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STUDY ON THE DEVELOPMENTAL TOXICITY OF THIMEROSAL

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Thimerosal is a mercury-containing compound used in trace amounts to prevent bacteria and other organisms from contaminating vaccines, especially in opened multi-dose vials. The toxicity of mercury is well known and those most at risk are occurred in unborn and newborn babies. Exposure to mercury from vaccines containing thimerosal in the first 6 months of life ranges from 0 to 187 μg based on which vaccines are administered. If all thimerosal containing vaccines are given, the total exposures exceed the limit of EPA guidelines, and possibly other guidelines, for the smallest infants. However, the precise cause of toxicity from low concentrations of exposure to thimerosal remains uncertain. Also clinicians are uncertain as to how much mercury can be safely given at 1 time when multiple thimerosal-containing vaccines are administered simultaneously. So, this study were performed to evaluate the toxicity of the thimerosal in rat embryos and neonates. Test methods included short-term in vitro battery system, such as whole embryo culture(WEC) system and midbrain micromass culture system, and in vivo test of neonatal toxicity in Wistar rats. Ethylmercury and methylmercury used as positive controls for the evaluating of toxic effects of mercury. In whole embryo assay, treated concentrations of thimerosal, ethylmercury and methylmercury were up to 0.01~5 $\mu\text{g}/\text{m}\ell$ respectively. All compounds didn't show any morphological abnormalities, but showed retardation of growth and development in dose dependent manner(>0.5 $\mu\text{g}/\text{m}\ell$). Also, in midbrain micromass assay, mercury compounds showed inhibition of growth and damages of midbrain cells. These data indicated that thimerosal showed developmental toxicity in vitro. In vivo test of neonatal toxicity, Wistar rats were administered subcutaneously with thimerosal, ethylmercury, or methylmercury(5~500 $\mu\text{g}/\text{kg}$) during from postnatal day(PND) 4 to 25. Significant effects of these compounds on relative organ weights and organ morphology were not observed in this experiment. But accumulation of

mercury was detected in the kidney and testis by treatment with thimerosal, ethylmercury, or methylmercury. These results suggest that thimerosal may be a harmful compound to embryo and neonate, but used concentration of thimerosal in these experiments is very higher than that of clinical application. In the future, further investigation is needed on the safety of vaccine components including a thimerosal in vitro and in vivo.

keyword : Thimerosal, Mercury, Vaccine, Whole embryo culture, Midbrain micromass assay