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Environmental contaminants and redox status of coenzyme Q10 and vitamin E in Inuit from Nunavik

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Abstract

The Inuit are heavily exposed to potentially prooxidant contaminants such as methylmercury (MeHg) and polychlorinated biphenyls (PCB) through their traditional diet. This diet is also an abundant source of n-3 polyunsaturated fatty acids (n-3 PUFA), selenium, and antioxidants, which might reduce cardiovascular risk. Although Inuit from Nunavik have low concentrations of plasma oxidized low-density lipoprotein (OxLDL) and elevated glutathione-related antioxidant defenses, the variance in OxLDL was predicted by PCB and blood glutathione, leaving the issue of contaminant-associated oxidative stress unresolved. The objective of the study was to assess oxidative stress in these Inuit by measuring the plasma concentrations and redox states of α-tocopherol and coenzyme Q10 (CoQ10), 2 sensitive biomarkers of oxidative stress, in relation to exposure. Plasma lipophilic antioxidants were determined by high-performance liquid chromatography–coupled electrochemical detection; and their relations to PCB, MeHg, n-3 PUFA, selenium, and OxLDL were assessed by multivariate analyses. Ubiquinol-10, ubiquinone-10, and ubiquinone-10 to $CoQ10_{total}$ ratio were elevated as compared with white populations but showed no associations with PCB, MeHg, or n-3 PUFA. Ubiquinol-10 ($\beta = .23$, $P = .007$) and $CoQ10_{total}$ ($\beta = .27$, $P = .009$) were predicted by blood selenium; and α-tocopherol, by PCB ($\beta = 4.12$, $P = .0002$), n-3 PUFA ($\beta = 9.16$, $P = .02$), and OxLDL ($\beta = 3.04$, $P = .05$). Unexpectedly, the α-tocopheryl quinone to α-tocopherol ratio, in the reference range, was negatively predicted by PCB ($\beta = -0.41$, $P = .02$). Using sensitive biomarkers of redox alterations, we found no evidence for MeHg- or PCB-associated oxidative stress in these Inuit. However, despite robust blood antioxidant defenses, the unusually elevated ubiquinone-10 to $CoQ10_{total}$ ratio (0.21 ± 0.11) suggests some form of oxidative stress of unknown origin.

1. Introduction

Studies in Inuit of Nunavik suggest that consumption of marine products, a major source of n-3 polyunsaturated fatty acids (n-3 PUFA), is beneficial to cardiovascular health [1]. Dewailly et al [1] concluded that the traditional Inuit diet was probably responsible for the low mortality rate from ischemic heart disease in this population. However, fish and sea mammals consumed by the Inuit are also highly contaminated by methylmercury (MeHg) [2] and other potentially prooxidant contaminants such as polychlorinated biphenyls (PCB) [3,4]. Both MeHg [5-8] and PCB [9-12] are documented sources of oxidative stress. The mean concentrations of PCB, MeHg, and selenium (Se) in Inuit of Salluit studied in the present report were, respectively, 16- to 18-fold, 10- to 14-fold, and 8- to 15-fold higher than reported for reference white populations consuming little fish as previously reported for the same subjects [13]. The low risk of cardiovascular disease (CVD) observed in an Inuit population highly exposed to MeHg stands in sharp contrast to the increased risk of CVD and acute myocardial infarction found associated with mercury exposure in Finnish men

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[14,15]. Susceptibility to MeHg toxicity likely depends on, besides the intrinsic genetic background, many environmental factors including the diet. The traditional Inuit diet is unusually rich in Se [16,17], coenzyme Q10 (CoQ10) [18], and vitamin E [16], which might be beneficial for cardiovascular health. Selenium is essential to human health [19], being a key component of several antioxidant proteins including selenoprotein P and glutathione peroxidase (GPx) and thioredoxin reductase enzyme families.

These Inuit also showed favorable lipid profiles and low levels of oxidized low-density lipoprotein (OxLDL) [13], a factor implicated in the pathophysiology of atherogenesis [20]. Low-density lipoprotein particle susceptibility to oxidation likely depends on blood and LDL antioxidant status. Circulating LDL contains 2 lipid-soluble antioxidants, α-tocopherol (α-TOH, the main component of vitamin E) and CoQ10. Coenzyme Q10 is found in 2 redox forms: the reduced form ubiquinol-10 (CoQ10H2) and the oxidized form ubiquinone-10 [21]. In addition to its classic role as an electron carrier in the mitochondrial respiratory chain, CoQ10 has gained much interest as a potential antioxidant in plasma and lipoproteins [22]. The antioxidant function of ubiquinol-10 has been related to a chain-breaking radical quencher in the oxidative cycle and as a regenerator of α-TOH from its oxidized derivative α-tocopheryl quinone (α-TQ) [23]. Most attention has focused on vitamin E because it is the major lipid-soluble antioxidant in LDL. Lipoproteins isolated from carotid plaques are apparently not grossly deficient in α-TOH [24], and the relative extent of TOH oxidation in human atherosclerotic lesions was found to be maximal early in the disease where it exceeded lipid oxidation [25]. The major LDL oxidation product was α-TQ, which only reached ~10% of LDL α-TOH, suggesting that vitamin E did not contribute much to prevent LDL lipid oxidation in the artery wall [25]. The respective roles of vitamin E and CoQ10 as potential antioxidants inhibiting LDL particle oxidation and as antiatherogenic agents remain controversial [20]. The results of vitamin E supplementation studies in animal models of atherosclerosis [26] and the outcome of clinical interventions with α-TOH supplements have been overall disappointing [20,27]. In contrast, ubiquinol-10 was reported to be much more efficient than α-TOH in inhibiting LDL oxidation [27a], suggesting that CoQ10 would be the first-line antioxidant defense in LDL particles. In support, CoQ10 proved to be a much more efficient antiatherogenic agent than α-TOH in apolipoprotein E–deficient mice [26,28].

Little is known on the potential effects of dietary Northern contaminants on vitamin E and CoQ10 antioxidant status in circulation, and LDL oxidation in exposed populations. In the present study, we assessed the possible associations of MeHg and PCB exposure of Inuit with changes in plasma levels and redox status of CoQ10 and vitamin E, in relation to Se, lipid PUFA, and LDL oxidation status. In particular, we looked whether MeHg and/or PCB would predict oxidation of ubiquinol-10 and α-TOH.

2. Methods

2.1. Study participants

This study was carried out in the Canadian Inuit village of Salluit (Nunavik, Northern Québec). The general characteristics of these randomly selected Inuit adult participants (n = 99) have been published elsewhere [13]. Selected participants had Inuit family names and spoke Inuktitut at home. Residents of white origins were excluded from the study. In summary, among these participants—aged 45 ± 13 years (mean ± SD); mostly women (71 women, 28 men); and featuring elevated body mass index (BMI) (29 ± 7 kg/m^2; range, 17-44 kg/m^2; 39% of them with BMI >30 kg/m^2), normal lipoproteinemia, and elevated concentrations of erythrocyte n-3 PUFA (11% ± 3%)—72% were smokers, 19% had hypertension, and 5% had diabetes. They signed an informed consent approved by the Université du Québec à Montréal Ethic Committee, the Nunavik Nutrition and Health Committee, and the Medical Board of the Povungnituk Hospital. Data related to participant health status, current health problems, and use of medication were obtained. Subjects taking medication affecting lipid metabolism and/or oxidative stress markers, such as statins, fibrates, and angiotensin-converting enzyme inhibitors, were excluded from the study. Blood samples were collected after an overnight fast. Plasma was immediately separated from red blood cells by centrifugation (1500*g*, 10 minutes) and stored at −84°C under argon until preparation for analysis. The time between blood sampling and freezing of the plasma was no more than 15 minutes.

2.2. Analyses of contaminants, OxLDL, and erythrocyte fatty acids

Blood contents of contaminants (Hg, Se, PCB) were determined at the Québec Toxicology Laboratory [13]. *PCB* was the sum of the most prevalent PCB congeners found in Northern Quebec subjects [4,29]. Plasma OxLDL was measured by enzyme-linked immunosorbent assay by use of monoclonal antibody mAb-4E6 (Mercodia AB, Uppsala, Sweden). Erythrocyte fatty acid profiles were obtained by gas-liquid chromatography (HP 5890; Hewlett Packard, Toronto, Ontario, Canada) using an Innowax capillary column (30 m × 0.25 mm × 0.25 μm; Agilent, Mississauga, Ontario, Canada) [13]. Chromatographies were calibrated using a mixture of 37 different fatty acids (FAME 37; Supelco, Bellefonte, PA). Fatty acid data were expressed as the percentage of total erythrocyte membrane fatty acids.

2.3. Determination of lipophilic antioxidants

Simultaneous monitoring of ubiquinol-10, ubiquinone-10, and tocopherols was carried out by high-performance liquid chromatography (HPLC) with coulometric electrochemical detection as described by Finckh et al [30]. The following calibration standards were purchased from Sigma-Aldrich (St Louis, MO) or VWR Scientific (Montreal, Quebec, Canada): α-TOH, α-tocopheryl quinone, γ-tocopherol, ubiquinone-10, ubiquinone-9, tocotrienol, and β-carotene. Ubiquinol-9 and ubiquinol-10 were prepared from their respective ubiquinones according to Yamashita and Yamamoto [31]. Plasma samples were extracted by a method adapted from Menke et al [32]. Briefly, after addition of 4 ng β-tocotrienol and 5 ng ubiquinol-9 as internal standards for post-HPLC quantification purpose, 300 μL plasma was thawed at 4°C in the dark and processed immediately by addition of 2 mL of a methanol-ethanol (1:1) mixture and vigorous shaking, followed by addition of 10 mL hexane. The solvent was evaporated under a nitrogen stream, and the dry sample was redissolved in 700 μL ethanol and injected in a Gold HPLC system (Beckman Coulter Canada, Mississauga, Ontario, Canada) with an autosampler connected to a Prontosil column (150 × 4.0 mm; Bischoff Chromatography, Atlanta, GA). The mobile phase contained methanol-ethanol-isopropanol (88:24:10) and 15 mmol/L lithium perchlorate. Oxidized and reduced forms of vitamins and CoQ10 were detected using a Coulochem III (ESA, Bedford, MA) coulometric electrochemical detector, as described [30,32]. Each compound's concentration was determined by use of calibration standard curves. No oxidation of the ubiquinol-9 internal standard was detected after plasma extraction and HPLC analysis.

2.4. Statistical analyses

Statistical analyses were carried out using JMP 4.0 software (SAS Institute, Cary, NC). Log-transformed continuous variables were used for pairwise correlations analyses. Correlations were considered statistically significant at $P < .05$. Multivariate stepwise models were built with each form of vitamin E and CoQ10 as independent variables and dietary contaminants MeHg and PCB, n-3 PUFA, Se, and OxLDL as predictor variables in a distinct model. Before regression analyses, data were log transformed to provide normal distribution. After age, BMI, sex, smoking status, and lipid profiles were forced into the models, independent variables were considered (Table 4). Only variables that had a P value of .05 or less were considered in the final fitted model.

3. Results

The chromatograms shown in Fig. 1A and B provide 2 examples of lipophilic antioxidant HPLC profiles selected

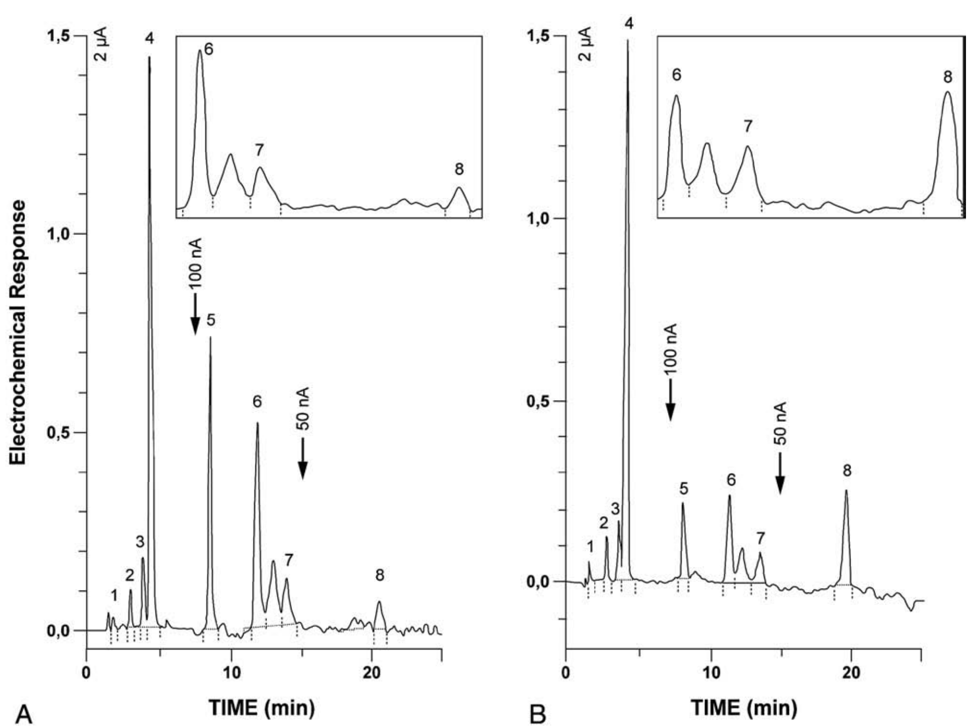

Fig. 1. Representative HPLC chromatograms of plasmatic lipophilic antioxidants from 2 Inuit presenting low and high redox ratio ubiquinone-10 to ubiquinol-10. Plasma samples (300 μL) contained (A) 4 ng β-tocotrienol (internal standard) (1), 0.74 μmol/L α-TQ (2), 3.09 μmol/L γ-TOH (3), 64.29 μmol/L α-TOH (4), 5 ng ubiquinol-9 (internal standard) (5), 4.82 μmol/L ubiquinol-10 (6), 0.24 μmol/L β-carotene (7), and 0.28 μmol/L ubiquinone-10 (8) and (B) 4 ng β-tocotrienol (internal standard) (1), 1.33 μmol/L α-TQ (2), 5.18 μmol/L γ-TOH (3), 49.75 μmol/L α-TOH (4), 5 ng ubiquinol-9 (internal standard) (5), 7.95 μmol/L ubiquinol-10 (6), 0.10 μmol/L β-carotene (7), and 5.91 μmol/L ubiquinone-10 (8). All compounds were separated according to their retention time. Detection sensitivity scales were adjusted to 2 μA for tocopherols, 100 nA for ubiquinols, and 50 nA for ubiquinone-10. The inserts show extensions of the chromatogram region upstream of ubiquinone-10 (8), where ubiquinone-9 elution was expected, but not detected.

to illustrate the wide range of CoQ10 redox states found in the Inuit group investigated. The ubiquinone-10 to $CoQ10_{total}$ ratio varied from virtually 0 to 0.53, with a mean value of 0.21 ± 0.11 (Table 1). All plasma samples contained β-tocotrienol and ubiquinol-9 added as internal standards for quantification of tocopherols and ubiquinol-10. Of importance, ubiquinone-9 potentially derived from artifactual ubquinol-9 oxidation was not detected in any plasma sample analyzed including those showing the highest ubiquinone-10 to $CoQ10_{total}$ ratio (Fig. 1B). Table 1 displays the plasmatic concentrations of the reduced and oxidized forms of tocopherols and CoQ10. The mean total CoQ10 concentration was 2.11 μmol /L, which comprised 77% ubiquinol-10 and 23% ubiquinone-10. The mean "total" vitamin E concentration was 31.91 μmoles/L comprising 87% α-TOH, 5% α-TQ, and 8% γ-TOH. Table 2 shows blood levels of MeHg and Se and plasma levels of the 14 most prevalent PCB congeners found in Inuit participants of Northern Quebec. The PCBs were determined in 97 of the 99 subjects.

Pairwise analyses of correlations between different forms of tocopherols, CoQ10, and dietary contaminants n-3 PUFA, Se, and OxLDL are shown in Table 3. Total vitamin E and α-TOH correlated significantly with all the variables, in contrast to γ-TOH. Of interest, both α-TQ and its redox state, α-TQ/TOH, a biomarker probe for oxidative stress, correlated negatively with PCB, MeHg, and n-3 PUFA, 3 potential sources of free radicals. The redox state α-TQ/TOH also correlated negatively with Se. Total CoQ10 and its reduced form, ubiquinol-10, correlated with PCB, MeHg, Se, and OxLDL, whereas its oxidized form, ubiquinone-10, was correlated with OxLDL only. The ubiquinone-10 to $CoQ10_{total}$ ratio, a second probe for oxidative stress, did not correlate with any of the variables tested.

The multivariate analyses presented in Table 4 show that α-TOH was positively predicted by PCB, n-3 PUFA, and OxLDL. α-Tocopheryl quinone, but not the α-TQ/α-TOH redox state, was negatively predicted by MeHg. The α-TQ/α-TOH ratio was negatively predicted by PCB. Neither reduced nor oxidized form of CoQ10, nor the ubiquinone-10 to $CoQ10_{total}$ ratio was predicted by PCB, MeHg, or n-3 PUFA. On the other hand, $CoQ10_{total}$ and ubiquinol-10 were positively predicted by Se.

Table 1
Plasmatic concentrations of lipophilic antioxidants

Compounds	Mean ± SD (n = 99)	Median	Range
$Tocopherols_{total}$ (μmol/L)	31.91 ± 8.63	30.27	13.65 to 53.47
α-TOH (μmol/L)	27.90 ± 7.50	26.35	12.65 to 45.14
α-TQ (μmol/L)	1.56 ± 1.73	1.13	ND to 7.27
γ-TOH (μmol/L)	2.45 ± 1.18	2.15	0.64 to 6.02
α-TQ/α-TOH	0.058 ± 0.05	0.04	ND to 0.24
$CoQ10_{total}$ (μmol/L)	2.11 ± 0.97	1.75	0.77 to 5.55
Ubiquinol-10 (μmol/L)	1.62 ± 0.69	1.38	0.70 to 4.59
Ubiquinone-10 (μmol/L)	0.48 ± 0.44	0.32	ND to 2.63
Ubiquinone-10 to $CoQ10_{total}$	0.21 ± 0.11	0.18	ND to 0.53
β-Carotene (μmol/L)	0.16 ± 0.23	0.11	0 to 1.58

ND indicates not detected.

Table 2
Levels of contaminants in study participants

	No. of individuals	Measures above detection limit	Average concentrations
Se (μg/L blood)	98	98	635.5 ± 38.7
MeHg (nmol/L blood)	98	98	106.2 ± 9.8
PCBs (μg/L plasma)			
28	97	10	0.05 ± 0.002
52	97	82	0.11 ± 0.013
99	97	97	0.54 ± 0.04
101	97	87	0.13 ± 0.01
105	97	77	0.16 ± 0.02
118	97	97	0.57 ± 0.06
128	97	50	0.04 ± 0.002
138	97	97	1.97 ± 0.17
153	97	97	3.17 ± 0.28
156	97	97	0.21 ± 0.02
170	97	97	0.50 ± 0.05
180	97	97	1.49 ± 0.15
183	97	96	0.19 ± 0.02
187	97	97	0.75 ± 0.07
Total PCBs	97	97	8.78 ± 0.79

Mean ± SEM.

4. Discussion

In this report, we looked for possible prooxidant effects of MeHg and PCB exposure on plasma concentration and redox status of 2 plasma antioxidants associated with LDL particles: α-TOH and CoQ10. The Inuit plasma vitamin E content, reflected by the sum of α-TOH, α-TQ, and γ-TOH, was similar or only slightly higher than that reported for other North American populations [33]. Multivariate analyses indicate that α-TOH was predicted by PCB, n-3 PUFA, and OxLDL. This observation is consistent with oxidative processes associated with each of these variables. The antioxidant function of vitamin E may prevent the oxidation of PUFA in membrane phospholipids and plasma lipoproteins [23,34,35]. The positive association observed between PCB and vitamin E in an earlier study on Baltic seals leads to the suggestion that elevated vitamin E status could be an effect of high PCB load [36]. Elevated vitamin E in Baltic seals was proposed to reflect an adaptive antioxidant response to PCB-mediated oxidative stress [37]. Exposure of rodents to PCB was also reported to increase the absorption of vitamin E and lipids by the intestine, thereby elevating plasmatic vitamin E levels [38]. We may therefore wonder whether PCB might have similar effects in the Inuit. Neither PCB, MeHg, nor red blood cell PUFA was a predictor of α-TQ, ubiquinone-10, or altered redox states. Mercury was even negatively associated with α-TQ; and PCB was found to predict a reduction of the α-TQ/α-TOH redox state, 2 unexpected results. Altogether, the tocopherol

Table 3
Pearson correlations (*r* values) from pairwise correlations between vitamin E or CoQ10 and biological variables including dietary contaminants, n-3 PUFA, Se, and OxLDL

	PCB	MeHg	n-3 PUFA	Se	OxLDL
$Tocopherols_{total}$	0.30 (0.003)	0.23 (0.02)	0.23 (0.03)	0.30 (0.003)	0.38 (0.0002)
α-TOH	0.41 (<0.001)	0.33 (0.001)	0.34 (0.0006)	0.36 (0.0006)	0.39 (0.0001)
α-TQ	−0.26 (0.01)	−0.26 (0.01)	−0.28 (0.007)	–	–
γ-TOH	–	–	–	–	–
α-TQ/α-TOH	−0.39 (0.0001)	−0.36 (0.0004)	−0.39 (0.0002)	−0.24 (0.02)	–
$CoQ10_{total}$	0.25 (0.02)	0.24 (0.02)	–	0.30 (0.004)	0.35 (0.0005)
Ubiquinol-10	0.25 (0.01)	0.24 (0.02)	–	0.31 (0.003)	0.32 (0.001)
Ubiquinone-10	–	–	–	–	0.33 (0.001)
Ubiquinone-10 to $CoQ10_{total}$	–	–	–	–	–

P values in parentheses; "–" indicates statistically not significant.

redox status data provide no evidence of oxidative stress associated with MeHg and PCB exposure in the adult Inuit investigated. Because of the limited number of participants, it was not possible to identify 3 subpopulations with various levels of PCBs and MeHg, but with low Se, and exhibiting differences in oxidative stress. It is of interest to note that individuals with high levels of PCBs and MeHg also exhibit high levels of Se, thus probably counteracting the oxidative effects induced by PCBs and MeHg.

Inuit plasma $CoQ10_{total}$ was about 2-fold higher than that in white [39] and Asian populations [31] and 1.5-fold that reported for Inuit Greenlanders [40]. Of note, ubiquinol-10 and $CoQ10_{total}$ were predicted by Se status of both women and men, in contrast to the results obtained with Inuit of Greenland, for whom a significant correlation between Se and $CoQ10_{total}$ was only observed in men [40]. We found that plasma ubiquinone-10 and the ubiquinone-10 to $CoQ10_{total}$ ratio used to assess CoQ10 redox status [31] were unusually high. The ubiquinone-10 to CoQ10 $_{total}$ mean value was 0.21 ± 0.11 (Table 4), which is 2- to 4-fold higher than that reported in white and Asian populations [31,32,39,41,42] and 50% to 75% higher than that in James Bay sport fishermen as determined by the use of exactly the same experimental protocol [43]. Because ubiquinols are extremely prone to autooxidation, possible artifactual oxidation of ubiquinols during extraction and HPLC analysis has to be considered first. Adequate precautions were taken to minimize ubiquinol oxidation during sample preparation and HPLC analysis, as recommended [30,32,42,44]. Secondly, formation of ubiquinone-9 from ubiquinol-9 internal standard was routinely checked in each sample analyzed and could not be detected. According to the definition of oxidative stress resulting from an "imbalance between oxidants and antioxidants in favor of the oxidants potentially leading to damage" [45], the observed shift of the CoQ10 redox state toward a more oxidized status provides a sensitive indicator of some form of "oxidative stress" in these Inuit. However, such oxidative stress would appear to affect CoQ10 specifically because neither α-TOH nor LDL oxidation status indicated an increased prooxidant balance. Moreover, the simultaneous observation of high levels of major antioxidant defense components including blood Se, GPx, and glutathione (GSH) reductase [13] and ubiquinol-10 (this study) may suggest an adaptive response of these Inuit to an oxidative challenge of unknown origin.

Of interest, plasma OxLDL concentrations of the Inuit (mean, 44.4 ± 1.7 U/L [13]) were lower than that reported for healthy white controls [46-49], despite exposure to potentially prooxidant PCB and MeHg. The correlation of OxLDL with plasma ubiquinone-10 is consistent with the view that LDL oxidation is associated with selective oxidation of ubiquinol-10 but not α-TOH [20]. In support, human studies

Table 4
Regression coefficient (*β*) from multivariate linear regression analyses preceded by stepwise analyses using vitamin E and CoQ10 as independent variables and PCB, MeHg, n-3 PUFA, Se, and OxLDL as predictor variables

	PCB	MeHg	n-3 PUFA	Se	OxLDL
$Tocopherols_{total}$	2.68 (0.0005)	–	–	–	4.47 (0.03)
α-TOH	4.12 (0.0002)	–	9.16 (0.02)	–	3.04 (0.05)
α-TQ	–	−0.30 (0.005)	–	–	–
γ-TOH	–	–	–	–	–
α-TQ/α-TOH	−0.41 (0.02)	–	–	–	–
$CoQ10_{total}$	–	–	–	0.27 (0.009)	0.08 (0.05)
Ubiquinol-10	–	–	–	0.23 (0.007)	0.18 (0.06)
Ubiquinone-10	–	–	–	–	–
Ubiquinone-10 to $CoQ10_{total}$	–	–	–	–	–

Models were adjusted for age, sex, BMI, smoking status, and plasma lipids. Before regression analyses, data were log transformed to provide normal distribution. *P* values in parentheses; "–" indicates statistically not significant.

showed that CoQ10 supplementation produced significant decreases in LDL hydroperoxides levels [39,50,51]. Stocker et al [52] suggested that ubiquinol-10 protects human LDL more efficiently against lipid peroxidation than α-TOH, despite the fact that α-TOH is the quantitatively dominant lipophilic antioxidant in LDL particles. In contrast to the low prevalence of CVD among the Inuit [1], studies in the Finnish population featuring low blood Se status reported significant associations between mercury exposure and an increased risk of CVD [14,15,53,54]. It is tempting to suggest that the low susceptibility of Inuit to LDL oxidation may be partly explained by high blood Se status and complex Hg-Se interactions that might reduce the deleterious effects of MeHg on cardiovascular health [19,55], in addition to n-3 PUFA–related beneficial effects [1]. On the other hand, the relatively high blood GPx activity of Inuit [13], falling in the activity range reported to be inversely associated with cardiovascular events [56], would also help prevent lipid peroxidation and could account, at least in part, for the low OxLDL oxidation [13]. In turn, low LDL oxidation status may be expected to contribute to reduce the risk of atherosclerosis development [47] in these Inuit.

In conclusion, the Inuit of Nunavik investigated here presented no evidence of alterations in plasmatic concentrations and redox states of α-TOH and CoQ10 associated with MeHg exposure. On the other hand, PCB exposure and erythrocyte n-3 PUFA content were positive predictors of plasma α-TOH, suggesting a tocopherol-mediated adaptive antioxidant response to PCB exposure and high n-3 PUFA intake. Plasma ubiquinone-10 concentration and ubiquinone-10 to $CoQ10_{total}$ redox ratio were unusually elevated in these Inuit, despite low LDL oxidation and high blood antioxidant defense status. Knowing that causality cannot be inferred from correlation studies, the physiological significance of this observation needs to be further investigated.

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