

Thimerosal and Vaccines — A Cautionary Tale

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In 1997, Frank Pallone, a U.S. congressman from New Jersey, attached a simple, 133-word amendment to a Food and Drug Administration (FDA) reauthorization bill. This amendment gave the FDA 2 years to “compile a list of drugs and foods that contain intentionally introduced mercury compounds and [to] provide a quantitative and qualitative analysis of the mercury compounds in the list.”¹ The bill — the FDA Modernization Act of 1997 — was signed into law on November 21, 1997. Neither the press nor the public took notice.

Eighteen months later, in May 1999, the FDA found that by 6 months of age, infants could receive as much as 75 μg of mercury from three doses of the diphtheria-tetanus-pertussis vaccine, 75 μg from three doses of the *Haemophilus influenzae* type b vaccine, and 37.5 μg from three doses of the hepatitis B vaccine — a total of 187.5 μg of mercury. The use of mercury in vaccines wasn't new; thimerosal, an ethylmercury-containing preservative, had been used to prevent bacterial contamination since the 1930s.

To determine whether the amount of mercury in vaccines was safe, FDA scientists examined safety guidelines from three sources: their own agency, the Environmental Protection Agency, and the Agency for Toxic Substances and Disease Registry. They found safety guidelines for methylmercury (environmental mercury), but not

for ethylmercury (thimerosal). Although these two molecules differ by only one carbon atom, the difference isn't trivial. Ethylmercury is excreted from the body much more quickly than methylmercury and is therefore much

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less likely to accumulate. For this reason, the safety guidelines that had been established for methylmercury weren't likely to be predictive of the safety of ethylmercury.

In mid-June 1999, FDA scientists held a meeting to discuss their findings. Present were representatives from the Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics (AAP) — the organizations that are principally responsible for making vaccine recommendations for U.S. children. Several attendees left the meeting concerned that infants might be receiving too much mercury from vaccines. Although they were largely reassured by studies of children who had ingested large quantities of mercury from fish in their diet,² they couldn't find a single study that compared neu-

rologic outcomes in children who had received thimerosal-containing vaccines with those in children who had not.

On July 9, 1999, after much wrangling, the CDC and AAP decided to exercise the precautionary principle. They asked pharmaceutical companies to remove thimerosal from vaccines as quickly as possible; in the interim, they asked doctors to delay the birth dose of hepatitis B vaccine in children who weren't at risk for hepatitis.³ A press release issued by the AAP revealed the ambivalence among its members: “Parents should not worry about the safety of vaccines,” it read. “The current levels of thimerosal will not hurt children, but reducing those levels will make safe vaccines even safer. While our current immunization strategies are safe, we have an opportunity to increase the margin of safety.” Critics wondered how removing something that hadn't been found to be unsafe could make vaccines safer. But many parents, frightened by a sudden change in policy, reasoned that thimerosal was targeted because it was harmful — and their faith in the vaccine infrastructure was shaken. Doctors were also confused by the recommendation.

In 2004, two studies performed in the United Kingdom examined whether thimerosal in vaccines caused neurodevelopmental or psychological problems⁴; neither found evidence that early expo-

sure to thimerosal was harmful. The study by Thompson and co-workers in this issue of the *Journal* (pages 1281–1292), the third and most comprehensive to date, also found no evidence of neurologic problems in children exposed to mercury-containing vaccines or immune globulins.

Although the precautionary principle assumes that there is no harm in exercising caution, the alarm caused by the removal of thimerosal from vaccines has been quite harmful. For instance, after the July 1999 announcement by the CDC and AAP, about 10 percent of hospitals suspended use of the hepatitis B vaccine for all newborns, regardless of their level of risk. One 3-month-old child born to a Michigan mother infected with hepatitis B virus died of overwhelming infection.

Then, beginning in 2000, parents founded several advocacy groups based on the belief that thimerosal had caused their children's autism. The notion that thimerosal caused autism has given rise to a cottage industry of charlatans offering false hope, partly in the form of mercury-chelating agents. In August 2005, a 5-year-old autistic boy in suburban Pittsburgh died from an arrhythmia caused by the injection of the chelating agent EDTA. Although the notion that thimerosal causes autism has now been disproved by several excellent epidemiologic studies, about 10,000 autistic children in the United States receive mercury-chelating agents every year. Furthermore, this notion has diverted atten-

tion and resources away from efforts to determine the real cause or causes of the disorder.

Meanwhile, some preparations of influenza vaccine still contain thimerosal, and all the negative media attention has made many parents reluctant to have their children receive this vaccine. Influenza virus causes hundreds of thousands of hospitalizations and about 100 deaths of children every year. By choosing not to vaccinate their children, these parents have elevated a theoretical (and now disproved) risk above the real risk of being hospitalized or killed by influenza.

The campaign against thimerosal has also caused legal, political, and social harms. Parents of 4800 autistic children have now taken their case to the federal Vaccine Injury Compensation Program, which was launched in 1988 to protect vaccine makers from frivolous litigation. If these claims are denied, it is possible that this litigation will spill over into civil courts, where decisions will be made by jurors, not federally appointed judges. Jurors are not always the best arbiters of scientific truth, and awards could be massive.

Politicians have used the thimerosal issue for political gain. On August 26, 2004, Arnold Schwarzenegger, governor of California, banned thimerosal-containing influenza vaccines from his state; others soon followed his lead.

Despite several years of reassuring studies, the thimerosal controversy continues to be emo-

tionally charged. Physicians, scientists, government policy advisors, and child advocates who have publicly stated that vaccines don't cause neurologic problems or autism have been harassed, threatened, and vilified, receiving hate mail and occasionally death threats. The CDC, in response to planned protests at its gates, recently beefed up security and instructed personnel about how to respond if physically attacked.

During the next few years, thimerosal will probably be removed from influenza vaccines, and the court cases will probably settle down. But the thimerosal controversy should stand as a cautionary tale of how not to communicate theoretical risks to the public; otherwise, the lesson inherent in the collateral damage caused by its precipitous removal will remain unlearned.

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4. Parker SK, Schwartz B, Todd J, Pickering LK. Thimerosal-containing vaccines and autistic spectrum disorder: a critical review of published original data. *Pediatrics* 2004;114:793-804. [Erratum, *Pediatrics* 2005;115:200.]
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