



Thiomersal and Vaccines

What is thiomersal?

Thiomersal (also known as thimerosal) is a mercury based preservative used in some vaccines and other pharmaceutical products such as antiseptics.

Should I be concerned?

No, firstly because extensive research has shown that thiomersal in vaccines is safe and secondly because there is no thiomersal in the routine schedule childhood vaccines given in New Zealand to children.

What is Mercury?

Mercury is a naturally occurring element found in the earth's crust, soil, water and the air. Mercury is released into the environment by volcanic eruptions, weathering of rocks and the burning of coal. Once released mercury can find its way through the food chain via fish and other animals. At high levels it can be toxic.

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 methylmercury and ethylmercury).

These various forms of mercury are found in the air, earth, aquatic sediment, in fish (particularly in long lived fish such as sharks and oily fish such as tuna) and some forms of mercury are used in industry.

Not all mercury is created equally and some forms pose a greater health risk than others. For example mercury vapour is extremely dangerous whereas amalgam, used in dental fillings, has not been shown to pose a health risk. In 2006 results from two large randomised clinical trials investigating the safety of amalgam dental fillings compared with other materials in children both suggest that amalgam fillings are safe and that it should remain a viable option for dental restoration.

Thiomersal and Mercury

Thiomersal (also known as thimerosal) is a mercury based preservative used since the 1930s in the manufacture of some vaccines and other pharmaceutical products. It is used to prevent bacterial and fungal growth. It has also been used during vaccine production both to inactivate certain organisms and toxins and to maintain a sterile production line.

Mercury in the body

The two organic forms of mercury, methylmercury and ethylmercury (in thiomersal), are closely related but they have important differences.

- Methylmercury (found in fish) 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.
- Ethylmercury (in thiomersal) does not accumulate in the body to such an extent, because its half life is only about 7-10 days. Ethylmercury is rapidly converted in the body to inorganic mercury and excreted.

Mercury can have harmful effects on the central nervous system, skin and kidneys, but most cases of the toxic effects of mercury have been from methylmercury, not ethylmercury.

How much mercury is safe?

Mercury becomes 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. Infants are therefore at greater risk than adults because they are smaller.

Safe levels of mercury have been estimated by different expert bodies and lie somewhere between 0.7- 3.3 $\mu\text{g}/\text{kg}$ body weight/week. These levels have been deliberately calculated to be much lower than the level at which harm might occur. For example the Environmental Protection Agency (USA) level has been set ten times below the lowest level calculated as causing harm, so there is a large built-in safety margin.

Importantly these levels refer to methylmercury, whereas thiomersal contains ethylmercury, which is broken down and excreted more rapidly and does not accumulate in the body like methylmercury. Therefore the safety limits for ethylmercury will be much higher.

Thiomersal in vaccines given to NZ children

In 2000 New Zealand moved to phase out all thiomersal-containing vaccines in the NZ childhood schedule vaccines. Note that some influenza vaccines contain thiomersal.

Thiomersal has never been present in the MMR vaccine or any other live vaccine.

When thiomersal-containing vaccines were being used prior to 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 ethylmercury, which is equivalent to about 1.9 $\mu\text{g}/\text{kg}$ body weight per week, for an average-sized baby. This level is well below the World Health Organization (WHO) limit for methylmercury discussed above. Studies measuring mercury levels in the blood of 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.

Thiomersal continues to be used in vaccines in many countries. The WHO's Global Advisory Committee on Vaccine Safety (GAVSC) 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 show this safety?

Many studies have been conducted including in Denmark, Sweden, the United States, and the United Kingdom. These have 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 *Paediatrics*. 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 conducted that suggest a link (notably only by one pair of authors) "have significant design flaws that invalidate their conclusions."

So why stop using vaccines that contain thiomersal?

Recommendations to remove thiomersal from 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 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, guidelines have been developed on limiting the consumption of certain types of fish, particularly in the diet of pregnant women and young children.

Thiomersal containing vaccines have been replaced with single dose vaccine vials or alternative preservatives have been used.

Mercury, vaccines and autism

In 1971 Iraq imported grain that had been inadvertently fumigated with methylmercury. People consumed bread baked from this contaminated grain resulting in one of the worst single source mercury poisonings in history. There were 6500 people hospitalized and 450 died. Pregnant woman delivered babies with epilepsy and mental retardation however they did not deliver babies with an increased risk of autism.

There have been several large studies comparing the risk of autism in children who received vaccines containing thiomersal to those who did not. The studies were well designed and reproducible, consistently finding that the incidence of autism was the same in both groups.

Studies of the head size, speech patterns, vision, coordination and sensitization of children poisoned by mercury show that the symptoms of mercury poisoning are clearly different from the symptoms of autism.

Causes of Autism

- **Autism clearly has a genetic basis. When one identical twin has autism, the chance that the other twin has autism is about 90% however for fraternal twins the chance is less than 10%**
- **There are also environmental causes of autism. Mothers who took thalidomide early in pregnancy had babies at increased risk for autism. Also, mothers who suffered rubella early in pregnancy have babies at increased risk of autism, however babies infected with the virus after birth do not develop autism. There are clearly windows early in development for viruses or drugs to cause autism however later in pregnancy or after birth the window appears closed.**
- **Women in the USA were occasionally exposed to mercury when they were given a product called RhoGam when their blood type was not compatible with their baby's blood type. This was to prevent the blood mismatch harming the baby. The product RhoGam contained thiomersal as a preservative. Babies exposed to RhoGam did not have a higher risk for autism than babies who never received RhoGam**

Although thalidomide and rubella virus can cause autism in pregnancy, evidence suggests mercury does not.

VACCINE	TRADE NAME	MANUFACTURER	THIOMERSAL
Hepatitis B	H-B-VaxII* preservative-free	CSL/MSD	Nil
DTPa	Infanrix and Tripacel	GSK, CSL	Nil
DTPa-hepatitis B	Infanrix-Hep B	GlaxoSmithKline	Nil
DTPa-IPV	Infanrix-IPV	GlaxoSmithKline	Nil
DTPa-hepatitis B-IPV	Infanrix-Penta	GlaxoSmithKline	Nil
DTPa-hepatitis B-IPV-Hib B PRPT	Infanrix-Hexa	GlaxoSmithKline	Nil
dTap	Boostrix (adult)	GSK	Nil
Hepatitis B - Hib B PRP-OMP	Comvax	MSD	Nil
Haemophilus influenza B OMP	Liquid PedVaxHIB	MSD	Nil
Haemophilus influenzae B PRPT	ActHib)	Pasteur Mérieux	Nil
Haemophilus influenzae B HbOC	HibTITER	Lederle	Nil
Measles, mumps, rubella	MMR II, Priorix	MSD, GSK	Nil
Meningococcal group B vaccine	MeNZB	Chiron	Nil
Meningococcal group C conjugate vaccines	Meningitec, Menjugate,	Wyeth, CSL, Baxter	Nil
Oral polio vaccine	OPV	CSL	Nil
Inactivated polio vaccine (IPV)	IPOL	Aventis Pasteur	Nil
Polysaccharide pneumococcal vaccine	Pneumovax 23	MSD	Nil
7-valent pneumococcal conjugate vaccine	Prevenar	Lederle	Nil
Varicella vaccine	Varilrix	GSK	Nil
Varicella vaccine	Varivax	CSL/MSD	Nil
Influenza vaccine	Vaxigrip, Fluvax	Aventis Pasteur, CSL	Nil
Combined diphtheria and tetanus vaccine	CDT	CSL	50 micrograms
Adult diphtheria and tetanus vaccine	ADT	CSL	50 micrograms
Diphtheria vaccine		CSL	50 micrograms
Hepatitis B	Engerix B Adult	GlaxoSmithKline	<2 micrograms
*Influenza vaccines	Fluarix, Influvac, Fluvax	GlaxoSmithKline, Solvay, CSL	50 micrograms
Japanese encephalitis vaccine	JE Vax	CSL	35 micrograms
Q fever vaccine	Q vax	CSL	50 micrograms
Tetanus	Tet-tox	CSL	25 micrograms
Hepatitis A	Havrix 1440	GSK	Nil
Hepatitis A	Havrix Jr	GSK	Nil
Hepatitis A	Vaqa (adult)	MSD	Nil
Hepatitis A	Vaqa (paed)	MSD	Nil
Hepatitis A	Avaxim	Aventis	Nil
Hepatitis A and B	Twinrix	GSK	Nil
Hepatitis A and B	Twinrix Jr	GSK	Nil
Cholera	Dukoral (oral)	Sanofi Pasteur	Nil
Meningococcal	Menomune ACYW-135	Sanofi Pasteur	Nil
Meningococcal	Mencevax ACYW-135	GSK	Nil
Pneumococcal	Pneumovax 23	MSD	Nil

Table 1. Vaccines available in New Zealand and their level of thiomersal

* This product should be considered equivalent to thiomersal-free products. This vaccine may contain trace amounts (<0.3 mcg) of mercury left after post-production thiomersal removal; these amounts have no biological effect. JAMA 1999;282(18) and JAMA 2000;283(16).

Further reading and online resources

- **Thiomersal in Vaccines.** WHO Global Advisory Committee on Vaccine Safety. http://www.who.int/vaccine_safety/topics/thiomersal/en/ (Accessed April 18, 2006)
- **Mercury and Vaccines.** National Immunisation Programme. Centre for Disease Control (CDC). <http://www.cdc.gov/nip/vacsafe/concerns/thimerosal/default.htm> (Accessed April 18, 2006)
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Other Links

- Synopses of articles from the scientific, peer-reviewed literature related to vaccines and immunization can be found at http://www.immunizationinfo.org/immunization_science.cfm?cat=1 (Accessed April 18 2006)
- Journal abstracts related to thiomersal can be found at <http://www.immunize.org/safety/thiomersal.htm#journalarticles> (accessed April 18 2006)
- American Academy of Pediatrics: "Vaccine Safety: at http://www.cispimmunize.org/ill/ill_main.html
- Centers for Disease Control and Prevention: "Vaccine Safety Issues" at <http://www.cdc.gov/nip/vacsafe/concerns/gen/of-interest.htm>
- Immunization Action Coalition: "Thiomersal Information" at <http://www.immunize.org/safety/thiomersal.htm>
- National Network for Immunization Information: "Thiomersal/Mercury" at http://www.immunizationinfo.org/thiomersal_mercury_issues.cfm
- U.S. Food and Drug Administration: "Thiomersal in Vaccines" at <http://www.fda.gov/cber/vaccine/thiomersal.htm>
- National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases at <http://www.ncirs.usyd.edu.au/>