Correspondence

Premature and neonate modeling of thimerosal exposure and neurodevelopment: additional comments

Health professionals in pediatrics, especially in neonatology, welcome the timely work of Chen et al.[1] Despite the widespread use of Thimerosal-containing vaccines (TCVs) in premature newborns, this is the first attempt to model exposure to thimerosal and neurodevelopment; that is why this study is both interesting and important. Given the special circumstances of the immature neurologic and immunologic systems of the premature-newborn, it is worth raising additional relevant issues to this revealing paper.

Metabolic stress is known to exacerbate Hg toxicity in rat model.[2] Body weight loss in human neonates (10%) occurs at the expense of body water and is more taxing in preterm babies;[2] neonates lose weight up to 5 days of life, but term-babies regain initial weight at a faster rate than preterm babies (10 days against 10 to 14 days respectively).

So far, all findings of low doses of ethylmercury relevant to vaccines demonstrated that infant animals (mice, rats, and monkeys) manifested neurological delays.[2] However, it is worth mentioning that another confounder not considered in any experimental study so far is TCV taken during pregnancy and other cumulative sources of environmental Hg exposure. Nowadays, expecting mothers are exposed to environmental Hg (fish-MeHg and dental amalgams) and likely to TCVs.

What is the vaccine equivalent of the modeled Thimerosal exposure? Actually Chen et al's Thimerosal doses used (32.2 μg/kg b.w. or 16 μgHg/kg b.w.) were close or relatively smaller than that actually reported (21.1 μgHg/kg b.w.) in premature babies;[3] additionally, the highest dose of Thimerosal (131.2 μg/kg b.w. or 65.6 μgHg/kg b.w.) was less than the cumulative doses received during the first six months, after correcting for weight gain.[3] In this regard, Chen et al's model is conservative and as a consequence the results are significant to model safety ranges of premature or neonate Hg exposure relevant to pediatric TCVs.

Before 2004, there are hardly any experimental studies addressing small doses of ethylmercury and neurological outcomes; these recent studies confirm well known impairment of nervous system functioning known to be caused by small doses of methylmercury.[2] It should be noticed that all these results focused on one mercury compound and a specific measured outcome. However, another important topic to consider in relation to experimental neurotoxicity of TCV is the obligatory occurrence of ethylmercury in association with aluminum as an adjuvant of such vaccines. In the specific case of hepatitis B vaccine, the ratio of Al:Hg is 20.[4] Given the susceptibility of young rats to aluminum toxicity[5] and translocation of intramuscular injection of alum-containing vaccine from muscle to the brain,[6] future experiments should explore the combined effect of Al plus Hg at ratios found in pediatric TCVs in order to address the actual range of combined Al and Hg in such vaccines used by the majority of infants in poor countries. Indeed, we are now learning that adjuvant-Al can produce neurological effects on its own,[7] but we have no clue as to the combined effect of ethylmercury plus adjuvant-Al as they occur in pediatric TCVs used in developing countries.

José G. Dórea
C.P. 04322
Faculty of Health Sciences, Universidade de Brasilia
70919-970 Brasilia, DF, Brazil
Email: jg.dorea@gmail.com

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We are grateful to your comments. The dose of thimerosal used in our study was according to the common mercury content in hepatitis B which was 12.5μg,[1] and converted into microgram per kilogram for rat by surface conversion formula. Next, according to the 1, 2, 3, 4 times, we designed 4 groups of thimerosal dose. Since thimerosal was dissolved in saline, we used saline group as a control in which main item was excluded for the saline interference.

We agreed that it was worth mentioning that aluminum is not considered in any thimerosal experimental study, which is an adjuvant of thimerosal-containing vaccines (TCVs). Given the reasons you suggested in the letter, we also strongly believed that it is urgent to study the combined effect of ethylmercury plus adjuvant-Al in TCVs. Of course, just as you said that TCV taken during pregnancy and other cumulative sources of environmental Hg exposure are not considered in experimental study now.

Yan-Ni Chen, Jue Wang
The Key Laboratory of Biomedical Information Engineering of Ministry of Education, Institute of Biomedical Engineering, School of Life Science and Technology and Affiliated Xi'an Children's Hospital of Medical College, Xi'an Jiaotong University, Xi'an 710002, China
Email:chenyannichil@163.com

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