

# ARE MERCURY AMALGAM FILLINGS SAFE FOR CHILDREN? AN EVALUATION OF RECENT RESEARCH RESULTS

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Two recent clinical trials on the safety of amalgam fillings in children found no evidence of harmful effects from mercury-containing dental fillings after following children for 5-7 years. This review suggests the studies' results are limited by (1) sample sizes that were too small to allow detection of genetic varia-

tions in mercury toxicity at a rate of 1 in 100 or lower, (2) a lack of control for other sources of mercury, and (3) a population that may have been skewed by excluding children with autism during a time when autism was escalating due, in part, to increased frequency of thimerosal-containing vaccine use.

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**T**wo thoughtfully designed and implemented clinical trials on the safety of amalgam fillings in children were published in *JAMA* in April. Neither of these National Institutes of Health (NIH)-funded studies found evidence of harmful effects from mercury-containing dental fillings after following children for 5-7 years. This paper reviews the studies and discusses their limitations in defining the safety of amalgams in children.

## UNITED STATES-BASED STUDY

In the United States study, 267 children receiving amalgam fillings and 267 children receiving resin composite fillings were followed for 5 years.<sup>1</sup> Eligible participants were children 6-10 years old with no prior amalgam fillings and no physician-diagnosed psychological, behavioral, neurological, immunosuppressive, or renal disease. This study was designed to detect an IQ difference of 3 points between children with caries filled with amalgam versus composite and also to explore potential differences in visuomotor ability, memory, and kidney function. There were no significant differences between the groups for any parameter at any time point. In addition, the 2 groups were monitored for development of new health conditions during the 5-year follow-up. The 2 groups reported similar incidences of new health conditions, including allergy, asthma, migraines, skin disorders, respiratory disorders, psychological disorders, and gastrointestinal disorders, among others. The researchers reported that children with amalgams had slight (0.9 µg/g creatinine) but significant increases in urinary mercury compared to controls (0.6 µg/g creatinine). There was no difference in hair mercury content between the 2 groups.

## LISBON, PORTUGAL-BASED STUDY

In the Portuguese study, 253 children receiving amalgam fillings and 252 children receiving resin composite fillings were followed for 7 years.<sup>2</sup> Eligible participants were children 8-10 years old with no prior amalgam fillings, urinary mercury below 10 µg/L, blood lead lower than 15 µg/L, IQ >67, and no interfering health conditions. This study also assessed memory, attention, visuomotor function, kidney function, and nerve conduction velocity. Endpoints were assessed annually, and there were no differences in any parameters at any time point. In this study, urinary mercury in the amalgam group was 1.5 µg/g creatinine greater than the composite group during the first 3 years and declined to an average 1.0 µg/g in later years, with no significant difference at year 7.

## MERCURY TOXICITY

Amalgams are made of approximately 50% mercury. Mercury is a known neurotoxin. Exposure resulting in urinary levels of 50 to 200 µg/L is associated with neurobehavioral defects, such as reduced metal capability, loss of fine motor coordination, mood alterations, and insomnia.<sup>3</sup> There is some evidence that urinary concentrations of mercury as low as 4 µg/L are associated with mood changes,<sup>4</sup> but in general, the effect of low-level mercury exposure is not well defined. Because of this deficiency, the World Health Organization has requested that researchers focus on investigating threshold effects at levels below 25 µg/L, as mean urinary levels in the general population are 3.1 or 9.0 µg/L.<sup>4</sup> These 2 amalgam studies should have provided useful information about low-level mercury exposure, but the similarity in urinary mercury excretion between the controls and the group receiving amalgams actually suggests similar mercury exposure.

## STUDY LIMITATIONS

Despite meaningful endpoints reflecting parameters

impacted by mercury, the studies failed to uncover any evidence of mercury toxicity from amalgams. The research has several key limitations, however. The researchers themselves admit, "This study was not designed to detect whether a very small fraction of children may have genetic predispositions to sequester elemental mercury at an extraordinarily high rate, or have rare allergic or other kinds of adverse reactions to elemental mercury."<sup>2(p1791)</sup> The small sample size of the studies does not allow for the detection of adverse effects if they occurred at a rate lower than 1 in 100.

Current research suggests that genetic variability may result in children that are susceptible to small amounts of mercury. This may be due to an inability to detoxify and eliminate mercury, resulting in manifestations of neurotoxicity and immune dysregulation as might be expected from higher mercury exposure. Indeed, recent research in human adults with occupational mercury exposure has demonstrated a correlation between neurobehavioral dysfunction from mercury exposure and genetic variants of an enzyme involved in heme synthesis as well as a neurotrophic protein.<sup>5,6</sup> Genetic variation of other enzymes also is suspected to contribute to mercury sensitivity, and multiple mutations may be a prerequisite to seeing clinical manifestations.

#### SKEWED STUDY POPULATION?

The slight differences in urinary mercury between the 2 groups in both studies suggest that exposure from the fillings may have been insignificant compared to exposure from vaccines and diet. Neither study reports on or controls for other sources of mercury, and the studies were conducted in a time period when immunization with thimerosal-containing vaccines was routine. It is possible that the recruitment of healthy school-age children may have excluded children with any and all genetic susceptibility to mercury. Research suggests that toxic metals, and mercury specifically, may play a role in autism.<sup>7,8</sup> Indeed, the phasing out of thimerosal-containing childhood vaccines in California has resulted in a decrease in the incidence of autism.<sup>9</sup> Given that autistic spectrum disorder (ASD) is typically diagnosed in the first 5 years of life and during the time period of the studies there was a 6-fold increase in ASD diagnoses,<sup>10</sup> one wonders if the children in the study may not have been truly representative of the general population. Considering the Centers for Disease Control and Prevention's estimates of ASD prevalence as high as 1 in 166 individuals,<sup>11</sup> the study may have ended up with a skewed population of only the fittest.

#### CONCLUSION

The 2 published amalgam studies reported unexpected results. However, given the extremely small differences in the urinary mercury levels between the children with amalgams and the composite controls, the studies may be lacking an adequate control group. Future studies aimed at determining the health risk of amalgams will need to ensure all other sources of mercury are removed and previous significant exposures from diet and vaccines are controlled for. In addition, research is

needed to determine the prevalence of genetic predisposition to mercury toxicity and the long-term health effects of decades of exposure to mercury from amalgams.

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