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Fetal exposure to tributyltin linked to obesity

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Exposing pregnant mice to low doses of the chemical tributyltin (TBT) – which was used in marine antifouling paints and is used as an antifungal agent in some paints, certain plastics and a variety of consumer products – can lead to obesity for multiple generations without subsequent exposure, a UC Irvine study has found.

After exposing pregnant mice to TBT at low concentrations, similar to those found in the environment and in humans, researchers observed increased body fat, liver fat and fat-specific gene expression in liver and stem cells in mouse "children," "grandchildren" and "great-grandchildren." The "children" were exposed as embryos, while the "grandchildren" may have been exposed as germ cells within the "children." The "great-grandchildren" had never been exposed to TBT. Such effects without exposure are termed transgenerational and thought to be permanently transmitted to future generations.

These findings demonstrate that early-life exposure to endocrine-disrupting compounds such as TBT can have permanent effects on fat accumulation, gene expression and stem cell programming without further exposure, said study leader Professor Bruce Blumberg with the UC Irvine Departments of Developmental & Cell Biology, Pharmaceutical Sciences and Biomedical Engineering.

The study appeared online Jan. 15 in *Environmental Health Perspectives*, a publication of the National Institute for Environmental Health Sciences.

Human exposure to TBT and related organotins can occur in a variety of ways. TBT contaminates particles derived from such products as shower curtains, vinyl flooring, carpet fibers, polyurethane foams, mold-resistant paints and other consumer products, where it is used as an antifungal agent. As a result, noteworthy levels of TBT have been reported in house dust, which may be particularly relevant for young children who can spend significant time on floors and carpets. Although TBT is now largely banned for use in marine hull paints, it remains pervasive in the environment, and people can be exposed by ingesting TBT-contaminated seafood. Organotins may also leach into liquids that come into contact with organotin-containing plastic pipes, containers and packaging materials.

Blumberg categorizes TBT as an obesogen, a class of chemicals that promote obesity by increasing the number of fat cells and the storage of fat in existing cells or by altering metabolic regulation of appetite and satiety. He and his colleagues identified TBT as an obesogen in a 2006 publication and showed in 2010 that TBT acts in part by modifying the fate of mesenchymal stem cells during development, predisposing them to become fat cells.

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