Breach of Security? Placental Uptake of Micro- and Nanoplastic Particles
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The placenta plays a critical role in fetal growth and development. In addition to delivering essential nutrients and oxygen, it removes waste products and can protect the fetus from harmful exposures. Uptake and transport processes across placental cells determine whether micro- and nanoplastic particles (MNPs) and environmental chemicals reach the fetus via maternal blood. In experiments recently published in *Environmental Health Perspectives*, researchers examined how placental cell lines responded to MNPs of two commonly used plastics: polystyrene (PS) and high-density polyethylene (HDPE).

The experiments involved two cell types unique to the placenta: cytotrophoblasts and syncytiotrophoblasts. Cytotrophoblasts differentiate from the fertilized egg very early in pregnancy. Some of these cells fuse into syncytiotrophoblasts, which form the outer layer of the placenta and come in direct contact with maternal blood. The authors analyzed syncytiotrophoblasts separately from cytotrophoblasts.

They were particularly interested in differences in the uptake, transport, and effects of pristine, freshly manufactured particles versus experimentally weathered particles, which were expected to better mimic real-life environmental exposures. The weathering process involved immersing the particles in water sampled from a ditch, shaking them, and exposing them to natural sunlight cycles at room temperature for 4 weeks. The researchers then used mass spectrometry to document the resulting changes in the particles’ chemical composition.

If environmental chemicals adhere to the particles during the weathering process, mass spectrometry should detect a more complex mixture of chemicals in weathered than pristine particles, says first author Hanna Dusza, a graduate student at Utrecht University, the Netherlands. However, the researchers observed the opposite, suggesting that MNPs can also leach chemicals during the weathering process. Thus, weathering may significantly change the chemical composition of particles, which in turn may influence their toxicity.

The researchers found that both PS and HDPE particles up to 10 μm in diameter readily entered both placental cell types within 24 hours of exposure. Using cytotrophoblasts to study the movement of particles from one cell to another, they found that such transport was limited and unaffected by coating the particles with human plasma, which served to mimic exposure through the maternal blood system.

To evaluate effects, cells were exposed to particles at doses ranging from 0.1 to 100 μg/mL, which reflected ranges used in...
earlier in vitro studies and included the recently reported mean concentration of 1.6 μg/mL in human blood.⁶ Consistent with earlier cytotoxicity studies, none of the doses affected cell viability.⁷-⁹ The smallest PS particles damaged plasma membranes of cytotrophoblasts but only at the highest concentration. Exposing syncytiotrophoblasts to PS at 10 μg/mL moderately reduced expression levels of a gene involved in estrogen synthesis, an effect that was weaker for weathered particles.

Phoebe Stapleton, an assistant professor of toxicology at Rutgers University who was not involved in the study, was surprised that the uptake of nanosized particles by placental cells took only an hour, and just slightly longer for larger particles. “We currently do not know if this rapid uptake involves simple diffusion or energy-dependent processes,” says Stapleton. “Studying transport mechanisms of nanoparticles is challenging, and the tools we need are still being developed.”

Erik Rytting, an associate professor of obstetrics and gynecology at the University of Texas Medical Branch, says the study’s dose range seemed high given that human blood concentrations of MNPs may be several orders of magnitude below 1.6 μg/mL.⁵⁰ owing to low particle transfer rates to blood.⁵¹-⁵³ But he was intrigued by the contrast between pristine and weathered particles.

“I think the simulated weathering process is important because humans are more likely to encounter weathered particles in the environment,” says Rytting, who was not involved in the study. “It would be interesting to explore potential reasons for the chemical differences between the pristine and weathered particles.” For example, he says, aquatic microorganisms may reduce the toxicity of weathered particles, or pristine particles may include harmful impurities.

Dusza agrees such follow-up efforts are warranted. “The chemical composition of MNPs may affect their toxicity more than the morphology, but we should also study exposure periods beyond 24 hours,” she says. More complex placental models⁵⁴ may be needed to learn how interactions between MNPs and associated chemicals affect placental functioning, as well as fetal and maternal health, adds Dusza.

Stapleton thinks that plastics have gone without intense scrutiny for a long time, perhaps because of their limited cytotoxicity in vitro. “But knowing that these particles exist in human lungs, blood, and placenta means that alternative end points are important to study,” she says. This is especially true for endocrine disruption, she adds, “because plasticizing chemicals like bisphenols and phthalates have long been implicated in that process.”

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