

11-1-2019

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### **Citation of this paper:**

Spence, J. David, "Trimethylamine N-oxide: Not just red meat - Egg yolk and renal function are also important" (2019). *Department of Medicine Publications*. 182.  
<https://ir.lib.uwo.ca/medpub/182>

# Trimethylamine N-oxide: not just red meat—egg yolk and renal function are also important

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Online publish-ahead-of-print 8 October 2019

**This commentary refers to ‘The red and the white, and the difference it makes’, by A. Davies and T.F. Lüscher, 2019;40:595–597.**

In their editorial about trimethylamine N-oxide (TMAO), Davies and Lüscher<sup>1</sup> said that the study referred to ‘proves that red meat, through L-carnitine, is the major source of elevated TMAO plasma levels in a healthy Western population’. That statement ignores the major contribution of egg yolk to TMAO production, from phosphatidylcholine. The yolks of two large (65 g) eggs contain 474 mg of cholesterol and 320 mg of phosphatidylcholine, i.e., more cholesterol and as much TMAO precursor as a Hardee’s Monster Thickburger, a 12-ounce beef burger. There is a linear dose response of plasma TMAO with egg consumption; two eggs more than double levels of TMAO.

In patients referred for coronary angiography, Tang *et al.*<sup>2</sup> measured plasma TMAO after a test dose of two hard-boiled eggs, and found that patients in the highest quartile of TMAO had a 2.5-fold increase in the 3-year risk of stroke, myocardial infarction, or vascular death.

Patients with severe atherosclerosis not explained by traditional risk factors (unexplained atherosclerosis) had significantly higher levels of TMAO, P-cresylsulfate, p-cresyl glucuronide, and phenylacetylglutamine than patients with high levels of risk factors and little/no carotid plaque (protected phenotype), despite no differences in dietary intake of TMAO precursors and no difference in renal function.<sup>3</sup> In backward linear regression, both TMAO and p-cresylsulfate were significant predictors of carotid plaque, and more significant than sex, diastolic blood pressure, total cholesterol, and diabetes mellitus.<sup>3</sup>

This suggests that approaches such as repopulation of the intestinal microbiome may be a way to treat atherosclerosis.

High levels of TMAO accelerate decline in renal function, and increase mortality in patients with severe renal disease. However, we found that plasma levels of TMAO and six other intestinal metabolites were significantly elevated by even mild renal impairment; an estimated glomerular filtration rate (eGFR) <66 mL/min/1.73 m<sup>2</sup>.<sup>4</sup> Renal function declines with age; above age 80 the mean eGFR among patients referred to our stroke prevention clinics was <60 mL/min/1.73 m<sup>2</sup>.

Thus, patients with impaired renal function, including the elderly, should not only limit intake of red meat, but should also avoid egg yolk. Egg whites and egg white-based substitutes can be used instead to make delicious omelettes, frittatas, and egg salad sandwiches.

**Conflict of interest:** none declared.

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