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EDITORIAL

Volatile organic compounds in the air of neonatal incubators

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Ambiant air pollution during pregnancy and infancy may affect the health in childhood. A meta-analysis showed that an increase in 10 mcg m^{-3} of particle concentration ($\leqslant$10 micrometer diameter) is associated with a 5% increase in postneonatal mortality for all causes and around 22% for postneonatal mortality for respiratory diseases.[1] Chemical air contamination has been demonstrated in incubators used for assisted reproduced technology.[2] One study showed that the atmospheric purification by an intraincubator air purification unit significantly increased pregnancy rate following transfer of *in vitro* produced bovine embryos.[3]

In this issue of *Journal of Perinatology*, Prazad *et al*.[4] report the result of a study that was carefully designed to identify and quantify any airborne volatile organic compound inside neonatal incubators. The authors used state-of-the-art technology, that is, gas chromatography/mass spectrometry, to identify and quantify these compounds. They report the novel observation that two volatile organic compounds, 2-heptanone and n-butyl acetate, were found at higher concentration in the air inside than outside of the neonatal incubators. Exposure to 2-heptanone may cause neurotoxicity, whereas n-butyl acetate may cause central nervous system excitation, sedation, hypoactivity and eye irritation. The concentrations of the two compounds increased when the incubators were at higher temperature and humidity, using settings routinely used in extremely preterm infants. The authors state (though data are not provided in the manuscript) that the concentrations of the two compounds were lower in experiments conducted 5 months after the first set of experiments, suggesting that the concentration decreased with the age of the incubator.

The authors have clearly highlighted some of the limitations of their study: (a) use of a single type incubator, (b) experimental conditions that may have resulted in higher concentrations in breathing air than in many situations of neonatal intensive care unit care, maintaining the windows of the incubator closed and lack of oxygen or airflow for respiratory management and (c) lack of neonatal data.

The highest observed concentrations of these two volatile organic compounds in this study, 2–heptanone 32.54 ± 10.17 p.p.b. and n-butyl acetate to 26.73 ± 7.82 p.p.b., were at least three orders of magnitude (that is, 1000-fold) less than those observed in studies of animal or human exposure showing toxicity with acute or chronic exposure. The concentration of 2-heptanone in air that kills 50% of the rats (LC50) in 6 h is 2000–4000 p.p.m.[5] Macaques and rats chronically exposed to 131 or 1025 p.p.m. for 6 h 5 days a week for 9–10 months tolerated exposure with minimal effects.[6–8] For n-butyl acetate, LC50 in the rat has been reported to range between 160 and 2000 p.p.m. (4 h exposure).[9,10] In contrast, guinea pigs exposed to 900 p.p.m. for 11 weeks have been reported to show no adverse effects.[11] As no data on 2-heptanone and n-butyl acetate are currently available in neonates including preterm infants, it is difficult to predict whether prolonged exposure to the levels of these two compounds in the ranges observed by Prazad *et al*.[4] could cause any toxicity in those patients. The history of neonatology has shown us that neonates, especially, extremely preterm infants, may be much more susceptible to toxins and medications than adults because of the differences in pharmacokinetics and pharmacodynamics, or interactions between multiple drugs and toxins. Furthermore, it is possible that specific patients may be genetically more susceptible to these compounds.

Prazad's study raises an entirely new set of questions: Could other brands or types of incubators expose preterm infants to other volatile organic compounds? Do preterm infants exposed to volatile organic compounds, single or in combination with medication or with other toxins, present with short- and long-term side effects? What is the developmental maturation of the metabolism of these compounds? Eventually, causality may be assessed by randomized trials. Thus, this study might open a new area of research in neonatal–perinatal medicine and help find out whether the benefit of using incubators outweighs the risk of environmental exposure, and whether alternative, less toxic materials, might ultimately improve the outcomes.

Could the risk of environmental toxin exposure be reduced by providing airflow inside the incubator, or in those who need respiratory support by providing air or oxygen? The answer is unclear, because many plastic medical devices (including those used for respiratory care) may be made from polyvinyl chloride.[12] Polyvinyl chloride includes a high percentage (up to 40% by weight) of di-(2-ethylhexyl) phthalate, a plasticizer approved by the US Food and Drug Administration for medical uses.[13] Although animal studies suggest that the antiandrogen effect of some phthalates may increase the risk for hypospadias, cryptorchidism and testicular toxicity, the potential health implications of prenatal and early childhood exposure to di-(2-ethylhexyl) phthalate remain to be determined.[14] Multiple other sources of toxicity have been described in the history of neonatology. We will need to stay alert.

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