More Smoke, Less Baby

Maternal ETS Exposure Means Low Birth Weight, Preterm Delivery

These days it's impossible to argue that smoking during pregnancy is good for the baby, but research is beginning to show that environmental tobacco smoke (ETS), too, may cause adverse effects in the unborn child. Jouni J. K. Jaakkola of the Nordic School of Public Health in Göteborg, Sweden, and colleagues used hair samples to gauge ETS exposure among new mothers during the last trimester, the period of greatest fetal growth [*EHP* 109:557–561]. They found evidence that maternal ETS exposure increases the risk of preterm delivery and affects fetal growth. This study is the first to support an increased risk in preterm delivery linked to ETS exposure.

Nicotine in hair, which accumulates through both internal and external routes, is considered a promising new biomarker for ETS exposure. Hair nicotine reflects exposure over the previous 2 months, whereas serum and saliva concentrations of cotinine (a metabolite of nicotine) have a half-life of only 2–3 days. This means that hair samples taken from mothers at delivery can tell how much ETS exposure the fetus received during the third trimester, the period when the fetus does the most growing in the least time, doubling in size. Hair nicotine may therefore provide an antidote to the problems (such as inaccurate subject recall) associated with the questionnaires and interviews often used in exposure assessments. Hair sampling also has the benefit of being noninvasive.

The scientists recruited 389 nonsmoking Finnish women from among all mothers who had given birth in two hospital districts between May 1996 and April 1997. The day after delivery, the women completed a questionnaire on maternal health, smoking and exercise habits, and details of their home and work environments. They also provided hair samples. A little over one-third of the women reported exposure to ETS in the home and/or at work. Another third of the women were married to smokers but reported no exposure to ETS. The rest were married to nonsmokers and reported no exposure to ETS.

For purposes of the study, the scientists defined low birth weight as less than 3,000 grams, which is higher than the traditional cutoff of 2,500 grams. The 2,500 gram cut point has been used since the early 1900s, although babies born today are heavier on average. Thus, says Jaakkola, including a larger proportion of newborns from the lower birth weight end conveyed the idea of studying the smallest babies but increased the number of outcomes and the power of the study. The team also considered whether children were small for gestational age and whether they were delivered preterm.

Jaakkola and colleagues found that mean birth weight among the women was consistent with the Finnish average; only 7 of the children were what is traditionally considered low birth weight (less than 2,500 grams). But they also found that the greater the mother's hair nicotine measurement, the lower the child's mean birth weight and the higher the prevalence of adverse pregnancy outcomes. Of children of mothers in the highest exposure group, 15.4% had low birth weight, 9.8% were small for gestational age, and 9.6% were preterm, compared to 9.9%, 8.0%, and 2.7%, respectively, for children of mothers in the lowest exposure group.

The researchers found that ETS exposure at work correlated with preterm delivery more than home exposure did, although hair nicotine due to reported exposures at both locations was similar, an irregularity that the team theorizes may be due to unknown confounding factors in the workplace. **–Susan M. Booker**

Baby bears the brunt. Recent research shows that as mothers are exposed to more environmental tobacco smoke while pregnant, their children's mean birth weight drops.

PhotoDisc

Childhood Brain Tumors

Little Risk from Well Water

Certain chemicals in drinking water including some *N*-nitroso compounds (NNCs) have demonstrated neurocarcinogenic potential. Well water in particular can be an important source of nitrate, which can be reduced to nitrite, a precursor of endogenously formed NNCs. Previous studies in rats and humans have reported evidence of a possible association between maternal dietary NNC exposure and childhood brain tumors (CBTs). Yet the association between prenatal environmental exposure to NNCs and CBTs remains unclear, possibly because it is difficult to measure such exposures in most epidemiologic studies. To gain insight into a possible relationship between NNCs and CBTs, Beth Mueller of the Fred Hutchinson Cancer Research Center in Seattle, Washington, and colleagues studied the link between maternal reliance on well water during pregnancy and BT incidence [*EHP* 109:551–556]. Overall they found no increased risk of CBTs among children whose mothers had drunk well water exclusively during pregnancy, although some populations exhibited either increased or decreased risk.

The subjects included 540 children who had been diagnosed with cancer of the brain, cranial nerve, or meninges, 801 controls, and the children's mothers. The children lived in one of three areas, Los Angeles County or the San Francisco Bay Area in California or the Seattle–Puget Sound area in Washington. The mothers were asked about the sources of household water during their pregnancies and into the children's early years. The mothers also estimated the proportion of bottled water consumed during that period. If the mother was still living in the same residence as during her pregnancy, tap water concentrations of nitrite and nitrate were measured. (A little under one-quarter of the mothers still lived in the homes where they had spent their pregnancies.)

An increased risk of CBT was observed among children in western Washington whose mothers reported using well water as their

sole source of drinking water during pregnancy. This phenomenon, however, was not reproduced at the California sites. In fact, a decreased risk was found in Los Angeles County, while San Francisco saw no statistically significant change in risk.

Mueller and colleagues say the increased CBT risk seen in western Washington may reflect the presence of some substance only in that region or some other factor unique to the rural residents who rely solely on well water. Also, residential water is only one source of dietary nitrate. Moreover, eating fruits and vegetables rich in vitamins C and E and other substances that inhibit endogenous nitrosation may counteract the effects of dietary intake of nitrate.

In addition, the mother's recollection of drinking water source may not always be reliable. Even if this factor is accurately reported, the mother may have consumed water outside the home. Also, say Mueller and colleagues, there are no data regarding the pathway by which nitrate might increase cancer risk, nor on whether high concentrations of nitrate might indicate the presence of other potentially carcinogenic contaminants in drinking water—such as metals and pesticides—that might be the real culprits.

Even though the results do not provide strong support for an association of well water with CBT occurrence, the researchers do suggest that, in western Washington at least, there may be a correlation with some other factor related to well water use. Because many people in some areas use well water and because there is evidence of increasing levels of contamination with nitrate (and perhaps other substances) along with a possible biological mechanism for NNCs to damage the fetal brain and induce CBTs, Mueller and her colleagues consider it important that this relationship be clarified further. **–Julian Josephson**

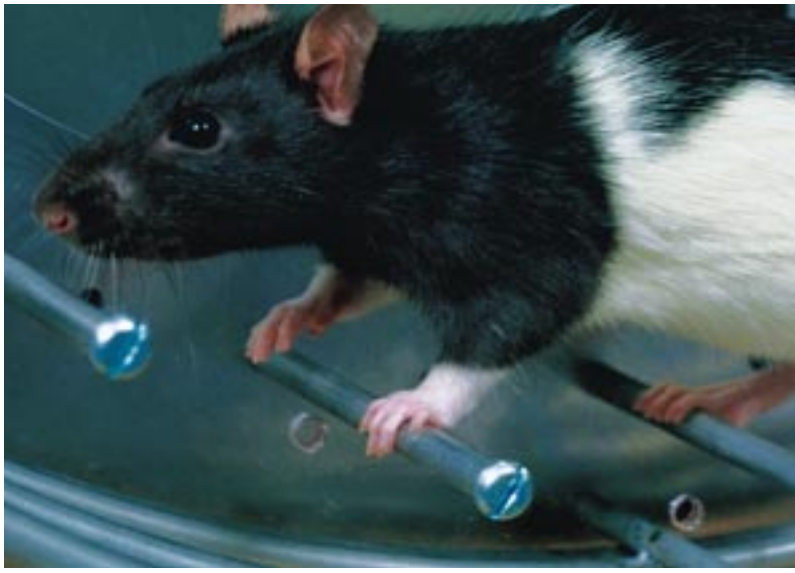
Slowing the Rat Race

Low-Dose Dioxin Alters Behavior

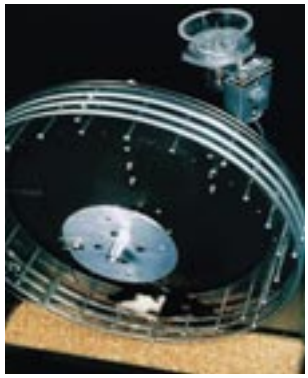
Concentrations of a common toxicant too low to cause reproductive abnormalities can still alter behavior in rats, according to a team of researchers led by Vincent Markowski of the University of Southern Maine in Portland [*EHP* 109:621–627]. The team studied the effects on female rats of perinatal exposure to the environmental contaminant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD. The study is one of very few to focus on TCDD's behavioral effects, says principal investigator Bernard Weiss of the University of Rochester School of Medicine and Dentistry in New York. Many studies over the past decade have centered instead on TCDD's capacity to interfere with the development of sexual organs and reproductive fitness.

Humans are exposed to the ubiquitous chemical mostly by eating meat, dairy, fish, and poultry products. TCDD is produced from the combustion of plastics and through some manufacturing processes, including paper bleaching. Air currents and water deposition scatter the contaminant, which settles on crops and waterways, where it begins its climb up the food chain. TCDD concentrates in fat and has a half-life in humans of 7–10 years.

The team limited their study to female rats because each sex is affected differently by TCDD, and many rat behaviors are sex-specific. One of those uniquely female behaviors is increased use of a running wheel during estrus, when the female is fertile and sexually receptive. To measure motivation, the researchers developed a running wheel with a brake. The rats were trained to press a lever a certain number of times to release the brake so they could run. The wheel could be rotated for a set time, then would stop. Each time the rats wanted to resume running, they had to release the brake.



A touch of toxicity? Concentrations of TCDD too low to cause reproductive effects can still alter behavior in rats.



Big wheel keeps on turnin'. A specially designed wheel allowed researchers to measure rats' motivation to run during estrus.

Female rats were exposed to TCDD through a single dose given to their mothers by gavage on the eighteenth day of gestation, when the fetal brain is developing a variety of different neural mechanisms. The mother rats received TCDD doses of 20, 60, or 180 nanograms per kilogram body weight (ng/kg). The lowest of these doses is comparable to the typical human body burden. The researchers then conducted the motivation portion of the experiment with the adult offspring.

The researchers found a direct correlation between the rats' exposure to TCDD and their motivation to run on the wheel: the more TCDD the rat was exposed to, the fewer running opportunities she earned. When the wheel was set to turn only after the rat pressed the release lever 20 times, for example, the control group ran an average of 8.3 times per hour. The group exposed to the lowest TCDD dose ran an average of 6.5 times per hour. The group exposed to the highest dose ran an average of 2.7 times per hour.

Whether TCDD causes analogous effects in humans is unknown, although the researchers point out that the average body burden in humans—estimated in 1995 by the U.S. Environmental Protection Agency at 13 ng/kg—was high enough to alter rats' behavior; the researchers extrapolated that a 10% change in the rats' behavior was noted at maternal TCDD exposures of 7–8 ng/kg.

The researchers believe that TCDD's damper on rat motivation extends beyond the running wheel. While other researchers have studied the anatomic and physiologic abnormalities that interfere with reproduction in exposed animals, Markowski and colleagues suggest that TCDD in the fetal brain also alters sexual motivation as well as copulatory behavior itself. They cite earlier research revealing that male rats exposed prenatally to TCDD take longer to begin copulating when allowed access to receptive females—perhaps, the researchers speculate, because of TCDD's motivational effects. **–Cynthia Washam**