

## Hydronephrosis in Mice Exposed to TCDD-Contaminated Breast Milk: Identification of the Peak Period of Sensitivity and Assessment of Potential Recovery

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Hydronephrosis in Mice Exposed to TCDD-Contaminated Breast Milk: Identification of the Peak Period of Sensitivity and Assessment of Potential Recovery. COUTURE-HAWS, L., HARRIS, M. W., McDONALD, M. M., LOCKHART, A. C., AND BIRNBAUM, L. S. (1991). *Toxicol. Appl. Pharmacol.* 107, 413-428. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) is a potent inducer of hydronephrosis in both fetal and neonatal mice. A critical period of sensitivity to TCDD could not be identified for prenatally induced hydronephrosis since the urinary tract appeared equally sensitive throughout organogenesis. To identify the critical period of susceptibility for development of lactationally induced hydronephrosis in neonatal mice, as well as to characterize the potential for recovery from this renal lesion, dose-response and time-course studies were conducted in the postnatal period. Pregnant C57BL/6N mice were allowed natural delivery. In the dose-response phase of this investigation, mothers were administered 0, 3, 6, or 12  $\mu\text{g}$  TCDD/kg once by gavage on Postnatal Day (PND) 1, 4, 8, or 14, and dams and pups were euthanized on PND 26. The kidneys were examined, and hydronephrotic severity was scored. The incidence and severity of hydronephrosis were significantly increased above controls only following treatment on PND 1 or 4, while on PND 8 the increase was marginal and pairwise tests were nonsignificant. Following treatment of dams on PND 1, the hydronephrotic response detected in 26-day-old pups was significantly greater than that for all later exposure days. In the time-course study, dams were given a single oral dose of 0 or 9  $\mu\text{g}$  TCDD/kg on PND 1, and mothers and litters were subsequently euthanized on PND 7, 13, 19, or 26. Both hydronephrotic incidence and severity increased with time to euthanization following treatment on PND 1. Thus with the dosing regimen used in this study, recovery does not appear to occur between PNDs 7 and 26. Sex-related differences were observed, as the hydronephrotic response in males was generally greater than in females. In conclusion, the postnatal window of sensitivity during which TCDD can induce hydronephrosis is very narrow. Nonetheless, the hydronephrotic response induced during this early postnatal time is dramatic. Finally, PND 1 is the peak postnatal period of susceptibility for development of TCDD-induced hydronephrosis.