

Association Between Thimerosal-Containing Vaccine and Autism

To the Editor: In their article on the association between thimerosal-containing vaccines and autism, Dr Hviid and colleagues¹ acknowledged their affiliations with Statens Serum Institut, Copenhagen, Denmark, but did not disclose that the institute is a for-profit, state-owned enterprise with roughly \$120 million in annual revenue. According to its 2002 Annual Report,² vaccines represent approximately one half of Statens Serum Institut's revenues and more than 80% of its profits. Furthermore, Statens Serum Institut manufactured the now discontinued monocomponent pertussis vaccine that contained thimerosal under investigation in their study. They were also the providers of diphtheria and tetanus components of a major thimerosal-containing diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) vaccine sold in the United States.³

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1. Hviid A, Stellfeld M, Wohlfahrt J, Melbye M. Association between thimerosal-containing vaccine and autism. *JAMA*. 2003;290:1763-1766.
2. Statens Serum Institut. 2002 Annual Report. Available at: <http://www.ssi.dk/sw3767.asp>. Accessed October 12, 2003.
3. Food and Drug Administration. Biologics license application approval letter to North American Vaccine. July 29, 1998. Available at: <http://www.fda.gov/cber/approvltr/dtapnor072998L.htm>. Accessed October 12, 2003.

To the Editor: Dr Hviid and colleagues¹ found no increase in relative risk of core autism from thimerosal in vaccines using the Danish autism registry. Denmark removed thimerosal from infant vaccines in mid-1992. The findings of Hviid et al are based on finding fewer older (born 1990-1992) thimerosal-exposed children than younger (born 1992-1996) unexposed children in the 2000 registry year. However, a sizable percentage of autism cases, skewing toward older children, are lost from the registry each year. Thus, the authors' finding is likely to be biased due to incomplete recordkeeping.

For instance, the 1995 registry² contains 97 cases among 5- to 9-year-olds. This same cohort, as it grows older, becomes the 10- to 14-year-old cohort in the 2000 registry, where its number has decreased to 75 children, a decline of 22 cases or 23% of the original 1995 group. Hviid et al stated that virtually all cases in their autism group were accurately diagnosed, and thus it is unlikely that cases were removed due to subsequent discovery of misdiagnosis and reclassification. Autism is a lifelong disorder with near-normal lifespan,³ and few registry cases are in older age groups likely to die. Therefore, virtually any case entered into the registry should remain there. That some do not suggests administrative error.

I calculated the extent of record loss for the 1991-2000 span studied by Hviid et al. For each year, I added the number of newly enrolled cases for that year to the number of previous year's cases. I compared this total to the number of cases actually recorded in the registry for that year. For 4 of the years, the proportion lost amounts to one fourth of the cases. For the 2000 registry year, 23% of the cases from the previous year are missing. Cumulatively, 815 cases were dropped between 1991 and 2000, more than the total number remaining in 2000.

Removed cases accumulate each year, so for any given registry year, proportionately more removed cases fall into older age groups, because with each successive year, the removed cases get older. The effect is a bias toward more accurate counting of younger age cohorts while undercounting older ones. The relative risk and conclusions of Hviid et al are predicated on finding fewer cases in the older thimerosal cohort and more in the younger nonthimerosal groups. This is an untenable approach given the recordkeeping problem, and thus Hviid et al should either adjust their 2000 data for record loss or use an alternative methodology.

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1. Hviid A, Stellfeld M, Wohlfahrt J, Melbye M. Association between thimerosal-containing vaccine and autism. *JAMA*. 2003;290:1763-1766.
2. Danish Institute for Computer-Assisted Reporting. *Registry Data Set*. Compiled 2003. Available at: <http://www.safeminds.org/sfpub/sfpub.html>. Accessed October 10, 2003.
3. Gillberg C, Coleman M. Adults with autism. In: Gillberg C, Coleman M. *The Biology of the Autistic Syndromes*. 3rd ed. London, England: Mac Keith Press; 2000: 73-78.

In Reply: In response to Dr Rimland, the Statens Serum Institut is the national center for prevention and control of infectious diseases in Denmark. It is a nonprofit state enterprise under the auspices of the Danish Ministry of Health and Interiors. Thus, any profit belongs to the state.

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