Reproductive and Developmental Toxicity Studies of Toluene. I. Teratogenicity Study of Inhalation Exposure in Pregnant Rats. Atsushi Ono, Kiyoshi Sekita, Akiniko Hirose, Yukio Ogawa, Minoru Saito, Katsushi Naito, Toyozo Kakeko, Tsuyoshi Furuya, *Kiyoshi Matsumoto, Satoru Tanaka and Yoji Kurokawa. Division of Toxicology, National Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, Tokyo 158, Japan and *Institute of Experimental Animals, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto-shi, Nagano 390, Japan

An abuse of volatile solvents abuse becoming a great public concern in Japan. In the present study, we focused on methylbenzene(toluene), the main component of paint thinner and one of the major subjects of abuse among the younger generation. Teratogenicity of toluene was examined in rats. Pregnant Sprague-Dawley rats, 10 weeks old, were exposed to 0 (control), 600 or 2000 ppm toluene for 6 h/day from day 7 to 17 of gestation and the effects on dams, fetuses and offspring were assessed serially. In dams exposed to toluene, significant body weight (BW) suppression and decreased food consumption were seen at 2000 ppm. Fetal mortality, and the number of the dams with high fetal mortality, was moderately increased in both exposure group. However, no external, internal or skeletal anomalies related to maternal toluene exposure were observed in the fetuses. BWs of offspring was remarkably suppressed in both sexes at 2000 ppm. Neither adverse effects was detected on the pre- and postweaning behavioral tests and any other examinations of the offspring. In conclusion, embryo-fetal toxicity of toluene was suggested in the present study and further studies are warranted at higher concentrations.


In our previous studies, dibutyltin dichloride (DBT) was found to be highly teratogenic after treatment on days 7 and 8 of pregnancy. It is known that tributyltin compound was metabolized to di- and monobutyltin derivatives and DBT was metabolized to butyltin trichloride (BT) in rats. The present study was conducted to compare the developmental toxicity of BT, DBT and tributyltin chloride (TBT) and to determine the roles of these butyltin compounds as a potential toxicant in teratogenesis when relatively high doses of butyltins were administered to pregnant rats during the susceptible period for the teratogenesis of DBT. Pregnant rats were given either BT at a dose of 1000, 1500 or 2000 mg/kg, DBT at a dose of 1 or 15 mg/kg or TBT at a dose of 40 or 80 mg/kg by gastric intubation on days 7 and 8 of pregnancy. Although maternal toxicity occurred, as evidenced by a significantly increased maternal lethality at 1500 and 2000 mg/kg and decreased maternal weight gain at 1000 and 1500 mg/kg, no significant increase in the incidences of postimplantation loss and malformed fetuses were observed after treatment with BT. Treatment with DBT resulted in a significantly lower maternal weight gain, lower fetal weight and higher postimplantation embryolethality. A significantly and markedly increased incidence of fetuses with malformations, such as exencephaly, cleft jaw, cleft lip, ankyloglossia, club foot, deformity of the vertebral column in the cervical and thoracic regions and of the ribs and ano- or microphthalmia, was observed in the treatment groups treated with BT. While treatment with TBT at 40 and 80 mg/kg caused a significantly decreased fetal weight gain and increased postimplantation embryolethality, no significantly increased incidence of malformed fetuses occurred. It could be concluded that the developmental toxicity of DBT is different from that of BT and TBT in the susceptibility and spectrum and the proximate teratogen of DBT is DBT itself.