A Safer Mosquito Treatment?

Minimizing Deltamethrin Risks to Children

Indoor spraying to control disease-carrying mosquitoes is the strategy of choice in Mexico's effort to reduce malaria. When Mexico discontinued the use of DDT for this purpose in 2000, the pyrethrum-derived compound deltamethrin became the primary pesticide in the battle against mosquitoes. To find out how deltamethrin is distributed, absorbed, and excreted, and how it affects human DNA, researchers at the Universidad Autónoma in San Luis Potosí, Mexico, tracked 32 Mexican children aged 3–12 years before and after their homes were sprayed with deltamethrin [***EHP* 113:782–786**]. Their findings suggest that with appropriate precautions, health risks to children exposed to deltamethrin can be minimized.

Deltamethrin is recommended by the World Health Organization for application to walls and mosquito nets, and is also used for other in-home insect control, and for agriculture. But during *in vitro* tests, deltamethrin has caused chromosome damage, which can be a precursor to cancer. There have also been published reports of neurotoxicity in exposed humans.

The children in the current study lived in four villages in the state of San Luis Potosí. The researchers sampled the soil of the homes' dirt floors and measured metabolites of deltamethrin in the children's urine at several time points in the 180 days after spraying. The urine metabolites served as biomarkers for systemic deltamethrin uptake.

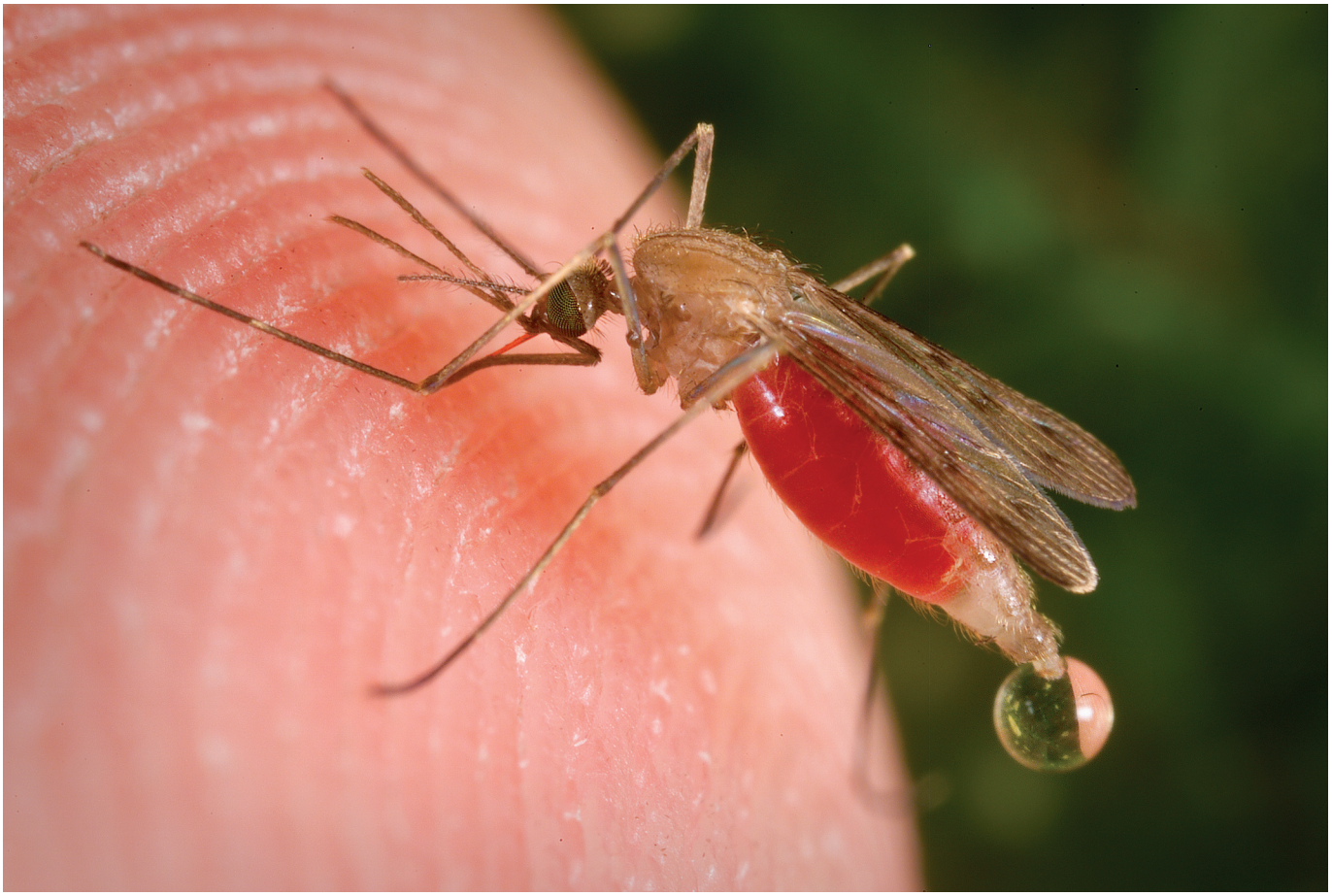
The researchers also took blood samples from 28 children before spraying and then 24 hours afterwards, and looked for chromosome breaks using the comet assay. In this assay, cells are broken apart to remove proteins, and the DNA is allowed to unwind. When the DNA undergoes gel electrophoresis (separation in an electric field), DNA fragments move away, and damage is measured by counting the fragments that have migrated.

Half of the deltamethrin degraded in indoor soil within 2.2 weeks. Indoor soil levels peaked above 2 parts per million 8 days after spraying, and declined to about 0.5 parts per million at 180 days. The highest urine metabolite concentrations appeared within 24 hours of spraying, and 91% of the metabolites were excreted within 3 days. Metabolite concentrations had returned to undetectable prespraying levels after 180 days. The results of the comet assay were statistically identical between prespraying and postspraying blood samples, indicating no DNA damage resulting from exposure.

Although peaks in urine biomarkers did not correlate with those of deltamethrin measured in the dirt floors—allowing the researchers to dismiss soil ingestion as the most important pathway of exposure—the study did confirm that children in treated houses had higher levels of deltamethrin metabolites than children in the general population, as measured in previous studies. Other studies have shown limited absorption of pyrethroids through the skin. The researchers therefore suggest that inhalation in the first hours or days after spraying is the most important pathway of deltamethrin exposure for children.

The researchers conclude that children may be protected by keeping them out of sprayed areas for one day, and then cleaning cooking surfaces and utensils before use. In addition, children should be monitored to minimize soil ingestion or contact with sprayed walls.

–David J. Tenenbaum



James Gathany/CDC

Taking the health bite out of mosquito fighters. Some simple precautions can protect children from the pesticide deltamethrin sprayed inside homes.

No Magic Bullet

Tungsten Alloy Munitions Pose Unforeseen Threat

"Better" bullets? New data show that tungsten alloy, used in munitions in hopes it would be an environmentally friendlier alternative to lead and depleted uranium, causes tumors in animals.

Don Farrall/Getty

In response to concerns about the human and environmental health effects of materials used to produce munitions, countries including the United States have begun replacing some lead- and depleted uranium–based munitions with alternatives made of a tungsten alloy. But this solution may not be the "magic bullet" it was once envisioned to be. Researchers from the Armed Forces Radiobiology Research Institute and the Walter Reed Army Institute of Research now report that weapons-grade tungsten alloy produces aggressive metastatic tumors when surgically implanted into the muscles of rats [*EHP* 113:729–734]. These findings raise new questions about the possible consequences of tungsten exposure, and undermine the view that tungsten alloy is a nontoxic alternative to depleted uranium and lead.

In the study, male F344 rats were implanted with pellets in each hind leg, an exposure protocol that mimicked shrapnel wounds received in the field. The rats were split into four treatment groups: a negative control implanted with 10 pellets of tantalum (an inert metal), a positive control implanted with 10 pellets of nickel (a known carcinogen), a high-dose group implanted with 10 pellets of tungsten alloy, and a low-dose group implanted with 4 pellets of tungsten alloy and 16 pellets of tantalum. The alloy used in this research was the same as that used in weapons: 91.1% tungsten, 6.0% nickel, and 2.9% cobalt.

By 6 months after implantation all the rats in the high-dose, low-dose, and positive control groups had developed leg tumors. None of the rats in the negative control developed tumors, and all survived beyond 12 months with no apparent health effects. All remaining rats were sacrificed at 24 months.

At sacrifice, blood samples were assessed for a range of hematologic parameters. The high-dose group exhibited statistically significant increases in levels of white blood cells, red blood cells, hemoglobin, and hematocrit as compared to the low-dose and control groups.

The rats also underwent a pathology exam, and tissues were collected for histology. Whereas the tantalum pellets in the low-dose group were surrounded by normal tissue, all of the tungsten alloy and nickel pellets were surrounded by tumors. Tumors in the tungsten alloy–treated animals metastasized to the lung. Histology further indicated that tungsten alloy pellets were surrounded by invasive neoplastic cells that had infiltrated into skeletal muscle tissue. No metastasis was observed in the positive controls.

Organ measurements identified significant increases in both spleen and thymus body-to-weight ratios in the high-dose group only. Both these organs are components of the immune system, leading the authors to suggest that embedded tungsten alloy may be immunotoxic at certain concentrations.

The authors write that the amounts of cobalt (a suspected human carcinogen) and nickel in the tungsten alloy material likely were too small to produce the effects seen in the two groups implanted with the alloy. However, they do cite recent evidence indicating that the combination of these metals may produce synergistic effects. The biological mechanism by which embedded tungsten alloy produces tumors is unclear, they add, and warrants further study. **–Charles W. Schmidt**

Roundup Revelation

Weed Killer Adjuvants May Boost Toxicity

Although the glyphosate-based herbicide Roundup is generally thought to be less toxic to the ecosystem than other pesticides, concerns about its effects on human reproduction persist. In a study in Ontario, Canada, exposure of male farmers to glyphosate-based herbicides was associated with an increase in miscarriage and premature birth in farm families. Seeking an explanation for these pregnancy-related problems, researchers at France's Université de Caen investigated the effects of the full Roundup formulation and glyphosate alone on cultured human placental cells [*EHP* 113:716–720]. The herbicide, they found, killed the cells at concentrations far below those used in agricultural practice. Surprisingly, they also found that Roundup was at least twice as toxic as glyphosate alone.

Virtually all previous testing of Roundup for long-term health damage has been done on glyphosate rather than on the full herbicide formulation, of which glyphosate makes up only around 40%. The remainder consists of inactive ingredients including adjuvants, chemicals that are added to improve the performance of the active ingredient. Roundup's main adjuvant is the surfactant polyethoxylated tallowamine, which helps glyphosate penetrate plant cells.

The Roundup concentration recommended for agricultural use is 1–2% in water. The authors incubated placental cells with various concentrations of Roundup (up to 2.0%) or equivalent concentrations of glyphosate. The viability of the cells was measured after 18, 24, and 48 hours. No one is sure how Roundup interferes with reproduction, so the team also tested whether it, like other pesticides, would disrupt the activity of aromatase (an

enzyme that regulates estrogen synthesis) in placental cells. Aromatase activity was measured after 1 hour and 18 hours.

The researchers found that a 2.0% concentration of Roundup and an equivalent concentration of glyphosate killed 90% of the cultured cells after 18 hours' incubation. The median lethal dose for Roundup (0.7%) was nearly half that for glyphosate, meaning Roundup was nearly twice as toxic as the single chemical alone. Further, the viability of cells exposed to glyphosate was considerably reduced when even minute dilutions of Roundup were added.

After an hour's incubation with Roundup, estrogen synthesis in placental cells (as shown by aromatase activity) was enhanced by about 40%. After 18 hours, however, synthesis was inhibited, perhaps reflecting an effect on aromatase gene expression. This effect was not seen with glyphosate alone.

The study showed that the effect of Roundup on cell viability increased with time and was obtained with concentrations of the formulation 10 times lower than those recommended for agricultural use. Roundup also disrupted aromatase activity at concentrations 100 times lower than those used in agriculture. The researchers suspect that the adjuvants used in Roundup enhance the bioavailability and/or bioaccumulation of glyphosate.

How these findings translate into activity of Roundup in the human body is hard to say. The French researchers point out that serum proteins can bind to chemicals and reduce their availability—and therefore their toxicity—to cells. Nevertheless, the authors conclude that the demonstrated toxicity of Roundup, even at concentrations below those in agricultural use, could contribute to some reproduction problems. **–Dorothy Bonn**

The Arsenic Differential

Metabolism Varies Between Children and Adults

Worldwide, millions of people drink water contaminated with arsenic, but not everyone who drinks contaminated water has the same severity of effects. It has long been speculated that this differing susceptibility to the adverse health effects of arsenic may be due to differences in the way people metabolize the element. Now researchers in Mexico and Arizona are finding that age may play a role as well: children may metabolize arsenic differently than adults, even if they share similar genetic traits [***EHP* 113:775–781**].

When arsenic is metabolized, it takes on new chemical identities that vary widely in their toxicity. Enzymes attach a methyl group to arsenic and convert it first to monomethylarsenic and then to dimethylarsenic. During this process, arsenic also changes its valence (the configuration of its electrons), which can affect its toxicity. The way a person metabolizes arsenic is reflected in a pattern of relative concentrations of arsenic metabolites in urine.

In the current study, researchers investigated urinary arsenic patterns of healthy residents of the Yaqui Valley in Sonora, Mexico. Participants fell into two age groups: children aged 7–11 and adults aged 18–79. The arsenic concentrations in the participants' water were between 5.5 and 43.3 parts per billion, a range found in many parts of the world. The researchers cataloged polymorphisms in a gene known to be involved in arsenic metabolism, arsenic (III) methyltransferase (*CYT19*), and used existing catalogs of polymorphisms in two others, purine nucleoside phosphorylase and glutathione-*S*-transferase omega. Then they tested the participants' urine to see how a subset of 23 of these polymorphisms related to urinary arsenic levels.

Among the children, polymorphisms on *CYT19* were strongly associated with a particular pattern of metabolites: a high ratio of dimethylarsenic to monomethylarsenic. Indeed, children with three polymorphic sites on *CYT19* were much more likely than any other participants to have the high ratio. No statistically significant association was seen in the adults—children and adults could have the same polymorphisms on their *CYT19* gene, yet have different ratios of dimethylarsenic to monomethylarsenic in their urine. However, even children with nonvariant *CYT19* had a higher ratio of dimethylarsenic to monomethylarsenic than adults.

Finding the association between the polymorphisms and urinary arsenic patterns only in children indicates that the association may be developmentally regulated, the researchers suspect. The *CYT19* gene may turn on during a certain developmental stage and be more or less active at different ages in a way that depends on a person's DNA sequence.

Whereas this study examined healthy subjects, planned follow-up studies will include individuals suffering from arsenic-related health effects to see if there is a relationship between their health effects, their urinary arsenic patterns, and their DNA sequences. The findings from such research may prove particularly important as new clinical uses for arsenic compounds are emerging in the area of cancer treatment, where differences in metabolism and toxicity are important to oncologists and their patients. **–Tina Adler**

New data on big and little dippers. Research in Mexico reveals differences in the way adults and children metabolize arsenic from drinking water.

Trygve Bolstad/Panos Pictures