

# Thimerosal distribution and metabolism in neonatal mice: comparison with methyl mercury

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**ABSTRACT:** Thimerosal, which releases the ethyl mercury radical as the active species, has been used as a preservative in many currently marketed vaccines throughout the world. Because of concerns that its toxicity could be similar to that of methyl mercury, it is no longer incorporated in many vaccines in the United States. There are reasons to believe, however, that the disposition and toxicity of ethyl mercury compounds, including thimerosal, may differ substantially from those of the methyl form. The current study sought to compare, in neonatal mice, the tissue concentrations, disposition and metabolism of thimerosal with that of methyl mercury. ICR mice were given single intramuscular injections of thimerosal or methyl mercury (1.4 mg Hg kg<sup>-1</sup>) on postnatal day 10 (PND 10). Tissue samples were collected daily on PND 11–14. Most analysed tissues demonstrated different patterns of tissue distribution and a different rate of mercury decomposition. The mean organic mercury in the brain and kidneys was significantly lower in mice treated with thimerosal than in the methyl mercury-treated group. In the brain, thimerosal-exposed mice showed a steady decrease of organic mercury levels following the initial peak, whereas in the methyl mercury-exposed mice, concentrations peaked on day 2 after exposure. In the kidneys, thimerosal-exposed mice retained significantly higher inorganic mercury levels than methyl mercury-treated mice. In the liver both organic and inorganic mercury concentrations were significantly higher in thimerosal-exposed mice than in the methyl mercury group. Ethyl mercury was incorporated into growing hair in a similar manner to methyl mercury. The data showing significant kinetic differences in tissue distribution and metabolism of mercury species challenge the assumption that ethyl mercury is toxicologically identical to methyl mercury. Copyright © 2007 John Wiley & Sons, Ltd.

**KEY WORDS:** thimerosal; methyl mercury; distribution; metabolism; mice; neonatal exposure

## Introduction

Thimerosal is an organic mercurial compound that has been used for over 60 years as a preservative in vaccines and other pharmaceutical products to prevent unwanted bacterial and fungal growth (U.S. Pharmacopeia, 1999). Thimerosal contains 49.6% mercury by weight and breaks down in the body to ethyl mercury and thiosalicylate (Tan and Parkin, 2000).

Public interest in the thimerosal content of vaccines began to develop after a report asserting that thimerosal in hepatitis B immunoglobulin caused severe ethyl mercury intoxication (Lowell *et al.*, 1996). Because of scarcity of toxicological information on ethyl mercury

exposure in humans, methyl mercury standards were used as surrogates for ethyl mercury based on the structural similarity of the two mercury species. In 1995, the Environmental Protection Agency introduced stricter guidelines for methyl mercury based on prenatal exposure (EPA, 1997). Public debate and the Food and Drug Administration (FDA) preliminary risk assessment prompted a joint statement of the American Academy of Pediatrics and the US Public Health Service calling for the removal of thimerosal from vaccines (AAP, 1999; AAP/USPHS, 1999).

Data on mercury levels in infants undergoing vaccination are scarce. A study on mercury disposition in 12 infants before and after hepatitis B vaccine administration (Stajich *et al.*, 2000) demonstrated increased mercury blood levels, especially in pre-term infants. However, this report did not provide a sufficient basis for exposure assessment due to the limited number of subjects and collection times of samples after vaccination. Ball *et al.* (2001) calculated that cumulative mercury exposure of infants up to age 6 months who undergo multiple

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