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Response to Letter to the Editor

Endotoxin and metabolic syndrome

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Dear Editor,

We are pleased that Dr. M. Manco has found our recent study [1] of interest. Dr Manco states that our data apart from showing important associations, may suggest a causative role for endotoxin in the development of metabolic abnormalities and metabolic syndrome. Whilst we agree that this is indeed plausible, we acknowledged that prospective evidence is required to establish causality. The possibility that endotoxin may represent the missing link between NAFLD/NASH and cardiovascular disease is certainly of interest. It is currently under investigation in our laboratory and we hope to submit our findings very soon.

The effect of diet is an important issue. Full dietary questionnaires were not carried out in the Wandsworth Heart and Stroke Study as at the time there were no validated dietary tools to be used with confidence in ethnic minority populations in the UK (a tool still not available to date). We were however, able to assess the impact of vegetarianism (Results (3.1) [1]). Whilst the issue of diet could not be fully addressed, it was shown that there are no differences in endotoxin levels between vegetarians and non-vegetarians [1].

It is incorrect to suggest that our study lacked obese individuals or subjects with abnormalities typical of the metabolic syndrome. Our population included both obese individuals and those with metabolic syndrome (please refer to Table 1; p. 496 [1]). Furthermore, we now report some additional analyses with participants categorised with different degrees of metabolic syndrome as defined by the ATPIII criteria [2] (Table 1).

In support of our hypothesis, there is a linear increase in endotoxin levels with increasing components of the metabolic syndrome across all ethnic groups. We agree that further studies are required to understand the mechanisms whereby lipopolysaccharide may lead to atherosclerotic development.

References

[1] Miller MA, McTernan PG, Harte AL, et al. Ethnic and sex differences in circulating endotoxin levels: a novel marker of atherosclerotic and cardiovascular risk in a British multi-ethnic population. Atherosclerosis 2009;203:494–502.
[2] Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III Final Report). 2002: 02-5215. http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm.

Table 1
Circulating endotoxin levels according to ATPIII criteria adjusted for ethnicity (total group only), age and sex.

Components of the metabolic syndrome	Total (men = 97, women = 96)		White (men = 32, women = 30)		African origin (men = 35, women = 33)		South Asian (men = 30, women = 33)	
	n	Endotoxin (Eu/mL)	*n*	Endotoxin (Eu/mL)	*n*	Endotoxin (Eu/mL)	*n*	Endotoxin (Eu/mL)
0	57	10.2 (9.2–11.3)	25	9.9 (8.3–11.8)	24	9.7 (8.5–11.1)	8	11.5 (8.5–15.6)
1	51	9.4 (8.4–10.4)	19	9.6 (7.8–11.7)	17	9.0 (7.7–10.4)	15	9.8 (7.8–12.3)
2	43	12.1 (10.8–13.5)	10	13.7 (10.9–18.1)	17	9.7 (8.3–11.3)	16	13.7 (11.1–16.9)
3	28	15.6 (13.4–18.0)	2	19.6 (10.6–36.1)	9	12.9 (10.4–16.6)	17	16.9 (13.8–20.9.)
4	11	13.3 (10.6–16.6)	6	13.3 (9.4–18.8)	0	–	5	14.7 (10.1–21.4)
5	3	22.6 (14.7–34.9)	0	–	1	21.7 (11.5–40.9)	2	23.3 (12.8–42.5)
Linear trend	$P < 0.001$		$P = 0.044$		$P = 0.015$		$P = 0.009$	

Results are geometric means (95% CI).

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