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Characterization of the Peak Period of Sensitivity for the Induction of Hydronephrosis in C57BL/6N Mice following Exposure to 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin[1]

L. A. COUTURE,*‡[2] M. W. HARRIS,† AND L. S. BIRNBAUM*

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Characterization of the Peak Period of Sensitivity for the Induction of Hydronephrosis in C57BL/6N Mice following Exposure to 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin. COUTURE, L. A., HARRIS, M. W., AND BIRNBAUM, L. S. (1990). *Fundam. Appl. Toxicol.* **15,** 142–150. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) is an extremely potent teratogen in mice. Hydronephrosis and cleft palate are the most sensitive measures of teratogenicity in mice following exposure to TCDD and other structurally related polyhalogenated aromatic hydrocarbons. Despite a relatively long half-life, investigators have identified a critical window for the induction of cleft palate in C57BL/6N mice. To characterize the critical period for renal teratogenesis, pregnant C57BL/6N mice were treated once by gavage with 0–24 μg TCDD/kg body wt on Gestation Day (GD) 6, 8, 10, 12, or 14. All dams were killed on GD 18, and the fetuses were examined for the presence of hydronephrosis and cleft palate. Maternal liver-to-body weight ratios were significantly elevated above controls on all days, while maternal weight gain was unaffected. Fetal mortality was increased relative to controls only at 24 μg TCDD/kg on GD 6. There was no significant difference in fetal body weights between control and TCDD-treated fetuses. The incidence of cleft palate increased in a dose-related fashion from GD 6 to GD 12, and identification of GD 12 as the critical window for induction of clefting of the hard palate was confirmed. Hydronephrosis was observed at all dose levels, regardless of exposure day, and the incidence was close to 100% at 3 μg TCDD/kg and higher doses on GD 12 and earlier. At all doses on GD 14, both the incidence and severity of hydronephrosis were decreased relative to all other days. There was a dose-related increase in the severity of the renal lesion on each day, but between GD 6 and 12 severity was constant. Thus, while palatal sensitivity to TCDD increased with gestational age between GD 6 and 12, there was no difference among these days in development of hydronephrosis. The data suggest, however, that on GD 14 the urinary tract may be less sensitive to TCDD.