



Combined Effects of Selenoneine, Ergothioneine, and Methylmercury on Blood Parameters of Nunavimmiut within the Qanuilirpitaa? 2017 Nunavik Inuit Health Survey

Alexandrine Roy¹, Pierre Ayotte^{1,2,3}, Matthew Little⁴, Azanmanvo Marcos Yedjenou², Mélanie Lemire^{1,2,5}

(1) Département de médecine sociale et préventive, Université Laval ; (2) Axe santé des populations et pratiques optimales en santé, Centre de recherche du CHU de Québec-Université Laval; (3) Centre de toxicologie du Québec, Institut national de santé publique du Québec ; (4) University of Victoria; (5) Institut de biologie intégrative et des systèmes, Université Laval

Introduction

- In Nunavik, anemia is prevalent and is a public health issue with multifactorial causes, including iron deficiency, chronic inflammation, and unexplained factors (1).
- Exposure to methylmercury (MeHg), found in some country foods like beluga meat (2), may contribute to anemia by binding to hemoglobin (Hb) and disrupting Nunavimmiut red blood cell (RBC) function and lifespan (3).
- The Nunavik country foods, highly nutritious, providing important sources of iron and other key nutrients, also contain exceptionally high levels of two structurally related antioxidants, selenoneine (SeN) and ergothioneine (ESH) (4), which may help reduce oxidative stress induced by elevated MeHg exposure (5).
- SeN, very elevated in beluga skin (6), binds to Hb, potentially protecting RBCs from oxidative stress and enhancing MeHg detoxification (7).
- ESH, quite elevated in caribou meat and beluga skin (6), may also help prevent Hb and iron oxidation, providing additional protection for RBC health (8).

Blood levels of Nunavimmiut are high in:



Schematic representation of MeHg toxicity mechanisms and protective effects of SeN and ESH in RBCs

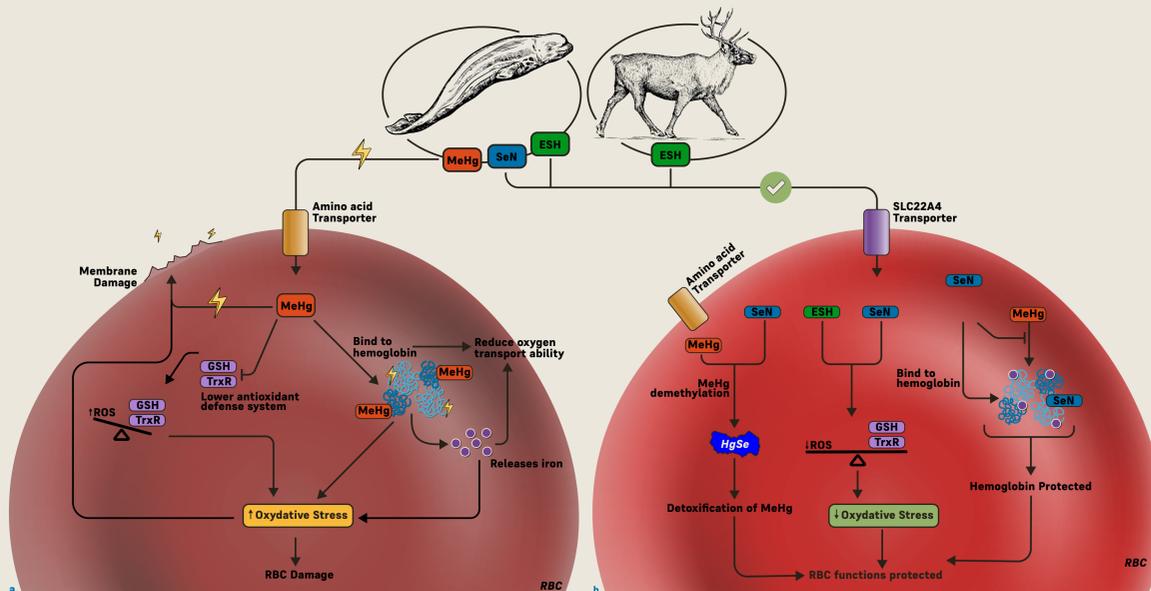


Illustration of how RBCs may be damaged by MeHg and potentially protected by SeN and ESH

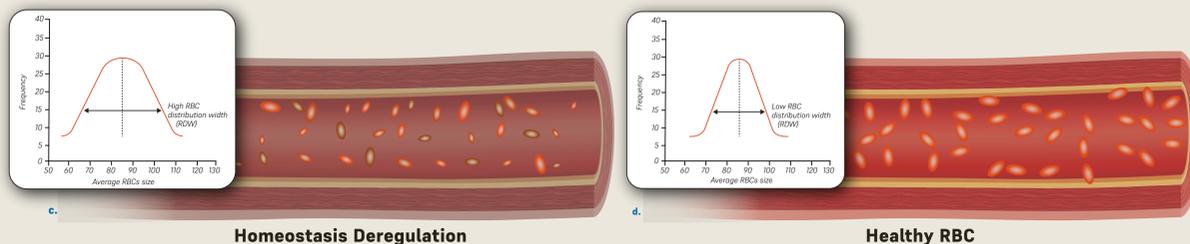
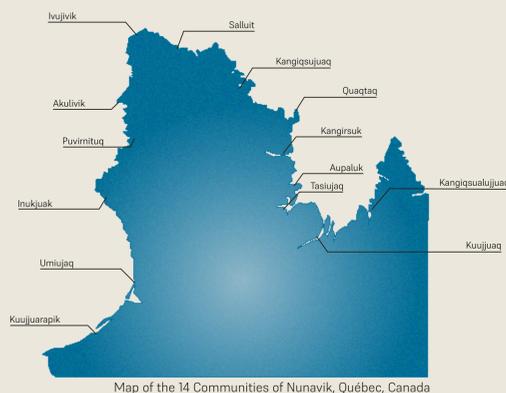


Figure 1. (a) MeHg toxicity on RBCs. (b) Protective effects of SeN and ESH on RBCs against MeHg exposure. (c) Potential effect of MeHg on RDW, showing increased variation in RBC size, which reflects deregulation of homeostasis and potential alterations in erythropoiesis, RBC metabolism, and viability. (d) Low RDW, indicating homogeneity in RBC size, associated with healthy and functional RBCs, that may reflect the positive impact of SeN and ESH.

What is Qanuilirpitaa? 2017

Meaning Where are we now? / How are we now?, this survey aimed to establish a health portrait of Nunavimmiut aged 16 and older, and identify health priorities to meet current needs and support the Nunavik Regional Board of Health and Social Services in their action plan to improve the population's health and well-being. The Qanuilirpitaa? 2017 Health Survey was conducted in all 14 communities of Nunavik between late August and early October 2017, using the Canadian Coast Guard research icebreaker Amundsen. Guided by the principles of Ownership, Control, Access, and Possession (OCAP®), all studies derived from Qanuilirpitaa? are developed in close collaboration with Nunavik institutions, which maintain ownership of the data.



Map of the 14 Communities of Nunavik, Québec, Canada

References

- Plante, C., Blanchet, C., Rochette, L., & O'Brien, H. T. (2011). Prevalence of anemia among Inuit women in Nunavik, Canada. *International Journal of Circumpolar Health*, 70(2), 154-165. <https://doi.org/10.3402/ijch.v70i2.17811>
- Lemire, M., Kwan, M., Laumonier, A. E., Muckle, G., Pirke, C., Ayotte, P., & Dewailly, E. (2015). Local country food sources of methylmercury, selenium and omega-3 fatty acids in Nunavik, Northern Québec. *Science of the Total Environment*, 509-510, 248-259. <https://doi.org/10.1016/j.scitotenv.2014.07.032>
- Bridle, T. G., Doroudian, M., White, W., & Geller, J. (2022). Physiologically relevant Hg²⁺ concentrations mobilize MeHg from rabbit serum albumin to form MeHg-Hg²⁺ complexes. *Metallomics*, 14(3), mfac010. <https://doi.org/10.1093/metmex/mfab010>
- Ayotte, P., Lemire, M., Dumais, P., Achoube, A., Yedjenou, M., Little, M., Allec, A., Dumais, P., Ouellet, N., Little, M., Lemire, M., & Ayotte, P. (2019). Selenoneine is a major selenium species in beluga skin and red blood cells of Inuit from Nunavik. *Chemosphere*, 229, 549-558. <https://doi.org/10.1016/j.chemosphere.2019.04.079>
- Yamaoka, M., Yamashita, Y., Suzuki, T., Kim, Y., Mizusawa, N., Inamura, S., Takemoto, K., Hara, T., Hossain, M. A., Noto, T., & Tsubota, K. (2013). Selenoneine, a Novel Selenium-Containing Compound, Mediates Detoxification Mechanisms against Methylmercury Accumulation and Toxicity in Zebrafish Embryo. *Marine Biotechnology*, 15(5). <https://doi.org/10.1007/s10261-013-9508-1>
- Thomas, T. A., Francis, R. D., James, G. Z., Koo, J. P., Nemkov, T., & Spitznagel, S. L. (2024). The Role of Ergothioneine in Red Blood Cell Biology: A Review and Perspective. *Antioxidants*, 13, 710. <https://doi.org/10.3390/antiox13060710>
- Ayotte, P., Gagnon, S., Piva, M., Muckle, G., Hamel, D., Bélanger, R. E., Fletcher, C., Furgal, C., Dawson, A., Galarneau, C., Lemire, M., Gauthier, M.-J., Labranche, E., Grey, L., Rochette, M., & Bourbonnais, F. (2024). The Qanuilirpitaa? 2017 Nunavik Health Survey: design, methods, and lessons learned. *Canadian Journal of Public Health - Revue Canadienne de Santé Publique*, 115(2), 111-119. <https://doi.org/10.17269/4499-223-00844-4>
- Furgal, C., Pirke, C., Lemire, M., Lucas, M., & Martin, R. (2023). Food Security. Nunavik Inuit Health Survey 2017 Qanuilirpitaa? How are we now? Québec: Nunavik Regional Board of Health and Social Services (NRBHSS) & Institut national de santé publique du Québec (INSPQ).



email: alexandrine.roy.4@ulaval.ca

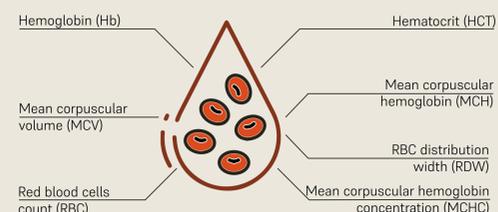
Objectives

This project aims to explore the associations between MeHg, SeN, and ESH with RBC parameters and anemia types, while assessing potential interactions among these molecules. The goal is to better understand the harmful effects of MeHg on RBCs and the protective roles of SeN and ESH in maintaining RBC health and quality.

Methods

This study uses data from blood measurements and questionnaires, collected during Qanuilirpitaa? 2017, a cross-sectional health survey conducted in Nunavik. More details on the survey methodology and laboratory analyses can be found in Ayotte et al. 2024 (9). Statistical analyses are conducted using SAS® software, including descriptive analyses, multiple linear regression with interaction terms, and moderation analyses.

Red blood cells parameters



These RBC parameters are essential indicators of red blood cell health. They assess hemoglobin levels (crucial for oxygen transport), if the number of RBCs is sufficient to meet the body's needs, and whether RBC size and uniformity fall within normal ranges.

1 290 Blood samples



*Pregnant women (n=33) were excluded from the analysis as RBC parameters are known to change significantly during pregnancy

Preliminary Results

Table 1: Preliminary results for the RDW show a negative association with blood Hg and a positive association with blood SeN in both sexes, suggesting an harmful effect of Hg and a beneficial effect of SeN on RBCs

Blood metabolite	Men		Women	
	β	95%CI	β	95%CI
Total mercury (THg)				
	+ .42**	.11 to .73	+ .28*	.03 to .53
Ergothioneine (ESH)				
	.05	-.30 to .40	.03	-.31 to .37
Selenoneine (SeN)				
	-.32*	-.58 to -.05	-.20*	-.39 to -.01

- Models adjusted for age, alcohol and cigarette consumption, which were all associated positively with RDW
 - No statistical interaction was found between THg, ESH and SeN
 - log-transformed
- *p < 0.05; ** p < 0.01

Conclusion

Country food plays an essential role for Inuit cultural and spiritual well-being. It is also a significant and nutritious food source in a context where 78% of Nunavimmiut experience some level of food insecurity (10). High levels of MeHg in certain country foods (beluga meat, big/old lake trout, seal liver) present challenges for Inuit. This study aims to provide insights to minimize the risks associated with MeHg exposure while promoting country food consumption.

Acknowledgment

We sincerely thank all Nunavimmiut who contributed to the Qanuilirpitaa? 2017 Nunavik Health Survey, as well as the teams and collaborators who planned and conducted this important initiative. We are incredibly grateful for the continued collaboration with the Nunavik Regional Board of Health and Social Services (NRBHSS) and members of the Health Surveys and Research Committees. We are also grateful for the assistance provided by Myrto Mondor in data analysis.

