Environmental exposure to lead: old myths never die

Based on an analysis of NHANES III, published in *The Lancet Public Health* (April, 2018), Bruce Lanphear and colleagues[1] propose that environmental exposure to lead, even at blood concentrations lower than 5 µg/dL, entails a population-attributable risk of cardiovascular mortality of 37·4%, thereby equalling the risk of smoking. This conclusion contrasts with expert opinion. Based on a comprehensive review of the literature, Navas-Acien and coworkers[2] concluded that there is sufficient evidence to infer a causal association of hypertension with lead exposure, but that the evidence is inconclusive to deduce a causal relation of cardiovascular outcomes with lead exposure. In our meta-analysis,[3] a doubling of blood lead was associated with minimally higher blood pressure, only averaging 1·0 mm Hg (95% CI 0·5–1·4) for systolic blood pressure and 0·6 mm Hg (0·4–0·8) for diastolic blood pressure. A common point of view is that hypertension explains the association of cardiovascular endpoints with lead exposure. However, our analysis of NHANES 2003–2010 showed weak and inconsistent associations of blood pressure with blood lead.[4] This finding excludes current environmental lead exposure as major causal contributor to hypertension in the USA.[4] Notably, in the report by Lanphear and colleagues, associations of cardiovascular and coronary mortality with blood lead remained significant after adjustment for hypertension.[1]

A major limitation of Lanphear and colleagues' study is its exclusive focus on mortality. The introduction of stroke units and the wide availability of invasive coronary care and thrombolysis reduced the case-fatality rate of most cardiovascular complications of hypertension. Not accounting for non-fatal events therefore limits the generalisability of their report. Moreover, the authors did not report on the association of non-cardiovascular mortality with blood lead, an issue of relevance because cardiovascular illness and renal impairment go hand in hand, and environmental exposure to lead might increase the vulnerability of people at risk of chronic kidney disease.[5] The effect sizes reported in Lanphear and colleagues' report inflate the estimates of the population-attributable risk, because they were computed for the 90th to the 10th percentile intervals of the blood lead distribution.[1] Computing this metric assumes causality, which cannot be deduced from an observational longitudinal study. Not surprisingly, all cardiovascular risk factors clustered within the highest third of the blood lead distribution.[1] Blood lead probably serves as a surrogate for socioeconomic disadvantage and unequal access to health care. The authors adjusted for household income,[1] but this adjustment is insufficient to correct for the differential impact of powerful social and ethnic confounders on morbidity and mortality. The authors might address this issue by reporting the interaction terms between ethnicity and blood lead and showing that the estimates of the risk function slopes are similar across income groups. In conclusion, in Lanphear and colleagues' report,[1] hypertension is unlikely to explain the association between mortality and blood lead, and the underlying mechanisms remain unknown, precluding informed preventive strategies and targeted allocation of resources to reduce cardiovascular disease risk.

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