Common disinfectants impair reproduction in mice

Quaternary ammonium compounds (QACs) are disinfectants that were first introduced in the 1950s and are now commonly used in laboratory settings. They are generally considered safe, although their toxicity has never been rigorously evaluated. Some toxicity testing was done by the compounds' manufacturers in which a slight weight reduction in offspring of exposed mice was reported as the only adverse effect, but the results were not peer-reviewed or published. Furthermore, these studies took place before toxicity testing practices were standardized: the Toxic Substances Control Act (TSCA) first created a system to oversee the production and use of chemicals in the US in 1976, and Good Laboratory Practices (guidelines for conducting research that is reproducible and reliable) were not developed until the 1980s. The TSCA does not mandate safety evaluations for all chemicals, and some can become widely used without ever undergoing direct toxicity testing. Such is the case for QACs. Furthermore, QACs are now often used in combination, yet no peer-reviewed studies have examined the toxicity of these combinations. Because chemical mixtures can have toxic effects that are greater than the sum of the effects of the individual components, toxicity testing of mixtures is essential.

gawriloff/iStock/Thinkstock

The lack of thorough toxicity testing of QACs recently came to light as two independent laboratories observed changes in the breeding performance of their mouse colonies. Terry Hrubec (Virginia Polytechnic Institute, Blacksburg) and Patricia Hunt (Washington State University, Pullman) both noticed declines in mouse productivity and maternal health that coincided with the introduction of disinfectants containing the QACs alkyl dimethyl benzyl ammonium chloride (ADBAC) and didecyl dimethyl ammonium chloride (DDAC).

Hrubec and Hunt collaborated on a 6-month breeding study to test the effects of a disinfectant solution containing ADBAC and DDAC on reproduction in laboratory mice (*Reprod. Toxicol.* doi:10.1016/j.reprotox.2014.07.071; published online 14 August 2014). Mice exposed to the QAC mixture had declines in fertility and fecundity compared with control mice: longer time to first litter (31 days versus 20 days) and fewer pregnancies (~5 versus ~7) and fewer pups (~500 versus ~800) in the first 100 days after exposure. Greater morbidity in near-term dams was also observed among mice exposed to the QAC mixture compared with control mice (40% versus 10%).

The results show that exposure to a common QAC mixture impairs reproductive health in mice. The study illustrates the importance of assessing mixture toxicity of commonly used products and highlights the paucity of information available on the potential health impacts of some commercially available products.

Monica Harrington

A COMMON FOE IN THE FIGHT AGAINST TYPE 1 AND TYPE 2 DIABETES

A new study has uncovered a connection between juvenile onset, or type 1, diabetes and type 2 diabetes, similar diseases with very different causes. Type 1 diabetes occurs in people who lack insulin because their immune systems have destroyed the insulin-producing beta cells in the pancreas, whereas type 2 diabetes occurs in people whose bodies are less responsive to insulin, leading the pancreas to produce less of it. Without the necessary insulin to control glucose levels in the blood, damage to organs such as the heart, kidneys, eyes and nerves can occur.

Previous research from Garth Cooper's group at University of Auckland, New Zealand, suggested that type 2 diabetes is caused by the formation of toxic clumps of a hormone called amylin in the pancreas. This hormone is produced by beta cells, just like insulin, and the two hormones typically work together to regulate the body's response to sugar. Some of the amylin that is produced can get deposited around pancreatic cells and tends to clump together; these clumps are toxic to beta cells and eventually destroy them. Cooper's team showed that the resulting decrease in the production of these hormones causes type 2 diabetes. Next, they wanted to determine whether toxic amylin deposits might be a causative mechanism in type 1 diabetes as well.

Modeling the activity of amylin in rodents is challenging because mouse amylin does not aggregate the way human amylin does. The researchers therefore created transgenic rodents that expressed human amylin for their studies. They compared mice with two copies of the human amylin gene (homozygous) and mice with one copy of the human amylin gene (hemizygous) in order to study the gene dosage effects. The homozygous mice developed clumps of human amylin in their pancreases and initially showed symptoms of prediabetes, including elevated insulin levels with transient insulin resistance, followed by a loss of beta cells similar to that seen in humans with type 1 diabetes. In contrast, the hemizygous mice had a prolonged prediabetes stage; extensive clumping of amylin and resulting dysfunction of beta cells did not occur until adulthood, similar to the symptoms and progression seen in humans with type 2 diabetes (*FASEB J.* doi:10.1096/fj.14-251744; published 19 August 2014).

The research provides strong evidence that type 1 diabetes results from the same mechanism as type 2 diabetes but starts at an earlier age and progresses more rapidly. This appears to be directly related to the level of amylin expression, providing a new potential target for future studies.

Kara Rosania