Mascitelli and Goldstein propose that lower levels of redox-active iron could explain some of the observed relationship between low serum bilirubin and the increased incidence of cardiovascular disease. Biliverdin/bilirubin, ferritin, and carbon monoxide are produced in equal quantities by heme-oxygenase–1, and the vascular effects of raised carbon monoxide may also contribute to the relationship between bilirubin and cardiovascular disease reported in our article.\(^1\) Disentangling the individual role of HO-1 products in cardiovascular disease will be difficult, although an independent effect of bilirubin is somewhat supported by Mendelian randomization designs using genetic variation strongly associated with bilirubin clearance.\(^2,3\) However, we should point out that these findings are not consistently replicated.\(^4\) We are not convinced that the results of our study can provide particularly strong support for the iron hypothesis, which remains an interesting area for research and debate.\(^5,6\)

Disclosures

None.

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