

## Precarious Balance

### Methylmercury, Selenium, and Cardiovascular Health

Inuit people living in Canada's Nunavik region consume large doses of methylmercury through their traditional diet, mostly from sea mammal meat. A new study set out looking for evidence of links between these native communities' exposure to the toxic metal and heart diseases [*EHP* 119(8):1077–1083; Ayotte et al.]. The results suggested an inhibitory effect of methylmercury on paraoxonase 1 (PON1), an enzyme whose activity may protect against cardiovascular problems. They also hinted unexpectedly that dietary nutrients, especially selenium, may counteract effects of methylmercury on PON1 activity. PON1 breaks down the oxidized lipids that may promote atherosclerosis.

The researchers collected blood plasma samples from nearly 900 people living in about 500 households in different communities across Nunavik. Each person provided biological samples and completed surveys on their medical history, diet, and lifestyle habits.

A simple correlation analysis indicated that higher blood mercury was associated with higher PON1 activity, contrary to findings from earlier *in vitro* studies. So the researchers turned to multivariate statistics to untangle other factors that might confound the mercury/PON1 relationship. These include intake of omega-3 polyunsaturated fatty acids (n-3 PUFAs) and selenium, important nutrients provided by the traditional Inuit diet.

In the multivariate model, higher blood mercury levels were associated with decreased PON1 activity whereas higher blood levels of n-3 PUFAs and selenium were associated with increased PON1 activity. The researchers also observed that PON1 activity decreased with age of participants, as previously reported in other populations.

Fish and sea mammal fats carry n-3 PUFAs that are beneficial for heart health, and have been known for some time to be a key nutrient in the traditional Inuit diet. This diet also includes such high-selenium foods as beluga whale *muktuk* (skin and fat). The researchers suggest that n-3 PUFAs and selenium in the Inuit diet may offset the inhibition of PON1 activity by methylmercury.

## A Different Diabetes

### Arsenic Plus High-Fat Diet Yields an Unusual Diabetes Phenotype in Mice

Obesity is the leading cause of type 2 diabetes mellitus. Because inorganic arsenic has been associated with type 2 diabetes in laboratory studies, chronic arsenic exposure has been hypothesized to heighten the risk of diabetes in obese individuals. A new study reveals a synergistic relationship between inorganic arsenic exposure and obesity that impairs glucose tolerance in mice [*EHP* 119(8):1104–1109; Paul et al.].

From age 4 weeks, male C57BL/6 mice, a strain susceptible to developing diet-induced diabetes, ate either a low- or high-fat diet and drank purified water (controls) or water with inorganic arsenic at 25 or 50 ppm. After 20 weeks, an oral glucose tolerance test was used to assess glucose homeostasis in the mice, and serum insulin was measured before and after glucose administration. Following sacrifice 7–10 days later, serum and tissue samples were collected to determine hydration, serum and hepatic triacylglycerol content, and body distribution of arsenic and arsenic metabolites. Statistical analysis focused on effects of diet, inorganic arsenic, and interactions between the two on the development of diabetes.

As expected, control mice on the high-fat diet weighed more and accumulated more fat than control mice on the low-fat diet. They



Beluga *muktuk* dries on racks at an Inuit whaling camp.

But as native populations shift to “modern” diets—for example, eating more fast food and prepackaged meals—the dietary balance between these nutrients and methylmercury could change, the researchers caution. For instance, if an individual consumes less dietary selenium, the negative effects of methylmercury may intensify. The researchers emphasize that followup studies are necessary to monitor dietary changes and cardiovascular health among these Arctic communities.

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exhibited higher fasting blood glucose, higher fasting and post-glucose challenge serum insulin, and greater insulin resistance, symptoms consistent with type 2 diabetes. In contrast, arsenic-exposed mice on the high-fat diet accumulated less fat than unexposed mice on the same diet and had lower serum triacylglycerol, fasting blood glucose, and insulin measures. However, glucose intolerance was high in these mice, even exceeding that observed in controls on the same diet.

The results suggest inorganic arsenic reduces diet-induced obesity in mice but acts synergistically with a high-fat diet to produce glucose intolerance, a symptom typically associated with prediabetes. The combination of glucose intolerance and elevated blood glucose levels with near-normal plasma insulin levels differs from the typical phenotype for type 2 diabetes.

The authors point out that the measures indicating near-normal insulin sensitivity, when paired with glucose intolerance, can reflect impaired insulin production by pancreatic  $\beta$  cells—a characteristic of advanced diabetes. However, the study did not measure  $\beta$  cell function and signals that regulate it and thus cannot offer insight on this possibility. More comprehensive investigation is needed to determine how inorganic arsenic exposure, alone and with a high-fat diet, may induce type 2 diabetes.

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