

Thiomersal

- Thiomersal (also known as thimerosal) is a mercury-based preservative that is used in some vaccines.
- None of the National Immunisation Program (NIP) vaccines currently supplied in Australia contain thiomersal.
- The removal of thiomersal-containing vaccines was a precautionary measure based on the ‘theoretical risk’ of harm from ethyl mercury, which is a metabolite of thiomersal.
- Where used in vaccines, the total amount of mercury derived from thiomersal is well below toxic levels.
- There is no evidence that thiomersal in vaccines has caused any serious health problems.

What is thiomersal?

Thiomersal is an organic compound containing 49.6% ethyl mercury by weight. It has been used in very small amounts in some vaccines since the 1930s to prevent bacterial and fungal contamination, particularly in multi-dose vials where withdrawing repeated doses from the same vial was more likely to result in contamination.¹

Do childhood vaccines contain thiomersal?

In Australia, thiomersal has been removed from all routine childhood vaccines since 2000. Multi-dose vaccine vials are no longer used for routine immunisation, so the risk of bacterial contamination from withdrawing repeated doses of vaccine is minimal. Most single-dose vaccine vials do not require preservatives; where needed, alternative preservatives to thiomersal are used.

What about vaccines for adults?

The levels of mercury in adults resulting from receiving thiomersal-containing vaccines are so low that experts do not recommend removal of thiomersal from vaccines for adolescents or adults.² Nevertheless, the only thiomersal-containing vaccine available in Australia is the Q fever vaccine (Q-VAX, CSL Biotherapies/Merck & Co Inc).

In many countries, thiomersal continues to be used in routine vaccines. The Global Advisory Committee on Vaccine Safety (GACVS) of the World Health Organization (WHO) has concluded that “there is currently no evidence of mercury toxicity in infants, children or adults exposed to thiomersal-containing vaccines” and that “there is no reason to change current immunisation practices with thiomersal-containing vaccines on the grounds of safety”.³

What is mercury?

Mercury is a natural element that occurs as a metal (metallic mercury which gives rise to mercury vapour); inorganic mercury (a form in the environment and in animal tissues); and organic mercury (the two main forms of which are methyl mercury and ethyl mercury).⁴ These various forms of mercury are found in the air, earth, aquatic sediment, in fish (particularly in long-lived fish such as sharks), and are used in industrial processes, dental fillings, thermometers and vaccines. The two forms of mercury that people are most likely to come into contact with are methyl mercury (in fish) and ethyl mercury (in vaccines).

Prior to 2000, very little was known about ethyl mercury, and recommendations for thiomersal-containing vaccines were based in part on extrapolations from analogies with methyl mercury and exposure limits for

mercury.⁴ It is now known that the two have very important differences in the way that they are absorbed and metabolised in the body.

Methyl mercury is more potent. It accumulates in the body because the time taken for the body to eliminate it (known as the 'half-life') is about 50 days. Ethyl mercury (in thiomersal), on the other hand, does not accumulate in the body to such an extent, because its half-life is only about 7–10 days.⁴ Ethyl mercury is rapidly converted in the body to inorganic mercury, which is excreted in the stool.⁴

Mercury can have harmful effects on the central nervous system, skin and kidneys, but most cases of the toxic effects of mercury have been reported as being from methyl mercury, not ethyl mercury.

How much mercury is harmful?

Mercury is harmful only after it reaches a certain level in the body. The toxicity depends on the amount of mercury consumed in relation to body weight, over a period of time. Therefore, infants are at greater risk from mercury than adults because of their size. Different expert bodies have determined that safe levels of mercury consumption lie somewhere between 0.7 µg/kg body weight/week (Environmental Protection Agency [EPA], USA) to 3.3 µg/kg of body weight/week (WHO).¹ These values indicate levels of exposure that can be tolerated, and have been deliberately calculated to be much lower than the level at which harm might occur. For example, the EPA level is 10 times below the lowest level calculated as causing harm, so there is a large built-in safety margin. In addition, these levels refer to methyl mercury, whereas thiomersal is converted to ethyl mercury, which is broken down and excreted more rapidly and does not accumulate in the body like methyl mercury.

How much mercury exposure results from vaccines?

In Australia, thiomersal has been removed from all routine childhood vaccines since 2000. When thiomersal-containing vaccines were being used before the year 2000, the maximum number of doses of thiomersal-containing vaccines a 6-month-old child might have received was as follows: 3 doses of diphtheria-tetanus-pertussis vaccine, 3 doses of hepatitis B vaccine and 3 doses of Hib vaccine. This would have resulted in a total intake of 175 µg of ethyl mercury, which is equivalent to about 1.9 µg/kg body weight/week, for an average-sized baby. This level is well below the WHO limit for methyl mercury discussed above. Two studies measuring mercury levels in the blood in infants who received thiomersal-containing vaccines indicated that their blood concentrations of mercury did not rise above designated levels, except possibly transiently in a premature infant less than 1kg in weight.⁵ These results were consistent with findings from studies investigating post-vaccination mercury levels in premature and low-birth-weight newborn infants² and adults.²

What studies have been done to look at the health effects of thiomersal in vaccines?

Several high-quality scientific studies in Europe, the United Kingdom, the United States of America (the USA) and Japan have shown that there is no evidence of developmental or neurological abnormalities resulting from the use of vaccines containing thiomersal.⁶⁻¹⁰

In 2004, a report by the Institutes of Medicine, an independent expert body in the USA, concluded that there is no association between autism and vaccines that contain thiomersal. Furthermore, in 2014, an extensive review and meta-analysis of all empirical studies on vaccines and autism and autism spectrum disorders (ASD) was published in the journal *Pediatrics*.¹¹ Case-control and cohort studies looking at the relationship between vaccine administration and development of autism and ASD were reviewed. Overall, pooled estimates indicated that autism and neurodevelopmental disorders are not associated with thiomersal in vaccines. Most of the epidemiological studies that do suggest a link between thiomersal and autism are notably by only one pair of authors and these studies "have significant design flaws", including a lack of appropriate controls and/or adjustment for confounders, "that invalidate their conclusions".^{12,13}

Why was thiomersal removed from childhood vaccines if there is no danger?

Although there has been a lack of evidence that thiomersal in vaccines is harmful, the recommendations to remove or to significantly reduce the amount of thiomersal present in vaccines were made for two main reasons. Firstly, it was to reduce exposure in premature babies with low birth weight in whom there was a theoretical risk that the intake of mercury from repeated doses of thiomersal-containing vaccines could

have been transiently high. Secondly, the intent has been to reduce total exposure to mercury in babies and young children in a world where other environmental sources (particularly in food such as fish) may be more difficult to eliminate.

In 1999, the US Food and Drug Administration (FDA) was authorised to assess mercury levels in all drugs and foods, not just vaccines. The results of these assessments raised concerns that the total amount of mercury derived from thiomersal (an ethyl mercury derivative) in vaccines used in the infant immunisation schedule could potentially exceed the recommended level.¹⁴ As a precautionary measure, the U.S. Public Health Service recommended that thiomersal be removed from many childhood vaccines to eliminate any potential risk. Since then more information has been gathered regarding ethyl mercury, and evidence shows that the rate at which ethyl mercury is broken down and excreted from the body makes it highly unlikely for it to be retained in the body at higher than recommended levels.

Online resources

- World Health Organization. Global Advisory Committee on Vaccine Safety. Thiomersal and vaccines: questions and answers. October 2011.
http://www.who.int/vaccine_safety/topics/thiomersal/questions/en/ Accessed September 2019
- Centers for Disease Control and Prevention (CDC). Vaccine safety. Thimerosal. October 2015.
<http://www.cdc.gov/vaccinesafety/Concerns/thimerosal/index.html>
- United States Food and Drug Administration. Vaccines, Blood and Biologics. Thimerosal in vaccines. February 2018.
<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/VaccineSafety/UCM096228>
- Immunization Action Coalition. Vaccine concerns. Thimerosal. June 2019.
<http://www.immunize.org/thimerosal/>
- The Children's Hospital of Philadelphia. Vaccine Education Center. Hot topics: thimerosal. April 2018..
<http://www.chop.edu/service/vaccine-education-center/hot-topics/thimerosal.html>

References

1. Institute of Medicine Immunization Safety Review C. In: Stratton K, Gable A, McCormick MC (editors). *Immunization Safety Review: Thimerosal-Containing Vaccines and Neurodevelopmental Disorders*. Washington (DC): National Academies Press (US) Copyright 2001 by the National Academy of Sciences. All rights reserved.; 2001.
2. Barregard L, Rekić D, Horvat M, et al. Toxicokinetics of mercury after long-term repeated exposure to thimerosal-containing vaccine. *Toxicological Sciences* 2011;120:499-506.
3. World Health Organization. Global Advisory Committee on Vaccine Safety, 20-21 June 2002 World Health Organization; 2002. Available from: <https://apps.who.int/iris/handle/10665/232032> (Accessed 9 September 2019).
4. Clifton JC, 2nd. Mercury exposure and public health. *Pediatric Clinics of North America* 2007;54:237-69, viii.
5. Pichichero ME, Gentile A, Giglio N, et al. Mercury levels in newborns and infants after receipt of thimerosal-containing vaccines. *Pediatrics* 2008;121:e208-14.
6. Heron J, Golding J. Thimerosal exposure in infants and developmental disorders: a prospective cohort study in the United Kingdom does not support a causal association. *Pediatrics* 2004;114:577-83.
7. van der Maas N, Dijs-Elsinga J, Kemmeren J, et al. Safety of vaccination against influenza A (H1N1) during pregnancy in the Netherlands: results on pregnancy outcomes and infant's health: cross-sectional linkage study. *BJOG: An International Journal of Obstetrics and Gynaecology* 2016;123:709-17.
8. Uno Y, Uchiyama T, Kurosawa M, Aleksic B, Ozaki N. Early exposure to the combined measles-mumps-rubella vaccine and thimerosal-containing vaccines and risk of autism spectrum disorder. *Vaccine* 2015;33:2511-6.

9. Barile JP, Kuperminc GP, Weintraub ES, Mink JW, Thompson WW. Thimerosal exposure in early life and neuropsychological outcomes 7-10 years later. *Journal of Pediatric Psychology* 2012;37:106-18.
10. Mrozek-Budzyn D, Majewska R, Kieltyka A, Augustyniak M. Neonatal exposure to Thimerosal from vaccines and child development in the first 3 years of life. *Neurotoxicology and Teratology* 2012;34:592-7.
11. Taylor LE, Swerdfeger AL, Eslick GD. Vaccines are not associated with autism: an evidence-based meta-analysis of case-control and cohort studies. *Vaccine* 2014;32:3623-9.
12. 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.
13. Bennett M, Webster A, Goodall E, Rowland S. *Life on the autism spectrum: translating myths and misconceptions into positive futures*: Springer Nature; 2019. Available from: <https://www.springer.com/gp/book/9789811333583#aboutBook>.
14. Centers for Disease Control and Prevention (CDC). Thimerosal in vaccines: a joint statement of the American Academy of Pediatrics and the Public Health Service. *MMWR Morbidity and Mortality Weekly Report* 1999;48:563-5.