Common pollutants undermine masculinity

Some widespread pesticides and chemicals in plastics can induce reproductive impairment in males, according to seven new animal studies. These compounds wreak their havoc by blocking the action of male sex hormones as they program sexual development.

Phthalates, ubiquitous oily solvents that make plastics flexible, have become the most abundant synthetic chemicals in the environment. One of the new studies examines the effects of fetal exposure to either diethylhexyl phthalate (DEHP), a softening agent found in most polyvinyl chloride (PVC) products, or di(*n*-butyl) phthalate (DBP), an additive in mosquito repellents.

L. Earl Gray Jr. and his colleagues at the Environmental Protection Agency in Research Triangle Park, N.C., administered the chemicals to female rats from weaning through lactation. They gave doses of 200 to 1,000 milligrams per kilogram of body weight. Then, they examined the exposed animals' offspring.

Compared with rats whose mothers had no phthalate exposure, these offspring produced far less testosterone and exhibited a range of abnormalities. Sometimes one testicle was absent or appeared as just a sac of blood. Says Gray, "We've never seen anything like this."

Prenatal exposure to either phthalate also markedly reduced the size of a muscle that runs from the colon to the base of the penis. In some offspring, the epididymis, a sperm-storing organ, was similarly just a fraction of its normal size.

Gray's team catalogued these and also many abnormalities that had already been seen with compounds that block male sex hormones, or androgens. Many test animals bore classically feminine features such as permanent nipples. The data were presented at the Society of Toxicology meeting in New Orleans 2 weeks ago and in the just-released January–March issue of TOXICOLOGY AND INDUSTRIAL HEALTH.

Paul M.D. Foster and his coworkers at the Chemical Industry Institute of Toxicology in Research Triangle Park, N.C., have also been exploring the antiandrogenic effects of phthalates. At the toxicology meeting, they reported that developmental defects in males can be triggered by as little as 100 mg of DBP per kg of body weight in the mom.

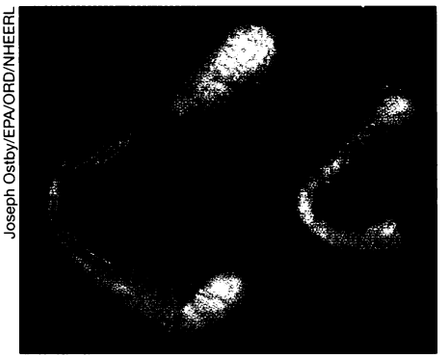
DBP halves testosterone production by the fetal testis, their data show. Foster says that the testis responds by making twice as many cells, a proliferation that resulted in testicular tumors after the animals became adults.

Many commercial chemicals possess antiandrogenic activity. In four other papers in TOXICOLOGY AND INDUSTRIAL HEALTH, Gray's group describes two fungicides (vinclozolin and procymidone), an herbicide (linuron), an insecticide (methoxychlor), and several other compounds that provoke various degrees of reproductive-organ abnormalities.

Linuron's devastating effect had a surprising aspect. Usually, external genital abnormalities hint at disruption of internal organs. However, although few linuron-exposed offspring had external malformations, "50 percent had a missing epididymis or malformed testis," Gray observes.

His group also showed that exposing young male animals to an antiandrogenic pesticide just before puberty dramatically delays the maturation of their sexual organs.

The doses at which all these adverse effects occurred in the rats approach the "range where people are actually being exposed," says Boston physician Ted Schettler, science director of the Science and Environmental Health Network. Dialysis patients and people receiving fluids in most plastic intravenous bags get substantial exposure to DEHP, he notes. Many PVC-based teething toys also leach this phthalate.



Joseph Ostby/EPA/ORD/NHEERL

Epididymis (left) from an unexposed adult rat is more than three times the size of this sperm-storing organ (right) from an animal exposed to DBP in the womb.

Peter L. deFur of Virginia Commonwealth University in Richmond worries, "I think there is more than just a possibility that [current human] exposures to antiandrogens are having measurable health effects." —*J. Raloff*

Allergy vaccine may take fear out of nuts

An experimental vaccine mitigates the worst effects of peanut allergies, at least in mice. The DNA-based oral vaccine immunizes the animals against a peanut protein that otherwise can kill them.

Food allergies are becoming more common and more dangerous (SN: 9/7/96, p. 150). Between 100 and 125 people in the United States die each year of allergic reactions to peanuts or true nuts, says Wesley Burks of the Arkansas Children's Hospital in Little Rock.

A further price of a peanut allergy is eternal vigilance. Peanuts pop up in many unexpected places, such as egg roll wrappers, chili fillers, and protein extenders in cake mixes. Once sensitized by exposure to peanut proteins, someone with a severe allergy may react the next time with hives or a swollen mouth and throat. In the most serious response, respiratory distress called anaphylactic shock, the person may die unless immediately given a shot of epinephrine.

Kam W. Leong and his colleagues at Johns Hopkins Medical Institutions in Baltimore successfully vaccinated mice against peanut allergens, they report in the April NATURE MEDICINE. The mice had been bred to develop peanut allergies.

Once sensitized, the mice react to the same peanut proteins that allergic humans do, one of which is called Arah2.

To make the vaccine, the researchers created balls of two molecules: the peanut DNA that encodes Arah2 and a compound called chitosan, which is found in crustacean shells. The chitosan protects the DNA and delivers it to cells in the intestines. Those cells then produce Arah2.

This result provides "a testament to the extraordinary ability of DNA to make itself at home wherever it can find the machinery for [making proteins]," comment Miriam F. Moffatt and William O.C. Cookson of John Radcliffe Hospital in Oxford, England, in an article accompanying the report.

Rather than triggering an allergic sensitivity, the vaccine protects the mice against a violent reaction. Vaccinated animals produce fewer of the antibodies, including immunoglobulin E, that fuel allergic reactions.

When subsequently exposed to peanut extracts, the vaccinated mice reacted more mildly than unprotected mice, which had been given either naked Arah2 DNA or chitosan alone.

"This is the first time that an oral vaccine against peanut allergens works," says Leong. The mice were vaccinated before they had their first allergic reaction to peanuts, when their immune systems were presumably more adaptable than those in mice that had already gone through an allergic response, he says.

Even if researchers develop a human version of this vaccine, Burks says, "people [with allergies] would not be able to go out and eat peanuts." A vaccine that weakens allergic reactions, however, could save lives. —*L. Helmuth*