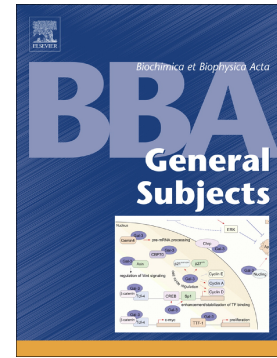


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## Mercury's Neurotoxicity is Characterized by its Disruption of Selenium Biochemistry

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### Abstract:

#### Background:

Methylmercury ( $\text{CH}_3\text{Hg}^+$ ) toxicity is characterized by challenging conundrums: 1) “selenium (Se)-protective” effects, 2) undefined biochemical mechanism/s of toxicity, 3) brain-specific oxidative damage, 4) fetal vulnerability, and 5) its latency effect. The “protective effects of Se” against  $\text{CH}_3\text{Hg}^+$  toxicity were first recognized >50 years ago, but awareness of Se's vital functions in the brain has transformed understanding of  $\text{CH}_3\text{Hg}^+$  biochemical mechanisms. Mercury's affinity for Se is ~1 million times greater than its affinity for sulfur, revealing it as the primary target of  $\text{CH}_3\text{Hg}^+$  toxicity.

#### Scope of Review:

This focused review examined research literature regarding distinctive characteristics of  $\text{CH}_3\text{Hg}^+$  toxicity to identify Se-dependent aspects of its biochemical mechanisms and effects.

#### Conclusions:

Research indicates that  $\text{CH}_3\text{Hg}^+$  irreversibly inhibits the selenoenzymes that normally prevent/reverse oxidative damage in the brain. Unless supplemental Se is provided, consequences increase as  $\text{CH}_3\text{Hg}^+$  approaches/exceeds equimolar stoichiometries with Se, thus forming  $\text{HgSe}$  and inducing a conditioned Se deficiency. As the biochemical target of  $\text{CH}_3\text{Hg}^+$  toxicity, Se-physiology provides perspectives on the brain specificity of its oxidative damage, accentuated fetal vulnerability, and latency. This review reconsiders the concept that Se is a “tonic” that protects against  $\text{CH}_3\text{Hg}^+$  toxicity and recognizes Se's role as Hg's molecular “target”. As the most potent intracellular nucleophile, the selenoenzyme inhibition paradigm has broad implications in toxicology, including resolution of conundrums of  $\text{CH}_3\text{Hg}^+$  toxicity.

#### General Significance:

Mercury-dependent sequestration of selenium and the irreversible inhibition of selenoenzymes, especially those required to prevent and reverse oxidative damage in the brain, are primarily responsible for the characteristic effects of mercury toxicity.

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