Near and Not-So-Dear TRI Facilities

Prenatal Proximity and Later Brain Cancer

The most clearly established environmental risk factor for childhood brain cancer is therapeutic radiation exposure (not including diagnostic X-rays). New research now suggests that children of mothers who lived near an EPA Toxics Release Inventory (TRI) facility while pregnant may be more likely to later develop brain cancer, especially if the site released carcinogens [***EHP* 114:1113–1118; Choi et al.**].

Prenatal exposure to chemicals can have profound long-term effects, as some toxic chemicals that are stopped by the blood–brain barrier in adults may reach the fetus via the placenta. This work is the first to specifically examine brain cancer risk in children and potential exposure to TRI releases, although some previous research has suggested slight increases in risk for certain birth defects associated with such emissions.

Of the more than 650 toxic chemicals listed in the TRI, 193 are known or suspected carcinogens, according to the EPA. Fifty-five known, probable, or possible carcinogens were actually released within 2 miles of the study participants. However, it is very difficult to accurately assess exposure to TRI releases. The TRI itself shows only the type and mass of chemicals released in a given year, not where the chemicals went or precisely when they were released. Because of the uncertainty built into using these data, studies such as this must be interpreted with caution.

The study included 382 children diagnosed with brain cancer before age 10 and an equal number of cancer-free controls analyzed as pairs. Mothers of children whose brain cancer was diagnosed before age 10 years were nearly 50% more likely to have lived within 1 mile of such a site during pregnancy; the likelihood was nearly 75% higher for children diagnosed before age 5. However, when looking at risk for two major childhood brain cancer types in particular, astrocytoma and primitive neuroectodermal tumors, there was no difference.

Location equation. New data point to a mother's residence near a Toxics Release Inventory facility while pregnant as a possible factor in brain cancer risk in children.

The team used EPA Region III's chronic toxicity index, which combines total mass released with toxicity factors including carcinogenic weight of evidence and cancer potency factors. For this study, inhalation and oral cancer potency factors were included. Other potential factors, such as mothers' exposures in the workplace during pregnancy, children's postnatal exposure, and exposure through contaminated drinking water, were not taken into account. The authors therefore caution that their results are not conclusive, but should be replicated and expanded using improved exposure measures. **–Valerie J. Brown**

A Killer Smell

Mold Toxin Destroys Olfactory Cells in Mice

Mold seems ubiquitous: it permeates spaces made damp by leaking water lines, faulty roofs, or storm flooding. Although no one contests that its slimy presence is a general nuisance, its related adverse health effects have been the subject of some controversy. Now researchers at Michigan State University's Center for Integrative Toxicology have found that a toxin produced by the black mold *Stachybotrys chartarum* can damage nerve cells key to the sense of smell, at least in the noses of mice [***EHP* 114:1099–1107; Islam et al.**]. The study is the first to probe how inhaling black mold toxins affects nasal passages.

Eau de *Stachybotrys*. The mold's toxin kills olfactory neurons.

Other researchers have previously reported links between *S. chartarum* exposure and human health effects including upper and lower respiratory illnesses. There is also evidence of an association between exposure to fungi in a damp indoor environment and effects such as asthma symptoms in sensitive individuals. However, in a recent Institute of Medicine report, a panel of experts concluded that there is limited or insufficient evidence to determine whether an association exists for other suggested health outcomes such as chronic obstructive pulmonary disease, neuropsychiatric symptoms, skin symptoms, and immune diseases.

The Michigan team found that a single low dose of satratoxin G administered directly into the noses of mice selectively killed sensory neurons involved in detecting odors and sending signals to the olfactory bulbs in the brain. Satratoxins are a type of mycotoxin found in the spores and other parts of *S. chartarum*. The toxins killed the olfactory neurons by apoptosis while apparently leaving bystander cells unharmed. The mice that inhaled the fungal toxins also developed inflammation of the nasal passages and rhinitis ("runny nose" symptoms), as well as milder inflammation of the olfactory bulbs.

It is still unclear how these findings apply to humans exposed to molds. Moreover, before broader health impacts may be assessed, both the amounts of mycotoxins in the air and the nature of human exposure need to be better understood, as do the effects of mold toxins on humans' sense of smell and nasal inflammation. On first examination, however, these mouse studies suggest that exposure to airborne mold toxins may adversely affect people's ability to smell. At a minimum, the study raises new questions about the hazards of exposure to black mold in water-damaged buildings. **–Julie Wakefield**

Top to bottom: Hal Smith/AP; unknown

Potential Immunotoxic Effect of Thimerosal

Compound Alters Dendritic Cell Response *in Vitro*

Thimerosal, an ethylmercury-based compound used for decades as a vaccine preservative, has previously been linked to neurotoxic effects. New research reveals that it may also affect the immune system by altering how dendritic cells respond to biochemical signals [***EHP* 114:1083–1091; Goth et al.**].

Dendritic cells are influential primary actors in the immune system's response to infectious invasion of the body. Once activated, a single dendritic cell can direct hundreds of T cells against an infectious agent. This ability, however, depends on the dendritic cell responding appropriately to signals.

Previous studies by other researchers have indicated that thimerosal is an immunotoxicant, but its specific targets were unknown. Hypothesizing that dendritic cells might be sensitive targets, the researchers cultured bone marrow–derived dendritic cells from mice and assayed how both mature and immature cells responded to activation following treatment with thimerosal. They especially focused on the responses of inositol 1,4,5-trisphosphate and ryanodine receptors (IP_3R and RyR, respectively), which are known thimerosal targets. These gatekeepers of intracellular calcium stores are essential for signaling activities affecting dendritic cell function and maturation.

The team showed for the first time that both mature and immature dendritic cells express isoforms of these receptors, IP_3R1 and RyR1. Upon activation with the cellular energy source adenosine triphosphate, immature control cells responded with a measurable rise and fall in intracellular calcium concentration that involved RyR1 building upon the initial IP_3R1-controlled calcium release and afterward working with IP_3R1 to bring calcium down to resting levels.

Exposure to thimerosal at concentrations as low as 20 ppb altered the time course of these responses, however, and prolonged the length of time that intracellular calcium levels remained elevated. One possible consequence of these sustained calcium levels is a change in the rate and timing of dendritic cells' secretion of interleukin-6, a chemical that triggers further immune system action. Exposure to thimerosal at concentrations above 200 ppb caused immature dendritic cells to die.

The continuing use of thimerosal in some vaccines and other products warrants further investigation of possible immunotoxic effects of this compound and its constituent ethylmercury. The researchers also note that the human *RyR1* gene is highly polymorphic, an observation that raises several questions about the role of RyR1 in the immune system's genetic vulnerability to mercury. **–Julia R. Barrett**

Remember *Pfiesteria*?

Occupational Exposure Unlikely to Cause Cognitive Effects

Case reports have suggested that exposure to the dinoflagellate *Pfiesteria* may contribute to deficits in human learning and memory. Until now, however, there has been no clear, objective documentation of health effects associated with regular occupational exposure to this organism. The results of the first systematic, multiyear study of *Pfiesteria*'s human health effects now demonstrate that commercial fishermen ("watermen") likely do not face significant health risks from routine occupational exposure to the organism [***EHP* 114:1038–1043; Morris et al.**].

Pfiesteria is a common inhabitant of estuarine waters in the U.S. mid-Atlantic region in the summer and fall. In 1997, watermen working along the Pocomoke River, an estuary off Chesapeake Bay, experienced a pattern of neuropsychological deficits in association with fish kills linked to *Pfiesteria* outbreaks. Researchers studying *Pfiesteria* in a lab environment had reported similar memory and learning deficits.

Using a cohort of 88 healthy watermen with regular occupational exposure to Chesapeake Bay waters and 19 controls with minimal contact to the waters (matched to the watermen by zip code, age, and educational level), a team of Maryland researchers collected data over four summers, from 1999 through 2002. They questioned the subjects biweekly about symptoms like those reported in the 1997 episode and about their exposure to the waters and to known chemical toxicants. Subjects were tested at the beginning and end of each summer season on sensory and motor functions, attention and concentration, memory, visual functions, and verbal functions. In addition, the research team analyzed more than 3,500 water samples taken from Chesapeake Bay to monitor the presence of *Pfiesteria* and other harmful species.

Photodisc

Safe from *Pfiesteria*. New data suggest commercial fishermen need not fear routine exposure to the organism.

P. piscicida was found in water samples drawn from a number of locations in all four years of the study, and *P. shumwayae* (recently renamed *Pseudopfiesteria shumwayae*) was found in the last two years. However, the investigators found no decline in neurological function among the watermen in any year of the study.

The scientists note that unique, isolated instances of *Pfiesteria* outbreaks or unusually toxic strains of the dinoflagellate may have been associated with the marked, reversible health effects documented in the past. They point out that the present study is congruent with similar studies in North Carolina and Virginia in providing reassurance that in the absence of these conditions, watermen do not appear to face significant health risks from routine occupational exposure to estuarine waters that contain *Pfiesteria*. **–Tanya Tillett**