Prevalence of apolipoprotein E epsilon4 allele may explain the geographical variation of coronary heart disease mortality rates in Western Europe

William B. Grant

Received: 5 July 2010 / Accepted: 16 July 2010 / Published online: 29 July 2010
© Springer Science+Business Media B.V. 2010

To the Editor,

A paper by Wong [1] reported an inverse correlation between incident solar radiation and coronary heart disease (CHD) mortality rates in Western Europe. It was hypothesized that the associated was mediated by vitamin D3 synthesis. This hypothesis is supported by a recent meta-analysis of prediagnostic serum 25-hydroxyvitamin D [25(OH)D] levels and incidence of cardiovascular disease [2]. However, vitamin D production is due only to ultraviolet-B (UVB) irradiance, not total insolation. Since Nordic countries experience about a six-month vitamin D winter [3], oral intake of vitamin D is higher in northern Europe than in southern Europe, resulting in higher serum 25(OH)D levels in the north, as shown in Figure 8 in [1].

An alternate explanation for the correlation with incidence solar radiation is the variation of the prevalence of apolipoprotein E epsilon4 (ApoE4) allele, which is a significant risk factor for CHD [4]. At higher latitudes, fresh fruits and vegetables are less readily available than at lower latitudes (see Figure 1 in [1]); as a consequence, prevalence of the ApoE4 allele increases with latitude. Based on data in Gerdes et al. [5], the prevalence of ApoE4 rises from 8.3% in Greece to 22% in Finland with a slope of 0.53% per degree latitude [6]. ApoE4 causes the liver to produce more cholesterol and the pancreas more insulin in order to store more food as fat when food is more abundant [6]. Average solar insolation falls from 4.7 kWh/m² per day at 37°N to 2.0 kWh/m² per day at 64°N [5]. The graph

of CHD mortality rate vs. insolation in Figure 4 of [1] has a very similar shape to the insolation vs. latitude graph in Figure 3 of [1].

Ecological studies of CHD in Europe can be difficult to do properly. In an ecological study I identified milk and sweeteners as important risk factors [7], but realized later that milk is not a risk factor [8] although sweeteners are [9].

References

1. Wong A. Incident solar radiation and coronary heart disease mortality rates in Europe. *Eur J Epidemiol*. 2008;23:609–14. doi:10.1007/s10654-008-9274-y.
2. Parker J, Hashmi O, Dutton D, Mavrodaris A, Stranges S, Kandala NB, et al. Levels of vitamin D and cardiometabolic disorders: systematic review and meta-analysis. *Maturitas*. 2010;65:225–36. doi:10.1016/j.maturitas.2009.12.013.
3. Webb AR, Engelsen O. Calculated ultraviolet exposure levels for a healthy vitamin D status. *Photochem Photobiol*. 2006;82:1697–703. doi:10.1111/j.1751-1097.2006.tb08353.x.
4. Bennet AM, Di Angelantonio E, Ye Z, Wensley F, Dahlin A, Ahlbom A, et al. Association of apolipoprotein E genotypes with lipid levels and coronary risk. *JAMA*. 2007;298:1300–11. doi:10.1001/jama.298.11.1300.
5. Gerdes LU, Klausen IC, Sihm I, Faergeman O. Apolipoprotein E polymorphism in a Danish population compared to findings in 45 other study populations around the world. *Genet Epidemiol*. 1992;9:155–7.
6. Grant WB. A multicountry ecological study of risk-modifying factors for prostate cancer: apolipoprotein E epsilon4 as a risk factor and cereals as a risk reduction factor. *Anticancer Res*. 2010;30:189–99.
7. Grant WB. Milk and other dietary influences on coronary heart disease. *Altern Med Rev*. 1998;3:281–94.
8. Grant WB. Commentary: Ecologic studies in identifying dietary risk factors for coronary heart disease and cancer. *Int J Epidemiol*. 2008;37:1209–11.
9. Stanhope KL, Schwarz JM, Keim NL, Griffen SC, Bremer AA, Graham JL, et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *J Clin Invest*. 2009;119:1322–34. doi:10.1172/JCI37385.

W. B. Grant (✉)
Sunlight, Nutrition, and Health Research Center (SUNARC),
P.O. Box 641603, San Francisco, CA 94164-1603, USA
e-mail: wbgrant@infionline.net
URL: www.sunarc.org