Vaccine Education Center

Thimerosal

Preservatives are used in some vaccines to prevent bacterial or fungal contamination. The requirement for preservatives in vaccines arose from many incidents in the early 20th century of children who developed severe and occasionally fatal bacterial infections after administration of vaccines contained in multidose vials. For example, in 1916, four children died, 26 developed local abscesses, and 68 developed severe systemic infections after receipt of a typhoid vaccine contaminated with the bacteria *Staphylococcus aureus*. As a consequence of this and similar incidents, preservatives have been required for vaccines contained in multidose vials (with some exceptions) since the 1930s.

Thimerosal, a mercury-containing preservative, has been the focus of intense scrutiny by the U.S. Congress and the news media following its removal from all routinely recommended childhood vaccines in 2001. Attention by the news media has caused some parents to fear that thimerosal contained in vaccines might have harmed their children.

Removal of thimerosal from vaccines

Removal of thimerosal from vaccines was precipitated by an amendment to the Food and Drug Administration (FDA) Modernization Act that was signed into law on November 21, 1997. The amendment gave the FDA two 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…." The amendment arose from a long-standing interest in lessening human exposure to mercury, a known neurotoxin and nephrotoxin.

At the time the FDA Modernization Act was passed, infants were recommended to receive three different vaccines that contained thimerosal — diphtheria-tetanus-acellular pertussis (DTaP), hepatitis B and *Haemophilus influenzae* type b (Hib). Infants receiving all of these vaccines could have been exposed to a cumulative dose of mercury as high as 187.5 ug by 6 months of age. The cumulative dose exceeded guidelines recommended by the Environmental Protection Agency (EPA) (see table below). Thimerosal was removed from all routinely recommended childhood vaccines by 2001 as a precautionary measure.

Exposure limits for mercury in infants less than or equal to 6 months of age by percentile body weight established by the Environmental Protection Agency (EPA), the Agency for Toxic Substance Disease Registry (ATSDR), and the Food and Drug Administration (FDA)

Agency	5th Percentile body weight	50th Percentile body weight	95th Percentile body weight
EPA	65 ug	89 ug	106 ug
ATSDR	194 ug	266 ug	319 ug
FDA	259 ug	354 ug	425 ug

Although no published studies to date have compared the incidence of developmental delay in children who received thimerosal-free or thimerosal-containing vaccines, several facts are reassuring that the level of mercury contained in vaccines was not likely to be harmful. Thimerosal contains 49.6 percent mercury by

weight and is metabolized to ethylmercury and thiosalicylate. Ethylmercury is contained in many drugs as well as biologicals. Adults and children inadvertently exposed to large quantities of ethylmercury acutely (quantities 1,000- to 1,000,000-fold greater than those found in vaccines) can suffer permanent neurologic damage and death. However, no data exist on the capacity of low-dose, chronic exposure to ethylmercury to harm the developing nervous system.

Methylmercury exposure guidelines
To develop guidelines for chronic exposure to ethylmercury, the EPA, FDA and ATSDR used data based on chronic exposure to methylmercury, the most common form of mercury found in the environment.

Guidelines from the EPA were based in part on data from pregnant women in rural Iraq exposed to large quantities of methylmercury. In October 1971 Iraq imported more than 90,000 metric tons of methylmercury-treated seed grain. The grain, distributed free-of-charge to farmers throughout the country, was used to make bread. Consumption of this bread caused an extensive outbreak of methylmercury poisoning resulting in more than 6,000 hospitalizations and 450 deaths. By examining the quantity of methylmercury contained in hair from mothers who ingested methylmercury, and comparing calculated exposures to methylmercury with the frequency of neurologic symptoms in their offspring (e.g., mental retardation, seizures and impaired vision or hearing), a dose of methylmercury required to cause neurologic damage in the fetus was established. **(Of interest, autism was not a consequence of exposure to methylmercury)**. The EPA determined “minimal dose” guidelines by taking the lowest quantity of methylmercury that might have resulted in harm to the fetus, and dividing by an “uncertainty” factor of 10. In other words, the guideline established by the EPA for infants exposed to ethylmercury in vaccines was one-tenth that found to be safe in fetuses exposed to methylmercury in the environment.

By using data from pregnant women in Iraq exposed to methylmercury in the environment to establish guidelines for chronic exposure of infants in the United States to ethylmercury in vaccines, two important (and incorrect) assumptions were made:

1. The toxicity and body’s disposal of methylmercury are the same as those of ethylmercury.
2. The central nervous system of the fetus and newborn are equally susceptible to the harmful effects of mercury. However, the body’s disposal of ethylmercury and methylmercury are not the same. One-half of the level of methylmercury in blood is eliminated from the blood in about 50 days compared with elimination in seven days for ethylmercury. Because ethylmercury is excreted from the body far more quickly than methylmercury, dosing guidelines would be very different. In support of this important difference, Pichichero and co-workers found that the level of mercury detected in the blood of 40 full-term infants 6 months of age or younger who received thimerosal-containing DTaP, hepatitis B and Hib vaccines were well within recommended guidelines. Further, the developing central nervous system of the fetus is far more susceptible to environmental and toxic insults than that of the newborn.

References
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