

Thiomersal

Thiomersal (also known as thimerosal) is a mercury-based preservative that has been used in some vaccines. There is no evidence that thiomersal in vaccines has caused any health problems except minor reactions, such as redness at the injection site. Follow-up studies in children and adults have not shown any harmful effects from thiomersal in vaccines. However, because of the ‘theoretical risk’ of harm from mercury, thiomersal was removed from most childhood vaccines as a precautionary measure. Current vaccines contain very little, if any, thiomersal.

What is thiomersal?

Thiomersal, also known as thimerosal, 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.

In 1999, concerns were raised in the United States that the total amount of mercury derived from thiomersal in vaccines given in the infant immunisation schedule would potentially exceed the recommended level set by a US government agency. There were no studies indicating that the ethyl mercury in thiomersal had caused harmful effects in children (except for occasional redness at the injection site). However, it was recommended that thiomersal be removed from many childhood vaccines to eliminate any potential risk. Since that time, much more information has been gathered regarding thiomersal (ethyl mercury).

What is mercury?

Mercury is a metal occurring naturally in the environment. Mercury is found in three main forms: 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). 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 organic forms of mercury, methyl mercury and ethyl mercury (in thiomersal), are closely related but they

have important differences. 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) does not accumulate in the body to such an extent, because its half-life is only about 7–10 days. Ethyl mercury is rapidly converted in the body to inorganic mercury, which is excreted in the stool. 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, because of their size, infants are at greater risk than adults. 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 (World Health Organization). 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. The exception is one type of hepatitis B vaccine which contains a greatly reduced amount of thiomersal (see Table 1 below). 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 World Health Organization (WHO) limit for methyl mercury discussed above. Two studies measuring mercury levels in the blood in infants given thiomersal-containing vaccines have 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.

In many countries, thiomersal continues to be used in vaccines. The Global Advisory Committee on Vaccine Safety (GACVS) of the 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”.

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

Many studies in Denmark, Sweden, the United States, and the United Kingdom have now shown that there is no evidence of developmental or neurologic abnormalities resulting from the use of vaccines containing thiomersal. In 2004, a report by the Institutes of Medicine, an independent expert body in the United States, concluded that there is no association between autism and vaccines that contain thiomersal. Also in 2004, an extensive review of all the studies on thiomersal-containing vaccines and autism and neurodevelopmental disorders was published in the journal *Pediatrics*. Studies looking at autism, mental retardation, speech disorders, and attention deficit disorder, as well as other conditions, were reviewed. Overall, the evidence indicated that autism and neurodevelopmental disorders are not associated with thiomersal in vaccines. The reviewers noted that the epidemiologic studies done that do suggest a link were notably only by one pair of authors and “have significant design flaws that invalidate their conclusions”.

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 significantly reduce the amount present in vaccines were made for two main reasons. Firstly, it was to reduce exposure in very small premature babies with low body 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. Along with these recommendations, Australian guidelines have been developed on limiting the consumption of certain types of fish, particularly in the diet of pregnant women and young children. This advice is available at <http://www.foodstandards.gov.au/foodmatters/mercuryinfo/ish.cfm> (accessed December 2009).

In the place of thiomersal, preservatives have either been eliminated from single dose vaccine vials, or alternative preservatives have been used. Multi-dose vaccine vials are no longer used for routine immunisation in Australia, so the risk of bacterial contamination from withdrawing repeated doses of vaccine is minimal. In the case of some vaccines, such as the Engerix-B paediatric formulation, thiomersal is no longer added specifically as a preservative. However, a very small amount or ‘trace’ of thiomersal may remain from the manufacturing process. The amount of thiomersal remaining is at least 25 times less than what the vaccine previously contained and is insignificant.

What about vaccines for adults?

The levels of mercury in adults resulting from thiomersal-containing vaccines are so low that experts do not recommend removal of thiomersal from vaccines for adolescents or adults. The vaccines available in Australia that currently contain thiomersal are listed in Table 2.

Which vaccines contain thiomersal?

All vaccines on the current National Immunisation Program (NIP) schedule for infants and children under the age of 8 years are now free of thiomersal. The exception is one of the infant hepatitis B vaccines, Engerix-B paediatric formulation, which contains a greatly reduced amount of thiomersal (<1 µg per dose) and this amount of thiomersal is considered to be insignificant from a clinical perspective. These conclusions are supported by recommendations in the United States where two hepatitis B vaccines, one without thiomersal, and one with <0.5 µg of mercury (<1.0 µg thiomersal/paediatric dose) have been in use since about 2000 for administration at birth and beyond. In 2000, the Centers for Disease Control and Prevention (CDC) issued a statement that both vaccines can be considered preservative-free for practical purposes. Similarly, in 2003, the Canadian National Advisory Committee on Immunization (NACI) recommended the

use of either vaccine stating that “Trace amounts of thimerosal, equivalent to <0.5 µg of mercury per dose, present in some paediatric vaccine formulations can be considered insignificant from a clinical perspective, except for people with a previous hypersensitivity to thimerosal.”

The following tables list the vaccines used in Australia that are thiomersal-free* (Table 1) and vaccines that contain thiomersal (Table 2). Please note that some of the vaccines listed below are not registered for use in children. Please consult the individual product information for each vaccine to obtain further information.

Table 1: Thiomersal-free vaccines available in Australia

Vaccine	Trade name	Manufacturer
Cholera	Dukoral	Sanofi Pasteur Pty Ltd
Diphtheria/tetanus	ADT Booster	Statens Serum Institut/CSL Biotherapies
Diphtheria/tetanus/pertussis	Adacel	Sanofi Pasteur Pty Ltd
Diphtheria/tetanus/pertussis	Boostrix	GlaxoSmithKline
Diphtheria/tetanus/pertussis/polio	Adacel-polio	Sanofi Pasteur Pty Ltd
Diphtheria/tetanus/pertussis/polio	Boostrix-IPV	GlaxoSmithKline
DTPa-hepatitis B-IPV	Infanrix Penta	GlaxoSmithKline
DTPa-hepatitis B-IPV-Hib	Infanrix hexa	GlaxoSmithKline
DTPa-IPV	Infanrix IPV	GlaxoSmithKline
<i>Haemophilus influenzae</i> B PRP-OMP	Liquid PedVaxHIB	CSL Biotherapies/Merck & Co Inc.
<i>Haemophilus influenzae</i> B PRP-T	Hiberix	GlaxoSmithKline
Hepatitis A	Avaxim	Sanofi Pasteur Pty Ltd
Hepatitis A	Havrix 1440	GlaxoSmithKline
Hepatitis A	Havrix Junior	GlaxoSmithKline
Hepatitis A – adult and paediatric/adolescent formulations	VAQTA	CSL Biotherapies/Merck & Co Inc.
Hepatitis A/hepatitis B	Twinrix (720/20)	GlaxoSmithKline
Hepatitis A/hepatitis B	Twinrix Junior (360/10)	GlaxoSmithKline
Hepatitis A/typhoid	Vivaxim	Sanofi Pasteur Pty Ltd
Hepatitis B-Hib	COMVAX	CSL Biotherapies/Merck & Co Inc.
Hepatitis B – paediatric and adult formulations*	Engerix-B*	GlaxoSmithKline
Hepatitis B – paediatric, adult and dialysis formulations	H-B-VAX II	CSL Biotherapies/Merck & Co Inc.
Human papillomavirus	CERVARIX	GlaxoSmithKline
Human papillomavirus	GARDASIL	CSL Biotherapies/Merck & Co Inc.
Inactivated poliomyelitis	IPOL	Sanofi Pasteur Pty Ltd
Influenza	Fluad	Novartis Vaccines and Diagnostics

Vaccine	Trade name	Manufacturer
Influenza	Fluarix	GlaxoSmithKline
Influenza	Fluvax	CSL Biotherapies
Influenza	Fluvirin	Novartis Vaccines and Diagnostics
Influenza	Influvac	Solvay
Influenza	Vaxigrip	Sanofi Pasteur Pty Ltd
Influenza	Vaxigrip Junior	Sanofi Pasteur Pty Ltd
Measles-mumps-rubella	Priorix	GlaxoSmithKline
Meningococcal serogroup C	Meningitec	Wyeth Australia Pty Ltd
Meningococcal serogroup C	Menjugate	CSL Biotherapies/Novartis Vaccines and Diagnostics
Meningococcal serogroup C	NeisVac-C	Baxter Healthcare
Meningococcal serogroup A, C, W ₁₃₅ , Y polysaccharide	Menomune	Sanofi Pasteur Pty Ltd
23-valent pneumococcal polysaccharide	Pneumovax	CSL Biotherapies/Merck & Co Inc.
7-valent pneumococcal conjugate	Prevenar	Wyeth Australia Pty Ltd
Rabies	Merieux Inactivated Rabies Vaccine	Sanofi Pasteur Pty Ltd
Rabies	Rabipur Inactivated Rabies Virus Vaccine	CSL Biotherapies/Novartis Vaccines and Diagnostics
Rotavirus (oral)	Rotarix	GlaxoSmithKline
Rotavirus (oral)	Rotateq	CSL Biotherapies/Merck & Co Inc.
Rubella	Meruvax II	CSL Biotherapies/Merck & Co Inc.
Typhoid	Typherix	GlaxoSmithKline
Typhoid	Typhim Vi	Sanofi Pasteur Pty Ltd
Typhoid (oral)	Vivotif Oral	CSL Biotherapies/Berna Biotech Ltd
Varicella	Varilrix	GlaxoSmithKline
Varicella	Varivax	CSL Biotherapies/Merck & Co Inc.
Yellow fever	Stamaril	Sanofi Pasteur Pty Ltd

* The paediatric formulation contains trace amounts of thiomersal, equivalent to <0.5 µg of mercury per 0.5 mL dose and the adult formulation contains <1.0 µg of mercury per 1 mL dose. This is considered insignificant from a clinical perspective, except for people with a previous hypersensitivity to thiomersal.

Table 2: Vaccines available in Australia that contain thiomersal

Vaccine	Trade name	Manufacturer
Japanese encephalitis	JE-VAX	Sanofi Pasteur Pty Ltd
Q fever	Q-VAX	CSL Biotherapies/Merck & Co Inc.

Further reading

Offit PA. Thimerosal and vaccines: a cautionary tale. *New England Journal of Medicine* 2007;357:1278-1279.

Thompson WW, Price C, Goodson B, et al. Early thimerosal exposure and neuropsychological outcomes at 7 to 10 years. *New England Journal of Medicine* 2007;357:1281-1292.

Pichichero ME, Cernichiari E, Lopreiato J, Treanor J. Mercury concentrations and metabolism in infants receiving vaccines containing thiomersal: a descriptive study. *Lancet* 2002;360:1737-1741.

Clifton JC, II. Mercury exposure and public health. *Pediatric Clinics of North America* 2007;54:237-269.

Eldred BE, Dean AJ, McGuire TM, Nash AL. Vaccine components and constituents: responding to consumer concerns. *Medical Journal of Australia* 2006;184:170-175.

Immunization Safety Review Committee, Board on Health Promotion and Disease Prevention, Institute of Medicine. Stratton K, Gable A, McCormick MC, eds. Immunization safety review: thimerosal-containing vaccines and neurodevelopmental disorders. Washington, D.C.: National Academy Press, 2001.

Thimerosal in vaccines: a joint statement of the American Academy of Pediatrics and the Public Health Service. *MMWR - Morbidity & Mortality Weekly Report* 1999;48:563-565.

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.

Immunization Safety Review Committee, Board on Health Promotion and Disease Prevention, Institute of Medicine. Stratton K, Gable A, Shetty P, McCormick M, eds. Immunization safety review: measles-mumps-rubella vaccine and autism. Washington, D.C.: National Academy Press, 2001.

Heron J, Golding J, ALSPAC Study Team. Thimerosal exposure in infants and developmental disorders: a prospective cohort study in the United Kingdom does not support a causal association. *Pediatrics* 2004;114:577-583.

Clements CJ. The evidence for the safety of thiomersal in newborn and infant vaccines. *Vaccine* 2004;22:1854-1861.

American Academy of Pediatrics. Study fails to show a connection between thimerosal and autism. May 16, 2003. Available at: <http://www.aap.org/profed/thimaut-may03.htm> (accessed Dec 2009).

Offit, PA, Jew RK. Addressing parents' concerns: do vaccines contain harmful preservatives, adjuvants, additives, or residuals? *Pediatrics* 2003;112:1394-1397.

Online resources (sites accessed December 2009)

World Health Organization. Global Advisory Committee on Vaccine Safety. Thiomersal and vaccines: questions and answers. July 2006. http://www.who.int/vaccine_safety/topics/thiomersal/questions/en/

Centers for Disease Control and Prevention (CDC). Vaccine safety. Thimerosal. December 2009. <http://www.cdc.gov/vaccinesafety/Concerns/thimerosal/index.html>

United States Food and Drug Administration. Vaccines, Blood and Biologics. Thimerosal in vaccines. June 2009. <http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/VaccineSafety/UCM096228>

Immunization Action Coalition. Vaccine concerns. Thimerosal. July 2009. <http://www.immunize.org/thimerosal/>

National Institute of Allergy and Infectious Diseases, National Institutes of Health, US Department of Health and Human Services. Vaccines. Thimerosal in vaccines. December 2009. <http://www.niaid.nih.gov/factsheets/thimerosal.htm>

Public Health Agency of Canada. Thimerosal in vaccines and autism: questions and answers. January 2008. http://www.phac-aspc.gc.ca/im/q_a_thimerosal_e.html

The Children's Hospital of Philadelphia. Vaccine Education Center. Hot topics: thimerosal. April 2008.. <http://www.chop.edu/service/vaccine-education-center/hot-topics/thimerosal.html>