

REGULAR ARTICLE

# Thimerosal exposure (from tetanus-diphtheria vaccine) during pregnancy and neurodevelopment of breastfed infants at 6 months

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## Abstract

**Aim:** We studied the effect on neurodevelopment of infants who are exposed to thimerosal in tetanus-diphtheria (Td) vaccines during pregnancy.

**Methods:** We compared Gesell Developmental Schedules (GDS) of exclusive breastfed infants at 6 months born to mothers who received Td (1 to 3 doses) against those who were born to mothers who did not take such vaccines.

**Results:** Compared with the group of infants not exposed to ethylmercury in utero, the infants of exposed mothers showed no significant difference in neurodevelopment delays. Although there was a significant correlation between hair-Hg of mothers and hair-Hg of neonates (Spearman  $r = 0.353$ ;  $p = 0.0011$ ), there was no significant correlation between the level of in utero exposure to ethylmercury in Td vaccines and neonate's hair-Hg concentrations (Spearman  $r = 0.060$ ;  $p = 0.5922$ ). However, regression analysis showed that GDS at 6 months was significantly associated with total mercury concentration of neonate's hair but was not sensitive to the number of vaccines taken by the mother.

**Conclusion:** Early neurodevelopment of exclusively breastfed infants is sensitive to in utero exposure to mercury, but maternal thimerosal exposure in tetanus-diphtheria vaccines per se cannot portend clinical neurodevelopment delays measured by GDS at 6 months.

## INTRODUCTION

Prenatal exposure to neurotoxic substances can cause morphological and functional anomalies in infants; Hg is one such substance. Long-term risk of neurological conditions or diseases can be the result of adverse responses to in utero exposures to environmental chemicals (arising from occupational hazards, drugs and tobacco smoking). Depending on the exposure, these chemicals can affect the central nervous system (CNS) leading to neurodevelopmental disabilities or can cause subtle changes capable of inducing adaptive responses (1); some of these responses are only noticeable through changes in behaviour in later years. Better protection of the CNS during the most vulnerable time includes avoiding exposure or remedying some of these early effects through breastfeeding (2).

Despite the universal use of small amounts of thimerosal as a preservative of vaccines since the 1930s, research on its toxicokinetics and toxicodynamics in neonates and infants is rare and very limited; and, as a consequence, knowledge of its Hg metabolite (ethylmercury – etHg) is derived mostly

from methylmercury (meHg) studies. The mechanistic understanding of organomercurials' neurotoxicity is unquestionable, and etHg is no exception. However, our ability to understand the safety of small quantities of etHg derived from thimerosal-containing vaccines (TCV) is still unsatisfactory (3); its limited toxicological understanding is the result of studies in animals and theoretical models (4). Although there is no proven causation of permanent neurological disorders in children exposed to TCV-etHg, its plausibility has been inferred from neurotoxic disasters caused by accidental exposure to high levels of organic Hg compounds (5).

The infant brain takes unusually a long period to form, with some higher functions being sensitive to initial anatomical and physiological conditions. Thus, the vulnerability of the developing brain to neurotoxic substances is amply recognized (6). Organic Hg compounds are among the neurotoxic substances whose effects depend on the CNS structure at time of exposure (6). Therefore, the use of TCV during pregnancy has been cautioned (3,7,8). Schilthuis and van Wijnen (9) raised an alert about the risk of thimerosal-containing gammaglobulin preparations for the prevention of hepatitis A in pregnant women, recommending alternatives without thimerosal. However, in the case of the tetanus vaccine, it has never been questioned (10). Tetanus vaccines are strategically used to increase protection of mothers and neonates and are considered safe. However,

## Abbreviations

CNS, vulnerable central nervous system; etHg, ethylmercury; GDS, Gesell Developmental Schedules; meHg, methylmercury; TCV, thimerosal-containing vaccines; Td, tetanus and diphtheria vaccine.