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Rethinking mercury: The role of selenium in the pathophysiology of mercury toxicity

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Introduction: the pathophysiological target of mercury is selenium, rather than the covalent binding of mercury to sulfur in the body's sulfhydryl groups. The role of selenium in mercury poisoning is multifaceted, bidirectional and central to understanding the toxicity of mercury.

Binding of mercury to thiol/sulfhydryl groups:
Mercury has a lower affinity for thiol groups and higher affinity for selenium-containing groups by several orders of magnitude. The established binding of mercury to thiol moieties does not explain the oxidative stress, calcium dyshomeostasis or specific organ injury seen with mercury.

Effects of mercury on selenium in the pathophysiology of mercury toxicity:
Mercury impairs control of intracellular redox homeostasis with subsequent increased intracellular oxidative stress. The primary cellular targets are the selenoproteins of the thioredoxin system (and the glutathione-glutaredoxin system. Mercury binds to the selenium site on these proteins and permanently inhibits their function, disrupting the intracellular redox environment. A number of other important possible target selenoproteins have been identified, including selenoprotein P, K and T. Impairment of the thioredoxin and glutaredoxin systems allows for proliferation intracellular reactive oxygen species which leads to glutamate excitosis, calcium dyshomeostasis, mitochondrial injury/loss, lipid peroxidation, impairment of protein repair and apoptosis. A second important mechanism is binding of mercury to selenium and the subsequent depletion of selenium stores needed for de novo generation of replacement selenoproteins.

The effects of selenium in biological response to mercury toxicity:
The roles selenium plays in this reduction of mercury toxicity partially depends on the form of mercury and may be multifaceted including: 1) facilitating demethylation of organic mercury to inorganic mercury; 2) redistribution of mercury to less sensitive target organs; 3) binding to inorganic mercury and forming an insoluble, stable and inert Hg:Se complex; 4) reduction of mercury absorption from the GI tract; 5) repletion of selenium stores; and 6) restoration of target selenoprotein activity and restoring the intracellular redox environment. There is conflicting evidence as to whether selenium increases or hinders mercury elimination.

Conclusions:
The interaction with selenium is a central feature in mercury toxicity. This interaction is complex depending on a number of features such as the form of mercury, the form of selenium, the organ and dose. The previously suggested "protective effect" of selenium against mercury toxicity may in fact be backwards. The effect of mercury is to produce a selenium deficiency state and a direct inhibition of selenium's role in controlling the intracellular redox environment in organisms.