



Letter to the Editor

Egg yolk consumption, smoking and carotid plaque: Reply to letters to the Editor by Sean Lucan and T Dylan Olver et al.

*Keywords:*

Egg yolk consumption
Smoking
Carotid plaque

We are not saying that egg yolks should be banished entirely – egg yolks are an essential ingredient in such culinary delicacies as Hollandaise and Béarnaise sauce, and whole eggs may be important nutritionally for starving children in third world countries. However, most vascular prevention patients in the Western world are over-nourished, not undernourished. Our recommendation that people at risk of vascular disease should limit their intake of egg yolks was based not only on the findings in our recent paper [1], but also on the totality of the evidence [2].

The point of view to which Dr. Lucan apparently subscribes is that dietary cholesterol is about fasting levels of LDL cholesterol. Certainly fasting LDL-C has been the gold standard for statin-like effects. However, fasting LDL cholesterol levels are determined mainly by cholesterol production in the liver overnight, and have little to do with what the patient consumed the previous day: they are like a baseline, on top of which the effects of diet can be assessed. Diet is mostly about the postprandial state [3]. Olver and colleagues assert that our study contained no data to support that statement, and it is obvious that it did not. They ask for experimental evidence of harm from dietary cholesterol; that evidence was reviewed by us in 2010, and as we reported [2], dietary cholesterol increases cardiovascular risk, probably mainly because of postprandial effects: for several hours after a high-cholesterol meal there is an increase in oxidative stress, vascular inflammation and adverse effects on endothelial function, and oxidation of LDL cholesterol is increased by nearly 40%. Dietary cholesterol is permissive of the harmful effect of saturated fats [4].

We believe a half-truth is promoted by the advertising slogan “eggs can be part of a healthy diet for healthy people”. Cohort studies are often cited to indicate that those who consume eggs may not be any more unhealthy than those who do not. This view should be tempered with Rose’s concept of a “sick population” [5] where ill health is ubiquitous and the range of “health” may not be sufficiently broad to establish a significant association. Furthermore, egg consumption “in a healthy diet” will displace “unhealthy” protein foods including saturated fat and cholesterol-laden meat dishes. Consequently, it has been recognized for many years that vegetarians may be at reduced CHD risk compared to non-vegetarians [6,7]. Many vegetarians are lacto-ovo-vegetarians [6,7]. We maintain that it is not the eating of eggs that makes them healthy, but their avoidance of

animal products in favour of plant foods. Furthermore, the two US-based studies that are often referred to as demonstrating no ill effects of eggs [8,9] also demonstrated that an egg a day doubled coronary risk among participants who became diabetic during followup. A Greek study in diabetics showed that an egg a day increased coronary risk 5-fold. Egg consumption also increases the risk of diabetes [10].

Our concern over dietary cholesterol is not new. Both Ancel Keys and Mark Hegsted included dietary cholesterol in equations designed to predict changes in serum cholesterol [11,12], and dietary cholesterol increases cardiovascular risk [2].

Egg yolks do contain a lot of cholesterol—more than 200 mg in the yolk of a large egg, i.e. more than the daily recommended intake of cholesterol for people at risk of vascular disease [13]. Egg whites are a good source of dietary protein, and are recommended in preference to whole eggs in the European guidelines for the management of dyslipidemia [14]. Njike et al. showed [15] that compared to whole eggs, egg-white-based egg substitutes improved endothelial function. As a substitute for meat-based meals, vascular patients should learn to make a tasty omelet or frittata, using egg whites or egg-white-based substitutes such as Egg Beaters® or Better ‘n Eggs®, or better still, a Tofu Scrambler (Amy’s Kitchen, Petaluma, CA), since soy proteins actually lower LDL-C [16–18].

However, there is another problem with egg yolks beyond the cholesterol content. A large egg yolk contains ~250 mg of phosphatidylcholine (lecithin), which is converted by intestinal bacteria to trimethylamine [19]. Trimethylamine in turn is oxidized in the liver to trimethylamine n-oxide (TMAO), which is toxic to the arteries [19,20]. Indeed, growing recognition of the interaction between diet, the intestinal microbiome and health [21] will revolutionize our understanding of these issues.

Olver and colleagues ask what the hypothesis was. Based on observations during 36 years of experience with patients at risk of stroke, and more than 20 years of studying carotid total plaque area, the hypothesis was that egg yolk consumption might affect carotid total plaque area in a manner similar to that of smoking. Like Dr. Lucan, they raise concerns about the inability to adjust for exercise and other dietary factors. We acknowledged the limitations of our data, which limited our ability to adjust for other dietary factors such as exercise, fat, and on starches and sugars, on which Dr. Lucan also focuses. However, body mass index, which

Table 1
Eggs per week by quintile of egg-yolk-years.

Egg-yolk-years	N	Eggs per week (mean)	Std. deviation	Minimum	Maximum
<50	220	0.47	0.44	0.0	2.5
50–110	207	1.37	0.54	0.7	3.0
110–150	263	2.30	0.53	1.5	4.0
150–200	238	2.76	0.59	1.9	4.5
≥200	302	4.68	3.03	2.5	30.0

Table 2
Effect of egg yolks and smoking on carotid total plaque area: interaction of egg yolks and smoking (all adjusted for age in the General Linear Model; $p = 0.0001$ for all comparisons of little-smoking little-egg eaters with other groups.).

Smoking and egg yolk consumption	Little-smoking little-egg eaters (pack-years <10, egg yolks quintile 1 or 2) $n = 95$	Little-smoking big egg eaters (pack-years <10, egg yolks quintile 4 or 5) $n = 284$	Smoking little-egg eaters (pack-years ≥10, egg yolks quintile 1 or 2) $n = 185$	Smoking big egg-eaters (pack-years ≥10, egg yolks top quintile) $n = 155$
Plaque area (mm ²)	69.16 ± 89.05	122.39 ± 114.48	153.73 ± 141.76	213.61 ± 164.62
Increase in plaque area (mm ²)	Comparator	53.23	84.57	144.45
Ratio	Comparator	1.77	2.22	3.09

was included in the multiple regression model, probably adjusts to a large extent for a high intake of those dietary factors.

With regard to the validity of the data on egg yolk consumption from dietary recall, this is an issue, as we stated in discussing the limitations of our study, that is common to all dietary studies relying on recall by patients, including those that can adjust for exercise, fat consumption and other dietary factors. Data on smoking history and exercise is similarly based on recall. With regard to the issue of dietary cholesterol and risk of diabetes, Dandona reviewed in 2010 [22] the effects of macronutrients on inflammation and insulin resistance, and van Bussel et al. [23] found in 2012 that dietary cholesterol was significantly associated with markers of inflammation and endothelial dysfunction in diabetics.

With regard to the need for additional experimental evidence, we offered [24], in a reply to letters to the Editor regarding our 2010 review, to carry out a randomized trial of eggs versus egg substitutes, and estimated that it could easily be funded out of the annual advertising budget of the egg industry. Olver and colleagues argue that we did not perform enough statistical analyses. To address a question sent by email by another reader, we analysed in our database the interaction between smoking and egg yolk consumption. Table 1 shows the number of eggs per week consumed by participants in the five quintiles of egg-yolk-years, and Table 2 shows the interaction between smoking and egg yolk consumption.

Compared to little-smokers (<10 pack-years) who were in the first quintile of egg consumption, egg yolks alone (quintiles 4 and 5 of egg-yolk-years) increased carotid total plaque area (TPA) 1.77-fold, smoking alone (>10 pack-years) increased TPA 2.22-fold, and the combination of smoking >10 pack-years and egg consumption in the top quintile increased TPA 3.09-fold (all significant after adjustment for age). Thus the effect of egg yolks and smoking appears to be additive, with egg yolks alone having approximately 62% of the effect of smoking alone.

Our study showed that compared to the increase of carotid plaque area by age alone, both smoking and egg yolk consumption accelerate carotid total plaque area, which is a very strong predictor of cardiovascular risk [25–28]. A 20-year old man might feel it would be safe to smoke and eat egg yolks, because his myocardial infarction is 45 years or so in the future – but why would he want to accelerate the progression of his atherosclerotic plaque to bring it on sooner? “Stopping egg yolks after the heart attack would be like quitting smoking after lung cancer is diagnosed” [2].

References

- Spence JD, Jenkins DJ, Davignon J. Egg yolk consumption and carotid plaque. *Atherosclerosis* 2012;224(2):469–73.
- Spence JD, Jenkins DJ, Davignon J. Dietary cholesterol and egg yolks: not for patients at risk of vascular disease. *Can J Cardiol* 2010;26:e336–9.
- Spence JD. Fasting lipids: the carrot in the snowman. *Can J Cardiol* 2003;19:890–2.
- Fielding CJ, Havel RJ, Todd KM, et al. Effects of dietary cholesterol and fat saturation on plasma lipoproteins in an ethnically diverse population of healthy young men. *J Clin Invest* 1995;95:611–8.
- Rose G. Sick individuals and sick populations. *Int J Epidemiol* 2001;30:427–32.
- Phillips RL, Lemon FR, Beeson WL, Kuzma JW. Coronary heart disease mortality among seventh-day Adventists with differing dietary habits: a preliminary report. *Am J Clin Nutr* 1978;31:S191–8.
- Fraser GE. Vegetarian diets: what do we know of their effects on common chronic diseases? *Am J Clin Nutr* 2009;89:1607S–12S.
- Hu FB, Stamper MJ, Rimm EB, et al. A prospective study of egg consumption and risk of cardiovascular disease in men and women. *JAMA* 1999;281:1387–94.
- Qureshi AI, Suri FK, Ahmed S, Nasar A, Divani AA, Kirmani JF. Regular egg consumption does not increase the risk of stroke and cardiovascular diseases. *Med Sci Monit* 2007;13:CR1–8.
- Djousse L, Gaziano JM, Buring JE, Lee IM. Egg consumption and risk of type 2 diabetes in men and women. *Diabetes Care* 2009;32:295–300.
- Keys A. Serum cholesterol response to dietary cholesterol. *Am J Clin Nutr* 1984;40:351–9.
- Hegsted DM. Serum-cholesterol response to dietary cholesterol: a re-evaluation. *Am J Clin Nutr* 1986;44:299–305.
- Healthy People. National health promotion and disease prevention objectives. United States Department of Health and Human Services; 2000. 1991.
- Catapano AL, Reiner Z, De BG, et al. ESC/EAS guidelines for the management of dyslipidaemias: the task force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). *Atherosclerosis* 2011;217(Suppl. 1):S1–44.
- Njike V, Faridi Z, Dutta S, Gonzalez-Simon AL, Katz DL. Daily egg consumption in hyperlipidemic adults—effects on endothelial function and cardiovascular risk. *Nutr J* 2010;9:28.
- Sirtori CR, Agradi E, Conti F, Mantero O, Gatti E. Soybean-protein diet in the treatment of type-II hyperlipoproteinaemia. *Lancet* 1977;1:275–7.
- Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med* 1995;333:276–82.
- Jenkins DJ, Mirrahimi A, Srichaikul K, et al. Soy protein reduces serum cholesterol by both intrinsic and food displacement mechanisms. *J Nutr* 2010;140:2302S–11S.
- Wang Z, Klipfell E, Bennett BJ, et al. Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. *Nature* 2011;472:57–63.
- Rak K, Rader DJ. Cardiovascular disease: the diet-microbe morbid union. *Nature* 2011;472:40–1.
- Clemente JC, Ursell LK, Parfrey LW, Knight R. The impact of the gut microbiota on human health: an integrative view. *Cell* 2012;148:1258–70.
- Dandona P, Ghanim H, Chaudhuri A, Dhindsa S, Kim SS. Macronutrient intake induces oxidative and inflammatory stress: potential relevance to atherosclerosis and insulin resistance. *Exp Mol Med* 2010;42:245–53.
- van Bussel BC, Soedamah-Muthu SS, Henry RM, et al. Unhealthy dietary patterns associated with inflammation and endothelial dysfunction in type 1 diabetes: the EURODIAB study. *Nutr Metab Cardiovasc Dis* 2012, epub ahead of print PMID: 22795869.

- [24] Spence JD, Jenkins DJA, Davignon J. Egg yolk consumption, smoking and carotid plaque: reply to letter to the Editor. *Canadian Journal of Cardiology* 2011;27:264.e7–8. www.onlinecjc.ca.
- [25] Inaba Y, Chen JA, Bergmann SR. Carotid plaque, compared with carotid intima-media thickness, more accurately predicts coronary artery disease events: a meta-analysis. *Atherosclerosis* 2011;220:128–33.
- [26] Spence JD, Eliasziw M, DiCicco M, Hackam DG, Galil R, Lohmann T. Carotid plaque area: a tool for targeting and evaluating vascular preventive therapy. *Stroke* 2002;33:2916–22.
- [27] Johnsen SH, Mathiesen EB, Joakimsen O, et al. Carotid atherosclerosis is a stronger predictor of myocardial infarction in women than in men: a 6-year follow-up study of 6226 persons: the Tromso study. *Stroke* 2007;38:2873–80.
- [28] Mathiesen EB, Johnsen SH, Wilsgaard T, Bonna KH, Lochen ML, Njolstad I. Carotid plaque area and intima-media thickness in prediction of first-ever ischemic stroke: a 10-year follow-up of 6584 men and women: the Tromso study. *Stroke* 2011;42:972–8.

J. David Spence*

*Stroke Prevention & Atherosclerosis Research Centre,
Robarts Research Institute, University of Western Ontario, 1400
Western Road, London, ON N6G 2V2, Canada*

David J.A. Jenkins
*Nutrition and Metabolism, Risk Factor Modification Centre, St.
Michael's Hospital, Toronto, Ontario, Canada*

Jean Davignon
*IRCM, Clinique de nutrition métabolisme et athérosclérose,
Institut de recherches cliniques de Montréal, Canada*
Faculty of medicine, University of Montreal, Canada
Experimental Medicine, McGill University, Montréal, QC, Canada

* Corresponding author. Tel.: +1 519 931 5731;
fax: +1 519 931 5737.

E-mail addresses: dspence@robarts.ca, [http://
www.imaging.robarts.ca/SPARC/](http://www.imaging.robarts.ca/SPARC/) (J.D. Spence)

5 October 2012
Available online 8 November 2012