CORRESPONDENCE

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Mercury in infants given vaccines containing thiomersal

Sir—In July 1999, the American Academy of Pediatrics (AAP) published recommendations to minimise exposure to the mercury-based vaccine preservative, thiomersal.[1] A main recommendation was to delay administration of the birth dose of hepatitis B vaccine (containing 12·5 μg mercury) until 6 months of age. This recommendation was made because blood mercury concentrations after injection of thiomersal are inversely related to bodyweight.

Given this relation, I am surprised that Michael Pichichero and colleagues (Nov 30, p 1737)[2] restricted their study to 2-month-old and 6-month-old infants and did not take blood samples within 72 h of vaccination. As shown in figure 1 of their report, the highest blood mercury concentrations were seen in infants 2 months of age and in samples obtained 5–7 days after injection. These results raise the possibility that some infants who received a thiomersal-containing vaccine at birth, as most in the USA did throughout the 1990s, would have had blood mercury concentrations within the first 3 days after vaccination that exceeded the safety threshold value of 29 nmol/L cited by Pichichero and colleagues.

The question of whether thiomersal increases the risk of neurodevelopmental disorders, as the Institute of Medicine's Immunization Safety Review Committee thought "biologically plausible", extends beyond childhood vaccines.[3] Until recently, the immune globulin (RhoGAM), which is given to rhesus-negative women one or more times during pregnancy or immediately postpartum, or both, contained thiomersal.[4] Organic mercury readily crosses the placenta, the blood-brain barrier, and is excreted in breast milk.[5]

Despite its use as a preservative in vaccines and other biological products for more than 60 years, the safety of thiomersal in infants has not been systematically studied. Future investigations, preclinical and clinical, need to define the pharmacokinetic profile and neurotoxic potential of thiomersal in the highest-risk populations: newborns and fetuses. Until such studies are done, every effort should be made to limit fetal and infant exposure to this mercury compound.

The above letter was written in the private capacity of the author, and the opinions expressed therein should not be construed as the official position of the US Food and Drug Administration.

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1 American Academy of Pediatrics, Committee on Infectious Diseases and Committee on Environmental Health. Thimerosal in vaccines: an interim report to clinicians. *Pediatrics* 1999; **104:** 570–74.
2 Pichichero ME, Cernichiari E, Lopreiato J, Treanor J. Mercury concentrations and metabolism in infants receiving vaccines containing thiomersal: a descriptive study. *Lancet* 2002; **360:** 1737–41.
3 Institute of Medicine. Immunization safety review: thimerosal-containing vaccines and neurodevelopmental disorders. http://www.nap.edu/books/0309076366 (accessed Dec 1, 2002).
4 Physicians' Desk Reference. Montvale, NJ: Medical Economics Company, 1998.
5 Yang J, Jiang Z, Wang Y, Qureshi IA, Wu XD. Maternal-fetal transfer of metallic mercury via the placenta and milk. *Ann Clin Lab Sci* 1997; **27:** 135–41.

Sir—Michael Pichichero and colleagues[1] provide important new data on mercury concentrations in blood after thiomersal exposure.

The estimated half-life of ethylmercury (7 days) is shorter than that of methylmercury, and there is no evidence that ethylmercury exposure accumulates over time from repeat exposures to thiomersal. Pichichero and colleagues, and D C Henderson,[2] note that mercury concentrations in blood did not exceed 29 nmol/L—the safety level recommended by a panel of the US National Academy of Sciences for methylmercury.[3] However, the authors did not measure the peak blood concentrations that occurred within hours after the injections. If the true half-life of ethylmercury is 7 days, the mercury concentrations in blood measured 7 days after exposure are about half the peak concentrations, and blood concentrations measured 21 days after exposure are about an eighth of the peak concentrations.

Pichichero and colleagues should generate a model for exposures that took place at birth after the administration of hepatitis B vaccine and at 6–8 weeks of age when infants received up to 62·5 μg ethylmercury. Their model should estimate mercury concentrations in blood for infants who are at the 5th and 50th percentiles in bodyweight. For example, what would be the estimated concentrations for a 2·5 kg 6-week-old infant who received 62·5 μg mercury?

The data are available for one child in their study: a 2-month-old with a blood mercury concentration of 20·55 nmol/L 5 days after vaccination. If the ethylmercury half-life is 7 days (and half lives are variable), the peak mercury concentration in blood would have been 29·4 nmol/L, which is right at the safety level. This leaves no margin of safety if there were other sources of mercury exposure as well, belying the authors' claim that "no children had a concentration of blood mercury exceeding 29 nmol/L". This child reportedly received 37·5 μg mercury; a dose of 62·5 μg could well have resulted in a peak blood mercury concentration of 48·3 nmol/L. Their figure 1 indicates that there was a 2-month-old with 7 nmol/L mercury in blood at day 21, which would imply a possible peak blood mercury concentration of 42 nmol/L if the half-life is indeed 7 days.

The infants studied by Pichichero and colleagues seem to have come from a population with low background exposure to methylmercury. The ability to measure any mercury in blood from thiomersal exposures is of potential concern for infants born to mothers with high blood concentrations of methylmercury from fish consumption if the effects of ethylmercury are additive to those of methylmercury.[4] The US National Research Council has estimated that about 60 000 children are born in the USA every year to mothers who have concentrations of methylmercury in blood that put their infants at potential risk of harmful effects.[3] Hopefully someone is doing animal studies to determine whether exposure to ethylmercury is additive to that of methylmercury.

Additional data should soon become available from neurodevelopmental testing of children who were exposed to