Mercury species in lymphoid and non-lymphoid tissues after exposure to methyl mercury: correlation with autoimmune parameters during and after treatment in susceptible mice.

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Abstract
Methylmercury (MeHg) is present in the environment as a result of the global cycling of mercury, although anthropogenic sources may dramatically increase the availability in confined geographical areas. Accumulation of MeHg in the aquatic food chain is the dominating way of exposure in mammals, which accumulate MeHg in all organs, including the brain. Demethylation has been described in the organs, especially in phagocytic cells, but mainly in the flora of the intestinal tract. While most of the inorganic mercury (Hg(2+)) formed in the intestine is excreted, a fraction is reabsorbed which together with the local demethylation increases the organ Hg(2+) concentration. MeHg is a well-known immunosuppressive agent, while Hg(2+) is associated with immunostimulation and autoimmunity especially in genetically susceptible rodents, creating a syndrome, i.e. mercury-induced autoimmunity (HgIA). This study aimed at exploring the effect of MeHg with regard to HgIA, and especially the immunological events after stopping treatment, correlated with the presence of MeHg and Hg(2+) in the organs. Treatment of A.SW mice for 30 days with 4.2 mg MeHg/L drinking water (corresponding to approximately 420 microg Hg/kg body weight/day) caused all the HgIA features observed after primary treatment with inorganic Hg, except systemic immune complex deposits. The total Hg concentration was 5-fold higher in the kidneys as compared with lymph nodes, but the fraction of Hg(2+) was similar (17-20%). After stopping treatment, the renal and lymph node MeHg concentration declined according to first order kinetics during the initial 4-6 weeks, but then slower. A similar decline in the organ Hg(2+) concentration occurred during the initial 2 weeks after stopping treatment but then ceased, causing the Hg(2+) concentration to exceed that of MeHg in the lymph nodes and kidneys after 3 and 8 weeks, respectively. The selective increase in lymph node Hg(2+) fraction is likely to be due to demethylation of MeHg in the macrophage-rich lymphoid tissue. The major autoantibody in HgIA, anti-fibrillarin antibodies, tended to increase during the initial 6 weeks after stopping treatment, while all other HgIA features including antichromatin antibodies declined to control levels after 2-4 weeks. This indicates differences in either dose requirement or induction mechanisms for the different HgIA parameters. The selective accumulation of Hg(2+) in lymph nodes following MeHg treatment should be taken into account when the effect of MeHg on the immune system is evaluated.

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