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# Phase-Specific Developmental Toxicity in Mice Following Maternal Methanol Inhalation<sup>1</sup>

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Methanol is toxic to embryos of mice and rats when inhaled by dams at high concentrations. The present studies examined methanol-induced developmental toxicity following inhalation exposure (6 hr/day) of pregnant CD-1 mice to 5000, 10,000, or 15,000 ppm either throughout organogenesis (GD 6–15), during the period of neural tube development and closure (GD 7–9), or during a time of potential neural tube reopening (GD 9–11). Transient neurologic signs and reduced body weights were observed in up to 20% of dams exposed to 15,000 ppm. Examination of near-term fetuses revealed embryotoxicity (increased resorptions, reduced fetal weights, and/or fetal malformations) at 10,000 and 15,000 ppm, while 3-day exposures at 5000 ppm yielded no observable adverse effects. Terata included neural and ocular defects, cleft palate, hydronephrosis, deformed tails, and limb (paw and digit) anomalies. Neural tube defects and ocular lesions occurred after methanol inhalation between GD 7–9, while limb anomalies were induced only during GD 9–11; cleft palate and hydronephrosis were observed after exposure during either period. These findings were consistent with prior reports that maternal methanol inhalation at high levels induces developmental toxicity in a concentration dependent manner. Furthermore, our data indicate that the spectrum of teratogenic effects depended upon both the timing (i.e., stage of embryonic development) and the number of methanol exposures.

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