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Letters to the Editor
All-Cause Mortality, Cholesterol and Eggs

To the Editor:

The review by Spence et al concludes that those at risk of vascular disease (which Canadian is not?) should avoid cholesterol, particularly eggs.[1] Before abandoning eggs, let us first consider total cholesterol and all-cause mortality. In most population studies, those with low(est) cholesterol die first. Typical is the Austrian Vorarlberg study with top mortality in the bottom quartile for cholesterol, an association not reaching full statistical significance only in men younger than 50 years.[2] Interestingly, the Quebec Cardiovascular Study found no link between cholesterol and coronary disease in men.

The article offers no placebo-controlled studies with cholesterol or egg feeding and clinical endpoints; 15 references are opinion pieces, and 41 are observational studies (epidemiologic, human, animal, in vitro) with surrogate endpoints such as flow-mediated dilation, lipid changes, and sudanophylic (lipid) stains in arteries.

The authors suggest that statins lower cholesterol approximately 5 times more than "low-fat" diets do, but there are no studies showing that even statins lower mortality in women, also a finding for anybody in all atorvastatin (Lipitor) studies ever done (references in[3]). How could egg avoidance do better?

The authors discuss oxidized cholesterol as confounder. Soft-boiled or poached eggs have none, as opposed to dried yolk (found in many processed foods), jerky, or crispy bacon. No cited rabbit, knockout mouse, primate, or pig study used fresh yolk.

The authors argue that dietary (cholesterol-raising) saturated fat and cholesterol may be as toxic as cigarettes: "[S]topping egg consumption after a myocardial infarction or stroke would be like quitting smoking after lung cancer." First, cholesterol is not a risk factor for stroke. Second, low and lowering cholesterol, especially after ages 50 or 60, is a risk factor for early death,[2,4(refs4-13)] cognitive decline, heart failure, and survival after infarcts, all among the dozens of "cholesterol paradoxes."

Eggs are tasty and cheap sources of unprocessed, high-quality nutrients, including carotenoids such as lycopene, and vitamin D3. Eggs may marginally raise high-density lipoprotein and total cholesterol, which, especially in older people, may be of overall benefit. If cardiac risk would be from oxysterols, the authors should have suggested the avoidance of products containing dried or overfried fats and cholesterol but mentioned that fresh boiled, poached, or "over easy" eggs are fine. Such a suggestion would have brought the authors in line with their references 1 through 5, which conclude that eggs are of no harm.

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Disclosures

The authors report no conflict of interest.

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Not All Eggs Are Created Equal: The Effect on Health Depends on the Composition

To the Editor:

A recent review addressed the increasing tendency to accept daily egg as optional in healthy diets, particularly in patients with or at risk for vascular disease. It emphasized that "diet is not all about fasting blood lipids," but rather the post-prandial effects of high cholesterol, ie, increased LDL oxidation (37% with 2 eggs/day), increased post-prandial lipemia (following >140mg cholesterol/meal), and potentiated adverse effects of dietary saturated fat (ie, bacon and butter, compared to egg consumed with salad oil). Eggs may further induce inflammation per observed elevations of CRP and amyloid A, with worsened macrophage accumulation in adipose tissue. The Physician's Health Study showed a 2-fold increase in CVD and all-cause mortality following onset of diabetes, and that egg consumption independently increased rates of new-onset diabetes.

It is worth noting that most of these deleterious effects could be addressed by egg composition modifications. Two/day eggs with reduced n-6 PUFA and increased n-9 MUFA and antioxidants (vitamin E, carotenoids, selenium) reversed egg-induced increased LDL oxidation to levels of 2-4 eggs/week (Figure 1).[1] One/day n-3 PUFA-fortified egg improved triglyceride and HDL levels,[2] ApoB:ApoA1 ratio, and fasting plasma glucose.[3] Similarly, 2/day eggs modified for reduced n-6 PUFA and enhanced n-9 MUFA and antioxidants reduced fasting glucose compared to 2/day regular western high n-6-PUFA eggs. Being an effective antioxidant delivery system, as shown by increased blood vitamin E and carotenoids,[1] and the finding that n-3 PUFA-fortified egg also reduced CRP,[4] suggests that "designer" eggs may provide protection against oxidative stress, inflammation, and acute effects of high glycemic load, recently linked to increased inflammation and reduced blood antioxidants, potentially associated with diabetes risk.

The above emphasize that not all eggs are created/prepared equal, and further, egg is not purely cholesterol, but rather a high nutritional value food with a unique capacity to transform and concentrate protective nutrients (ie, DHA, antioxidants) that can modify metabolic/physiological effects. Moreover, eggs' high "satiety index" makes them an important candidate against obesity, and much lower carbon footprint than chicken, beef, or pork yields environmental advantages.

Designing protective compositions and preparation, ie, based on advantageous Mediterranean/Greek-type eggs and dietary principles – high n-3 PUFA, n-9 MUFA, and antioxidants, with low n-6 PUFA – could significantly influence egg-related benefits vs risks. Modifications more suited to requirements of subpopulations could differentially widen recommendations to accept vs reject eggs. Most of us will benefit, though consumption may remain advised against in some metabolically/genetically-sensitive and/or hyperlipidemic individuals.

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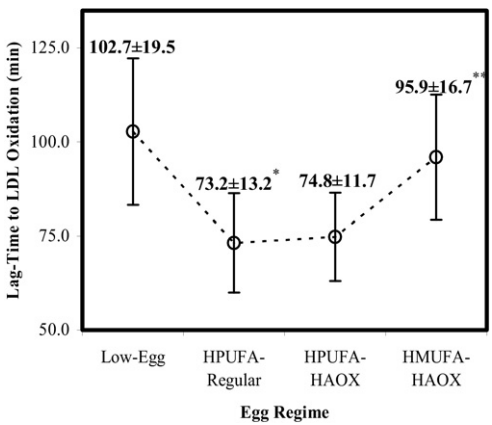

Figure 1. Lag-time to plasma LDL oxidation following low-egg (2-4/week) or high-egg (2/day) regular high n-6 PUFA (HPUFA-Regular), high n-6 PUFA+high-antioxidant (HPUFA-HAOX), or high n-9 MUFA+high-antioxidant (HMUFA-HAOX) 3-week regimes (n=17)[1]. $^{*}P < 0.01$ (vs. low-egg); $^{**}P < 0.01$ (vs. regular egg).

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Eggs and Health Benefits

To the Editor:

Spence et al.[1] send a strong message against eggs as the "target food" for dietary cholesterol (DC). The purpose of my letter is to draw attention to the published and well-established facts regarding the effects of eggs on health.

A review of the current dietary guidelines for DC reports that the European Union, *Canada,* India, Korea, New Zealand, and other countries have *no guidelines* regarding DC.[2] In contrast, there is a worldwide consensus limiting saturated fat intake. Further, recent epidemiologic studies[2] have demonstrated that there is no correlation between egg consumption and coronary heart disease risk, which is not surprising given that (1) eggs consistently increase high-density lipoprotein (HDL) maintaining the low-density lipoprotein (LDL)/HDL ratio[3] even under conditions where LDL is not raised[2]; (2) eggs contain lutein, a carotenoid known to protect against macular degeneration,[3] oxidative stress, inflammation, and atherosclerosis[2]; (3) eggs are a good source of choline, a key nutrient for normal fetal development, which may also protect against Alzheimer's disease[4]; (4) eggs suppress appetite and decrease caloric intake during the next 24 hours[2]; (5) eggs are nutrient dense and an affordable source of high-quality protein[5]; and (6) decreased egg consumption has been correlated with protein malnutrition in underdeveloped countries.

Spence et al.[1] cite a study where the equivalent to 9500 mg/day of DC (1.25%) increases endothelial dysfunction in mice. Other cited animal studies also used DC challenges not related to human intake. In contrast, egg consumption is not related to detrimental endothelial function.

Dietary recommendations should not be based on eliminating eggs, an excellent source of nutrients and other components that provide benefits that extend beyond nutrition.

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Disclosures

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Reply to Letters from Dr Maria Luz Fernandez, Eddie Vos, and Dr Niva Shapira

To the Editor:

The letter of Dr Shapira rightly points out that the question of cholesterol oxidation is related to what happens in vivo as much as to what may occur in the frying pan, and that low-density lipoprotein (LDL) oxidation is part of the problem. It is worth remembering that elevated circulating cholesterol has deleterious pleiotropic effects that are exerted via LDL cholesterol (LDL-C) and that may affect several physiological functions. Elevated LDL-C has been associated with an increased atherogenic potential related to enhanced susceptibility to oxidation (malondialdehyde modification), hypercoagulability (increase in beta-thromboglobulin, thromboxane B2), enhanced platelet reactivity (increase in soluble P-selectin, reduction of eNOS), reduced fibrinolysis (increase in plasminogen activator inhibitor-1), endothelial dysfunction (reduced nitric oxide), increased vascular reactivity (increased thromboxane B2 and decreased prostacyclin), increased vascular permeability, and increased plasma viscosity (increased fibrinogen, decreased erythrocyte deformability). It is also proinflammatory (action on nuclear factor κB, macrophages, and IL-1β). The majority of these effects are improved by statins.[1] It would be valuable if the "improved egg product" alluded to shared several of these beneficial pleiotropic properties besides the interesting antioxidant effect. It is important to state, however, that simply giving antioxidant supplements, such as vitamin E, failed to offer protection for coronary heart disease in a number of clinical trials, for example the Heart Outcomes Prevention Evaluation study.

Eggs are clearly not all the same. The Canadian Nutrient File at Health Canada, accessible online at http://webprod.hc-sc.gc.ca/cnf-fce/start-debuter.do?lang=eng, shows that a jumbo chicken egg contains 237 mg cholesterol; a duck egg, 619 mg; and a goose egg, 1227 mg. Eggs from chickens fed flax seed have a higher content of omega-3 fatty acids; however, their cholesterol content is similar to that of other chicken eggs. For patients at risk of vascular disease, it would be better to eat the flax seed and leave the egg cholesterol out of the issue.

Mr. Vos is right about two things: (1) Most Canadians are at risk of vascular disease—the only ones who could eat egg yolk regularly with impunity would be those who expect to die prematurely from nonvascular causes, and (2) it would be good to have a randomized clinical trial. A feasible design would be to randomize vascular patients to consume eggs or egg white–based substitutes, provided in identical containers, with recipes for omelettes and frittatas, and follow these patients for cardiovascular events. We invite the egg marketers to fund it and would be happy to conduct it. We estimate that the costs would be approximately equivalent to their annual costs of advertising.

Unfortunately, Mr Vos confuses fasting serum cholesterol levels with the effect of dietary cholesterol. The more important issue is the postprandial effects of consuming cholesterol, including egg yolk. Focusing on fasting serum cholesterol levels misses the bulk of the problem. Even though serum cholesterol rises very little after a meal, dietary cholesterol increases the susceptibility of LDL-C to oxidation, vascular inflammation, oxidative stress, and postprandial hyperlipemia and potentiates the harmful effects of saturated fat, impairs endothelial function, and increases cardiovascular events (all referenced in our paper). Some of these effects may be related to consumption of oxidized cholesterol, taken up into LDL. Egg yolk consumption also decreased by half the postprandial clearance of atherogenic chylomicron remnants.[2]

Not only cardiovascular mortality,[3] but all-cause mortality (Strandberg et al 2004) is clearly related to elevated serum cholesterol levels, in a graded fashion. Lower serum cholesterol levels in cachectic patients with cancer likely explain reverse associations with all-cause mortality in some studies. The effect of cholesterol levels on stroke risk was for many years obscured by the overwhelming effect of uncontrolled hypertension; in a community where blood pressure was controlled, serum cholesterol was a significant risk factor for stroke.[4] In the Stroke Prevention by Aggressive Reduction in Cholesterol Levels trial, among patients with carotid atherosclerosis, statin treatment reduced recurrent stroke by 33%.[5] Amarenco has shown clearly in meta-analyses that statins reduce stroke risk.

People at risk of vascular disease (indeed, as Mr. Vos points out, most Canadians) should not regularly consume egg yolks. As discussed in Spence's book, *How to Prevent Your Stroke* (Vanderbilt University Press, 2006), they should learn to make a delicious omelette or frittata using egg whites or egg white–based substitutes such as Egg Beaters, Egg Creations, or in the United States, Better'n Eggs. As eggs are required to make these substitutes, the egg marketers would serve us all better by promoting healthy consumption of egg whites rather than dangerous consumption of yolks. For those wishing to lower serum cholesterol levels, tofu scrambler (Amy's Kitchen, Petaluma, CA) is a useful substitution for scrambled eggs since soy consumption per se may lower serum cholesterol.

It is curious how Dr Fernandez, like many others, simply doesn't want to look at the evidence. We summarized clearly the evidence that cholesterol has a permissive effect on, and amplifies the effect of, saturated fat. Dietary cholesterol clearly increases coronary risk. The same large, frequently cited studies that showed no harm from egg yolks among participants who remained healthy showed that egg yolks doubled coronary risk among participants who became diabetic during follow-up. The apparent absence of harm from egg yolks among people who remained healthy during the period of observation is probably an issue of statistical power.

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