Toxicological effects of thiomersal and ethylmercury: Inhibition of the thioredoxin system and NADP\(^{+}\)-dependent dehydrogenases of the pentose phosphate pathway

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**Abstract**

Mercury (Hg) is a strong toxicant affecting mainly the central nervous, renal, cardiovascular and immune systems. Thiomersal (TM) is still in use in medical practice as a topical antiseptic and as a preservative in multiple vaccine preparations. Exposure to mercurial compounds such as thiomersal (TM) in medicines and antiseptics is decreasing it is still used as a preservative in some formulas, namely vaccines with TM are the main route of mercury exposure in clinics containing vaccines; TM, thiomersal; Trx, thioredoxin; TrxR, thioredoxin reductase.

Mercurial compounds have shown a wide range of toxicological effects on human beings, involving especially the central nervous system, causing damage to the brain, but also to the kidneys, the cardiovascular and immune systems (Clarkson et al., 2003; Dórea et al., 2013). Exposure to mercurial compounds such as methylmercury (MeHg) and mercutic mercury (Hg\(^{2+}\)) at levels above the toxicity threshold occurs either by regular fish consumption or occupational contact, respectively, and represents a major concern in toxicology (Clarkson et al., 2003; Carvalho et al., 2008a; Nunes et al., 2014). Not less important is mercury exposure in dental practice for both dentists and patients due to the use of dental amalgam fillings that release mercury vapour (Clarkson et al., 2003). Even though the use of mercury compounds such as thiomersal (TM) in medicines and antiseptics is decreasing it is still used as a preservative in some formulas, namely vaccines (Sykes et al., 2014).

Although mercurial compounds are not new toxicants, there is a significant lack of knowledge about their molecular mechanisms of toxicity, especially about TM and its breakdown product ethylmercury (EtHg). TM, a mercury derivative composed of EtHg and thiosalicylic acid has been widely used as a preservative in vaccines, dermatological (topic) and ocular preparations. Indeed, vaccines with TM are the main route of mercury exposure in clinics (Bigham and Copes, 2005) and while children in most of the developed countries receive normally TM-free vaccines, children in developing countries may receive several doses of different vaccines; TM, thiomersal; Trx, thioredoxin; TrxR, thioredoxin reductase.

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