

## **Homozygous gene deletions of the glutathione S-transferases M1 and T1 are associated with thimerosal sensitization.**

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Int Arch Occup Environ Health. 2000 Aug;73(6):384-8.

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**OBJECTIVE:** Thimerosal is an important preservative in vaccines and ophthalmologic preparations. The substance is known to be a type IV sensitizing agent. High sensitization rates were observed in contact-allergic patients and in health care workers who had been exposed to thimerosal-preserved vaccines. There is evidence for the involvement of the glutathione system in the metabolism of thimerosal or its decomposition products (organomercury alkyl compounds). Thus detoxification by polymorphically expressed glutathione S-transferases such as GSTT1 and GSTM1 might have a protective effect against sensitization by these substances. **METHODS:** To address this question, a case control study was conducted, including 91 Central European individuals with a positive patch-test reaction to thimerosal. This population was compared with 169 healthy controls and additionally with 114 individuals affected by an allergy against para-substituted aryl compounds. The latter population was included in order to test whether possible associations were due to substance-specific effects, or were a general feature connected with type IV immunological diseases. Homozygous deletions of GSTT1 and GSTM1 were determined by polymerase chain reaction. **RESULTS:** Glutathione S-transferase M1 deficiency was significantly more frequent among patients sensitized to thimerosal (65.9%,  $P = 0.013$ ) compared with the healthy control group (49.1%) and the "para-compound" group (48%,  $P = 0.034$ ). Glutathione S-transferase T1 deficiency in the thimerosal/mercury group (19.8%) was barely elevated versus healthy controls (16.0%) and the "para-compound" group (14.0%). The combined deletion (GSTT1-/GSTM1-) was markedly more frequent among thimerosal-sensitized patients than in healthy controls (17.6% vs. 6.5%,  $P = 0.0093$ ) and in the "para-compound" group (17.6% vs. 6.1%,  $P = 0.014$ ), revealing a synergistic effect of these enzyme deficiencies (healthy controls vs. thimerosal GSTM1 negative individuals,  $OR = 2.0$  [ $CI = 1.2-3.4$ ], GSTT1-,  $OR = 1.2$  [ $CI = 0.70-2.1$ ], GSTM1/T1-,  $OR = 3.1$  [ $CI = 1.4-6.5$ ]). **CONCLUSIONS:** Since the glutathione-dependent system was repeatedly shown to be involved in the metabolism of thimerosal decomposition products, the observed association may be of functional relevance.



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