Lawn care herbicide linked to reproductive problems in mice

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Researchers at UW-Madison found that exposure to low levels of a common lawn herbicide mixture led to reduced litter sizes in laboratory mice. This research builds on other studies showing possible links between pesticide exposure and reproductive and/or developmental problems in animals and humans.

While previous epidemiological studies have linked herbicide exposure and birth defects, others have found no link between pesticides and reproductive problems. UW-Madison Zoology Professor Warren Porter says, "The present study shows that there may be cause for concern. Further study on the effects of low doses of off-the-shelf herbicide *mixtures* on reproductive performance are needed. Levels that were previously assumed safe by the EPA have now been shown to have possible biological effects. Since the greatest effects were at the lowest dose, we still don't know how low an exposure can be and still induce effects."

The herbicide mixture tested was composed of 2,4-D (7.59%), mecoprop (3.66%), dicamba (0.84%), and inert ingredients (87.91%), as reported by the manufacturer. These chemicals are also used in agriculture to control broadleaf weeds, although application rates are typically lower for agriculture than for lawns.

Of mice and herbicides

UW-Madison Zoology researchers James Jaeger and Warren Porter and University of Valparaíso, Chile, faculty member María Fernanda Cavieres exposed pregnant female mice to the commercial herbicide mixture via drinking water in 2000-01.

The mice were assigned to four groups receiving different dosage levels, and a control group. All dose levels were confirmed by State of Wisconsin lab analysis. The researchers closely monitored water consumption to make sure that water intake did not differ significantly between the groups of mice and that each mouse received the right dose.

At birth, each litter of mice was checked for the total number of live pups. Pups born dead and cannibalized pups were not included. Once counted, the litters were culled to 8 pups to ensure comparable growth. These pups were weaned at three weeks and kept until they were 6 weeks old for additional studies. The researchers also examined each female mouse to determine how many embryos it carried at the beginning of the pregnancy.

All experiments were conducted in accordance with laboratory animal use and care protocols as established by the UW-Madison Research Animal Resource Center.

Effects of herbicide exposure

"We found that herbicide doses at all levels caused a decrease in the number of embryos in early pregnancy and live born pups compared to the control group," says Porter. These decreases were significant in the low and very low dosage groups (ANOVA, Bonferroni $p<0.05$). Mice exposed to herbicides had a decrease of about 20 percent in the number of pups born compared to the control group. "What is most important from these data is the decrease in the number of embryos that survived at the very low and low doses," says Porter (see figure on back).

The difference between the number of initial embryos and number of live born pups represents fetuses that aborted and were re-absorbed. Resorptions weren't significantly affected by dose.

Compared to the control group, pups exposed to the herbicide as fetuses did not show a large decrease in weight or length from head to tail, common measures of chemical toxicity. This may be related to the fact that pups from small litters tend to be larger than pups in large litters.

Herbicide treatments on lawns may pose a risk to fertility.

"These data do not fit with the common currently accepted toxicology models for dose-response relationships—one would expect that litter size would decrease as dosage increases," states Porter. However, U-shaped dose response curves (greatest effects at lower doses) have been reported for neurological, endocrine, and immune functions. Porter says, "We speculate that the greatest effect occurs at the lower dosage levels because of the interaction between hormones." For example, there may be negative feedbacks between hormones, or responses to subtly different levels may be very different, or there may be subtle shifts in the chemical environment of the enzymes creating the hormones.

In the world of endocrinology and immunology, it is well established that the body's enzymes, hormones and other chemicals tend to be controlled over very narrow concentration ranges—often in the parts per trillion. Most of the reproductive problems that occurred in this study were produced by doses at which other environmental chemicals have been shown to produce similar effects.

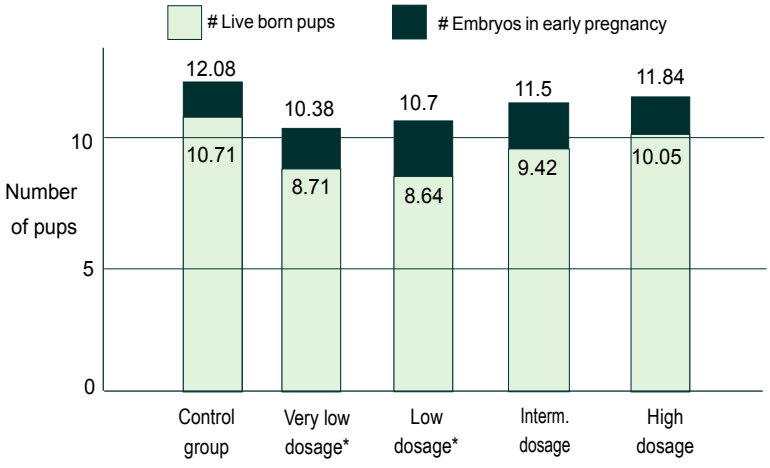
More research is needed to replicate these results.

Seasonal variations

There were seasonal differences in the responses to varying herbicide doses. In fall, the largest decrease in litter size occurred at the high dose level; in all other seasons, the largest decrease occurred at low and very low doses.

The researchers speculate that these seasonal differences may be due to normal seasonal influences on animal hormone levels, even though the mice were kept under controlled laboratory conditions. "Extreme care was taken in our procedures to minimize inter-experimental variation so that the animal supplier, the age of the animals, the sources of food and water, room temperature and humidity, and length of daylight were always the same in all experiments," says Porter. He reports that other studies have found seasonal variations in the release of reproductive hormones in experimental animals.

Initial litter size and # live born pups at 4 dosage levels



See text for explanation of largest effect at very low and low dosages.

*Statistically significant: p<0.05 Bonferroni

Links to human health

Mice, as mammals, provide a model system on which to test the effects of toxic compounds, but there are differences in how mice and people react to some chemicals. However, these findings are significant enough to cause concerns about herbicide exposure and reproductive problems in humans.

People can be exposed to chemicals like those in the study by drinking contaminated groundwater, breathing air containing the chemicals, or having their skin come into contact with a treated lawn. "All three chemicals in this mixture are found in groundwater, which is why EPA has established standards for each of them," Porter notes. Certain substances in commercial herbicide formulations allow the rapid movement of chemicals through the skin, bypassing the body's primary defenses in the liver. "Due to the ability of these chemicals to pass through fat, once in the blood they have the potential of crossing the blood-brain barrier and gaining access to the brain," according to Porter. "Once the chemicals gain access to the brain, the potential for reproductive problems like infertility and miscarriages arises."

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