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Mercury toxicokinetics—dependency on strain and gender

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ABSTRACT

Mercury (Hg) exposure from dental amalgam fillings and thimerosal in vaccines is not a major health hazard, but adverse health effects cannot be ruled out in a small and more susceptible part of the exposed population. Individual differences in toxicokinetics may explain susceptibility to mercury. Inbred, H-2-congenic A.SW and B10.S mice and their F1- and F2-hybrids were given $HgCl_2$ with 2.0 mg Hg/L drinking water and traces of ^{203}Hg. Whole-body retention (WBR) was monitored until steady state after 5 weeks, when the organ Hg content was assessed. Despite similar Hg intake, A.SW males attained a 20–30% significantly higher WBR and 2- to 5-fold higher total renal Hg retention/concentration than A.SW females and B10.S mice. A selective renal Hg accumulation but of lower magnitude was seen also in B10.S males compared with females. Differences in WBR and organ Hg accumulation are therefore regulated by non-H-2 genes and gender. Lymph nodes lacked the strain- and gender-dependent Hg accumulation profile of kidney, liver and spleen. After 15 days without Hg A.SW mice showed a 4-fold higher WBR and liver Hg concentration, but 11-fold higher renal Hg concentration, showing the key role for the kidneys in explaining the slower Hg elimination in A.SW mice. The trait causing higher mercury accumulation was not dominantly inherited in the F1 hybrids. F2 mice showed a large inter-individual variation in Hg accumulation, showing that multiple genetic factors influence the Hg toxicokinetics in the mouse. The genetically heterogeneous human population may therefore show a large variation in mercury toxicokinetics.

Introduction

All living organisms are exposed to low levels of mercury due to its eternal presence in the environment, but exposure leading to health hazards are generally related to specific human activities and of multitude origin: from unintentional occupational exposure (Rohling and Demakis, 2006), to ingestion of Hg as an ingredient in folk remedies, religious attributes, and skin-lightening creams (Pollard and Hultman, 2007; Risher and De Rosa, 2007). However, the main forms of Hg exposure recently discussed (Clarkson and Magos, 2006) as a source of adverse health effects are amalgam fillings (inorganic Hg) (Bates, 2006; Martin and Woods, 2006), food, especially fish (methyl Hg) (Grandjean et al., 2003; Passos et al., 2007), and as a preservative in vaccines (thimerosal) (Clifton, 2007).

A number of recent studies in cohorts of humans exposed in the above ways (Bellinger et al., 2006; de Burbure et al., 2006; DeRouen et al., 2006; Passos et al., 2007; Woods et al., 2007, 2008; Barregard et al., 2008; Pichichero et al., 2008) have tried to establish association between exposure to mercury and any adverse health effects. In addition, case reports of disease conditions after various forms of Hg exposure regularly appear in the medical literature (Mahaffey, 2005; Risher and De Rosa, 2007). Furthermore, experiments in mammals (Havarinasab et al., 2007) also including non-human primates (Burbacher et al., 2005) have been used to increase the knowledge of Hg toxicokinetics and related health effects.

The majority of the studies on these forms of Hg exposure have concluded that there is no clear evidence for significant health effects except in special situations such as methyl mercury exposure due to high consumption of Hg-rich fish and seafood (Grandjean et al., 2003). However, increased urinary Hg excretion (Woods et al., 2007; Dunn et al., 2008; Ye et al., 2008) , and increased urinary protein excretion (microalbuminiuria) has been described following exposure from dental amalgam fillings (Barregard et al., 2008). However, even after studies in large exposed cohorts, uncertainty remains with regard to possible adverse health effects due to Hg exposure in susceptible individuals (Barregard, 2005; Bellinger et al., 2008). Individual susceptibility may be due to unexpected high exposure caused for example by gum chewing or bruxism in dental amalgam bearers (Sallsten et al., 1996; Isacsson et al., 1997; Barregard et al., 2008), or genetic factors causing differences in the toxicokinetics of

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