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Urinary Metabolites of Chloroprocaine

To the Editor:—In their recent article, Krohg and Jellum[1] reported no evidence of conjugated 2-chloro-4-aminobenzoic acid (CABA) in either maternal or neonatal urine following epidural anesthesia with 2-chloroprocaine. In addition, they found only small amounts of unmetabolized CABA in neonatal urine. They studied four mothers and one neonate.

In contrast to their data, we are finding on the average 36 per cent of the total excreted CABA to be conjugated. Our data are from a similar ongoing study which presently includes 22 mothers. O'Brien *et al.*[2] have reported similar findings in four subjects. In addition, we have observed that the urine from the resulting infants contains amounts of unmetabolized CABA comparable to those excreted by the mother (data expressed on a μg drug/mg creatinine basis). In agreement with Krohg and Jellum, we did not find significant amounts of conjugated CABA in neonatal urine during the first 48 h of life. However, on the third day of life, trace amounts of conjugated CABA were detectable.

There are two differences between our methodology[3,*] and the methodology used by Krohg and Jellum which may explain these conflicting results. First, Krohg and Jellum collected specimens from mothers at the time of delivery and two hours later which corresponds to approximately one and three hours after epidural injection. Only one neonatal urine sample was studied and it was "voided shortly after delivery." In contrast, we collect urine samples from delivery through the first 72 h postpartum in both mother and neonate. Possibly, there was not enough time for sufficient amounts of conjugated CABA to be produced, concentrated, and excreted by Krohg and Jellum's patients. In support of this interpretation, O'Brien *et al.* reported that the proportion of conjugate to free metabolite increased with time following intravenous administration of chloroprocaine. Secondly, to free conjugated CABA, we pretreat 1-ml aliquots of diluted urine for 20 h at 90°C prior to extraction; O'Brien *et al.*[2] used even harsher hydrolysis conditions. However, no mention is made of conjugate hydrolysis techniques by Krohg and Jellum.

For these reasons, it does not seem reasonable at this time to accept Krohg and Jellum's conclusions regarding maternal levels of conjugated CABA and neonatal levels of unmetabolized CABA.

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3. Kuhnert BR, Kuhnert PM, Prochaska AL, et al: Plasma levels of 2-chloroprocaine in obstetric patients and their neonates after epidural anesthesia. ANESTHESIOLOGY 53:21–25, 1980

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* Technique modified to include 4-amino-3,5,-diiodobenzoic acid as the internal standard and detection by electron capture gas chromatography.

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In reply:—In reply to the letter from Kuhnert, Kuhnert, and Reese we have the following comments. The above authors claim to find on the average 36 per cent of the total CABA to be conjugated, but they have been unable to identify the conjugate. We have conclusively shown using gas chromatography-mass spectrometry and reference compound that the major metabolite is N-acetyl CABA.

Whether this should be called a conjugate or not is a matter of definition. One should realize that N-acetyl CABA readily undergoes alkaline hydrolysis to yield free CABA (shown by GC-MS experiments in our labora-