



Good review and references list here ... but some considerations:

- need for complementing plant proteins is not correct
- citing India's vast vegetarianism as proof that meat is not required is not a good reference point, at least without more nuance, since many there engage in suboptimal vegetarian diet practices that could be improved
- there may be a good role for concentrated plant proteins in optimizing plant diets (protein powders for smoothies, soy milk, healthy high protein snacks, plant based meats)
- What is latest update with TMAO and CVD?



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See the Authors references re eggs

Editorial

Reducing Cardiovascular Risk: The Potential of Plant-Based Meat Alternatives and Egg Substitutes

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See article by Nagra et al., pages XXX-XX of this issue.

In an excellent review of plant-based meat alternatives in this issue of the *Canadian Journal of Cardiology*, Nagra et al.¹ focus on reduction of cardiovascular risk factors, and the effects of various individual dietary factors on cardiovascular risk. For example, “Soy consumption may reduce risk of CVD, CHD, and stroke by 16%, 17%, and 18% respectively, while also reducing risk of several cancers, including breast cancer.” And, “Canola oil significantly reduced TC, LDL-C, and apoB compared with other oils.” They found improvement in cardiometabolic risk profiles with plant-based meat alternatives, but no reduction of blood pressure. However, what really matters is not the effect of individual components of a diet, nor the effect of diet on cardiovascular risk factors; what matters is the effect of diet on the actual risk of cardiovascular events such as myocardial infarction and stroke. Most physicians markedly underestimate the cardiovascular benefit of diet and place far too little emphasis on diet in the management of patients at high risk of cardiovascular events.

In recent years there has been much controversy about the potential benefits of various approaches to diet, including low-carbohydrate diets, the keto and paleo diets, alternate-day fasting, and so on. However, it's not all that complicated: Based on the evidence from randomised clinical trials, the Cretan Mediterranean diet is the best for cardiovascular risk, although it's possible that a vegetarian diet might be as good or better. The reduction of actual cardiovascular risk with diet is much greater than the reduction of cardiovascular risk factors.

The Cretan Mediterranean diet is a mainly vegetarian diet,² high in whole grains, fruits, vegetables, legumes, and monounsaturated fat, and low in meat and dairy products. In the Seven Countries Study, the 10-year coronary risk among men in Crete was 1/15th that in Eastern Finland (200 vs 3000 events).³ The percentage of calories from fat was 40% in

Crete vs 38% in Finland, but in Crete it was olive oil and in Finland animal fat, which is always accompanied by cholesterol. Dietary cholesterol markedly increases the adverse effects of saturated fat.⁴ Notwithstanding controversy (probably largely industry generated), it is clear that dietary cholesterol intake is harmful.^{5,6}

An excellent randomized controlled trial in Israel (> 90% adherence at 1 year and > 80% at 2 years) showed the same weight loss with a low-carbohydrate (Atkins-style) diet and the Mediterranean diet, and both were better than a low-fat diet. Importantly, the Mediterranean diet was the best for lowering fasting glucose, fasting insulin, and insulin resistance.⁷

The Spanish Primary Prevention of Cardiovascular Disease with a Mediterranean Diet (*Prevención con Dieta Mediterránea* [PREDIMED]) study randomised overweight nondiabetic persons with risk factors to a low-fat vs a Mediterranean diet, and there were 2 arms in the Mediterranean diet: supplementation with olive oil or mixed nuts. The primary end point was a major cardiovascular event (myocardial infarction, stroke, or death from cardiovascular causes). In the intention-to-treat analysis including all the participants and adjusting for baseline characteristics and propensity scores, the hazard ratios, compared with the control diet, were 0.69 (95% confidence interval [CI] 0.53-0.91) for a Mediterranean diet with extra-virgin olive oil and 0.72 (95% CI, 0.54-0.95) for a Mediterranean diet with nuts.⁸

Regarding protein intake, supplements are not necessary, nor is animal flesh. Approximately 600 million people in India do just fine on a vegetarian diet. Legumes are missing some of the essential amino acids, whereas grains are missing different ones, so combining grains and legumes (eg, rice and beans or lentils) gives a complete protein. Furthermore, a vegetarian diet, in addition to being better for the environment, saves the consumer money.⁹ (Have you noticed the price of chicken and other kinds of animal flesh in our supermarkets lately?)

Besides plant-based meat substitutes, there is great potential for reduction of cardiovascular risk with the use of egg substitutes. Cardiovascular harm from meat and egg yolks is not only due to the high content of cholesterol and saturated fat in meat, and the very high cholesterol content in egg yolks; it is also due to elevation of plasma levels of toxic metabolites of the intestinal microbiome, such as trimethylamine N-oxide

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See page 2 for disclosure information.

Table 1. Egg yolk vs Hardee's Monster Thickburger: content of cholesterol and TMAO precursors

	Cholesterol content	TMAO precursor
2 large egg yolks*	474 mg	320 mg phosphatidylcholine
Hardee's Monster Thickburger [†]	265 mg	320 mg carnitine

TMAO, trimethylamine N-oxide.

*Jumbo (75 g) eggs.

[†] 12 ounces of beef, 3 slices of cheese, 4 slices of bacon.

(TMAO). Plasma levels of TMAO increase linearly with egg consumption.¹⁰

The toxic metabolites of the intestinal microbiome have been of increasing interest in recent years. In a study of extreme phenotypes of atherosclerosis, patients with unexplained atherosclerosis (severe atherosclerosis despite absence of traditional risk factors) were compared with a protected phenotype (normal arteries despite high levels of cardiovascular risk factors). "Plasma levels of TMAO, p-cresyl sulfate, p-cresyl glucuronide, and phenylacetylglutamine were significantly lower among patients with the protected phenotype, and higher in those with the unexplained phenotype, despite no significant differences in renal function or dietary intake of nutrient precursors of gut-derived uremic toxins. In linear multiple regression with a broad panel of risk factors, TMAO ($P < 0.011$) and p-cresyl sulfate ($P < 0.011$) were significant independent predictors of carotid plaque burden."¹¹

Carnitine in meat (particularly red meat) and phosphatidylcholine in egg yolk are converted by intestinal bacteria to trimethylamine, which is then oxidised in the liver to TMAO. The intestinal metabolites are renally eliminated; even moderate renal impairment (an estimated glomerular filtration rate < 66 mL/min/1.73 m²) significantly raises plasma levels of the toxic intestinal metabolites,¹² and that level of renal function is normal in patients aged > 75 years.¹³ This has important dietary implications: Patients with impaired renal function, including the elderly, should limit meat intake and avoid egg yolk.

Thanks, no doubt, to inexplicably successful propaganda of the egg industry,¹⁴⁻¹⁶ most of the public, as well as most physicians, have no idea how harmful egg yolk is. Cardiovascular harm from meat and egg yolks was reviewed in 2021.⁵ Table 1 compares egg yolk with a dietary monstrosity, the Hardee's Monster Thickburger. Two large egg yolks contain much more cholesterol, and as much TMAO precursor, as the monster burger, which contains about 4 days' worth of meat on a healthy diet. Over a year, the harmful contents of 2 eggs a week would be equivalent to those of about 200 extra days' worth of meat!

An important clinical trial by Hazen's group showed that switching from red meat to white meat or meatless meals significantly reduced plasma TMAO within a month.¹⁷ Egg substitutes such as No Fat Egg Creations, Just Egg, Better'n Eggs, and others can be used to make tasty omelets, frittatas, egg salad sandwiches, and most other egg dishes. (Recipes are available from the author on request.) Like plant-based meat substitutes, they should be used much more frequently by persons at risk of cardiovascular disease.

Persons at risk of cardiovascular disease should limit meat intake and avoid egg yolk, so plant-based meat substitutes and egg substitutes are helpful to patients wishing to reduce their cardiovascular risk. Their effect on reducing actual cardiovascular risk is undoubtedly much greater than their effect on cardiovascular risk factors.

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