, poultry or fish because they may make muscle grow faster; whether muscle from such livestock have higher levels of these compounds remains unknown.

"Knowing that gut flora generates a pro-atherosclerotic metabolite from a common dietary lipid opens up new opportunities for improved diagnostics, prevention and treatment of heart disease," Dr. Hazen said. "These studies suggest we can intelligently design a heart healthy yogurt or other form of probiotic for preventing heart disease in the future. It also appears there is a need for considering the risk vs. benefits of some commonly used supplements."

Journal Reference: 1.Zeneng Wang, Elizabeth Klipfell, Brian J. Bennett, Robert Koeth, Bruce S. Levison, Brandon DuGar, Ariel E. Feldstein, Earl B. Britt, Xiaoming Fu, Yoon-Mi Chung, Yuping Wu, Phil Schauer, Jonathan D. Smith, Hooman Allayee, W. H. Wilson Tang, Joseph A. DiDonato, Aldons J. Lusis, Stanley L. Hazen. Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. Nature, 2011; 472 (7341): 57 DOI: 10.1038/nature09922