

Response to Comments by J.R. Mann

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We thank Mann for his insightful comments concerning our manuscript (1). Mann suggests we should have analyzed the same periods following immunizations with and without thimerosal. We have done this in a subsequent analysis, and we still found statistically significantly increased relative risks for neurodevelopmental disorders following thimerosal-containing vaccines in comparison to thimerosal-free vaccines based upon analysis of the Vaccine Adverse Event Reporting System (VAERS) (2).

Mann suggested that by focusing on thimerosal-containing DTaP we may have missed the effects of other thimerosal-containing vaccines on neurodevelopmental disorders. Subsequently, we analyzed the United States' Department of Education (USDEA) datasets, where we were able to evaluate the complete mercury burden from all thimerosal-containing childhood vaccines in each birth cohort examined (2, 3). Our analyses have shown close significant dose-response relationships between increasing mercury burdens per birth cohort and increasing prevalence of neurodevelopmental disorders per birth cohort (2, 3). We generated dose-response curves from VAERS for increasing dose of mercury from thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines, and found that the slopes from our VAERS and USDEA dose-response neurodevelopmental disorder analyses were similar (2, 3).

We agree with Mann that some epidemiologists use attributable risk to be a measure of the absolute (not relative) difference in risk between people "exposed" and "unexposed." In a number of our previous studies we have used attributable risk as a measure of the relative risk, allowing one from the attributable risk to determine the attributable percent association [(attributable risk/relative risk) \times 100 = attributable percent association]. We believe that the attributable percent association value derived is very significant for those in the practice of medicine because it allows one to be able to quantify what the relative effect of a given

treatment is in a percentage scale, instead of in absolute terms of number of cases, as described by Mann.

Finally, as Mann suggests, our assessment of the relative risk from VAERS for the effects of increasing doses of mercury from thimerosal-containing vaccines in comparison to thimerosal-free vaccines was based upon cases of neurodevelopmental disorders believed to have a relationship with vaccination that developed within a defined temporal period following vaccination. At the time of our publication, we believed that overall our results demonstrated that an association existed between thimerosal-containing childhood vaccines and neurodevelopmental disorders based upon the Institute of Medicine of the U.S. National Academy of Sciences concluding that it was biological plausible for there to be an association between mercury from thimerosal-containing vaccines and neurodevelopmental disorders and our own epidemiological results. Subsequently, we published that the instantaneous mercury doses from thimerosal-containing childhood vaccines administered resulted in infants being exposed to in some cases more than 100-fold in excess of the Federal Safety Guidelines for the oral ingestion of methyl mercury, and we have shown similar significant dose-response curves from two independent databases (i.e. VAERS and USDEA) closely correlating increasing mercury from childhood thimerosal-containing vaccines with neurodevelopmental disorders (2, 3). We have evaluated the Centers for Disease Control and Prevention's Vaccine Safety Datalink (VSD) studies that showed statistically significant dose-response curves closely correlating increasing mercury doses from thimerosal-containing childhood vaccines and various neurodevelopmental disorders. We have co-authored a case-control study on the mercury burden among children with autistic spectrum disorders, and found that age, sex, and vaccine status matched cases with autistic spectrum disorders had statistically significantly ($p < 0.005$) 5.94 relative increased urinary mercury concentrations in comparison to normal controls following a three-day challenge with an oral chelating agent (4). Similarly, Holmes et al. have shown in a case-control study that there was direct connection between decreasing first baby hair cut levels of mercury and increasingly severe autism (5).

In addition, we have conducted a PubMed search on thimerosal, and found hundreds of publications on its adverse effects. Kravchenko et al. (6) published, "Thus thi-

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merosal, commonly used as a preservative, has been found not only to render its primary toxic effect, but also capable of changing the properties of cells. This fact suggests that the use of thimerosal for the preservation of medical biological preparations, especially those intended for children, is inadmissible." Similarly, Seal et al. (7) published, "Thimerosal is a weak antibacterial agent that is rapidly broken down to products, including ethylmercury residues, which are neurotoxic. Its role as a preservative in vaccines has been questioned, and the pharmaceutical industry itself considers its use as historical." Also, the National Toxicology Program of the U.S. Government reported clumsiness, speech impairment, emotional disturbances, and mental retardation in children are among the commonly observed symptoms of thimerosal exposure (8). Even authors from the Division of Neurotoxicology, National Center for Toxicological Research at the Food and Drug Administration (9) have published, "Thimerosal (sodium ethylmercurithiosalicylate) crosses the blood-brain and placental barriers and results in appreciable mercury content in tissue including brain."

Therefore, in conclusion, based upon what now appears to be an overwhelming amount of scientific/medical literature from many different sources on the direct adverse effects of thimerosal, as we have published recently, one must consider that there is a causal relationship between thimerosal-containing childhood vaccines and neurodevelopmental disorders.

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