

ORIGINAL ARTICLE

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

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Abstract 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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Introduction

The predisposition to acquire a sensitization towards certain contact-allergens was proposed to be heritable. This proposal was based mainly on family and twin studies (reviewed by Menné and Holm 1986). Among