Neonic Pesticides: Potential Risks to Brain and Sperm

January 06, 2021 Jennifer Sass

Neonicotinoid insecticides or "neonics"—the most widely class of insecticides worldwide—have long been linked to massive losses of bees and butterflies, despite industry efforts to downplay their leading role. Science also ties neonics to declining bird species, dramatic losses of fish populations, and birth defects in white-tailed deer.

But neonics may be a problem for more than just the birds and the bees. Commonly found in water supplies, food, and human bodies across the country, these popular chemicals are increasingly becoming part of our daily lives. That's also of increasing concern to health professionals as new studies illuminate the serious risks that these everyday exposures may pose for people, especially children.

While more research on neonics' possible human health harms is sorely needed, what we already know is worrying, and scrutiny is growing. For example, California is currently considering whether to list some of the neonic pesticides under Proposition 65 based on their neurodevelopmental and reproductive effects (i.e., brain and sperm damage), with a committee of experts (the "DARTIC" committee) discussing it last month (see NRDC's comments here). However, since the evidence we have on neonics' potential human health impacts to date is little known to the public, often ignored by regulators, and (as with the wildlife data) downplayed by industry, it's worth a quick review:

How Neonics Work: They Target the Brain and Nervous System

Neonics are neurotoxic insecticides. They permanently bind to insect nerve cells, overstimulating and destroying them—commonly causing uncontrollable shaking or twitching, paralysis, and (eventually) death. Neonics bind to nicotinic acetylcholine (nACh) receptors, so

called because they are activated by nicotine. Neonicotinoids (meaning “new nicotine-like” substance) get their name because they activate nACh receptors too.

But nACh receptors aren’t only in insect nerve cells, they’re also in the brain cells of people, where they play a central role in the operations of our brain and nervous systems, including learning, memory, mood, sensory processing, and pain. And there’s reasons to fear the impacts of nicotine-like substances on the brain, particularly for young, developing brains. In fact, health experts have long warned pregnant women to avoid nicotine because we know it isn’t safe for the fetus.

To get even more fine-grained, neonics are designed to bind to a subunit of the nACh receptor, called the alpha-4-beta-2 (α4β2) subunit. This subunit is a part of all insect nACh receptors, but a lesser fraction of those in people. Nonetheless, critical areas of the human brain are densely populated with nACh receptors containing the α4β2 subunit, including: the cortex (responsible for planning, judgment, creativity, inhibition, attention, memory, language); the thalamus (emotion, memory, relay sensory information between the cortex and the cerebellum); and, the cerebellum (posture, balance, coordination, speech). In other words, this receptor subtype may number fewer in people than in insects proportionally, but it’s all over critically important areas of the brain.

To make an analogy, a needle poke will hurt an insect more than a human, but it is still important to ask what happens if a person gets that needle poke in a sensitive area like the eye. With neonics, the concern is about getting a needle poke (or many) in critical regions of the brain during sensitive life-stages of brain development.

Evidence of Exposure: Half the U.S. Population Regularly Dosed with Neonics

To continue the metaphor, the first key question is how many people are getting poked with neonic needles? As it turns out, you don’t need to go looking in haystacks.

The Centers for Disease Control and Prevention (CDC) finds that roughly half the U.S. population is exposed to at least one neonic chemical on a regular basis (Ospina et al. 2019). That analysis looked for neonic breakdown products or “metabolites” in urine from a random population sample of thousands of people, finding acetamiprid (35% of samples) and imidacloprid metabolites (20% of samples) most commonly and also at the highest levels (95th percentile concentrations were 1.29 and 1.37 µg/L respectively).

Compared with adults, young children age 3 to 5 years old had higher neonic exposures, likely from eating non-organic (conventionally grown) foods. While the CDC study does not include children under 3 years old, the EPA has estimated that infants up to 1 year old are exposed through diet (food and water) to roughly 70-80% of the maximum acceptable limit (called the acute Population Adjusted Dose, or aPAD) for each of acetamiprid (69% of aPAD, 0.071 mg/kg-day) and imidacloprid (84% of aPAD, 0.08 mg/kg-day). Had EPA evaluated the cumulative toxic impacts of all neonics together (which it should have) then exposure to infants would exceed EPA's acceptable limit.

So how are these neonics entering people's bodies? Most people exposed would have to search no further than their refrigerator or the tap at their kitchen sink.

Favorite Kids Foods Contaminated with Neonics (Good news: Organics are mostly neonic-free)

Based on USDA data, acetamiprid was detected in many non-organic foods that are children's favorites, including: 60% of cherries; 30% of strawberries; 30% of apples; 20% of nectarines; and 16% of pears. Even apple sauce, a common food staple of babies and young children, had acetamiprid in about 60% of non-organic samples tested. The neonic imidacloprid was found in 41% of non-organic U.S. grapes and—while possibly not kid-favorites—also on non-organic leafy greens like spinach, kale, and collard greens. Other research has also detected neonics in baby food.

Pesticide Action Network, https://www.whatsonmyfood.org

On organic foods—where neonic use is prohibited—neonics were rarely detected. However, in a sign of how pervasive neonic contamination is, research has shown that neonics even show up in a very small percentage of organic produce too, likely as a result of neonic-contaminated irrigation water.

What's on Tap? Neonics!

In addition to our favorite foods, neonics also run off farm fields, lawns, and gardens into waterways and groundwater—with federal government research showing neonics in about half of U.S. streams tested. While modern filtration systems can remove neonics, standard chlorination treatment doesn't, meaning homes that pull from groundwater or older treatment systems are at higher risk of finding neonics in their tap. For example, one study found neonics "ubiquitously" in tap water at the University of Iowa. Even worse, some government and

university experts are warning that neonics have the potential to form even more toxic compounds when they are chlorinated during routine tap water treatment (see details in my previous blog; Klarich Wong et al. 2019).

Poisoning from Household Products

Imidacloprid is the most common neonic used in household products (e.g., bed bug and pet flea treatments), and, in the last decade, there's been an astounding 1,630 imidacloprid poisoning incidents according to data collected by EPA (see here). The reported symptoms include skin rash, muscle tremor, difficulty breathing, vomiting, wheezing, lock jaw, memory loss, and renal failure. Other severe symptoms are described in EPA's Pesticide Poisoning Handbook:

"Patients have presented with disorientation, confusion and agitation—severe enough to require sedation—headache, drowsiness, dizziness, weakness, tremor and, in some situations, loss of consciousness."

(EPA 2013, P. 90)

These poisonings are evidence that consumers using these neonic products are getting exposed to imidacloprid at levels that cause poisoning symptoms severe enough for them to seek medical attention, but they likely represent only a fraction of actual poisonings. Note: To report a pesticide poisoning—including to people, pets, and wildlife—call a Poison Control Center, or follow the instructions on EPA's webpage.

Evidence of Hazard: Developmental and Reproductive Risks

Science has long recognized that even small toxic exposures that occur during early development are more likely to lead to permanent or debilitating effects throughout life (for example, see NAS 1993, and FQPA 1996). A growing body of scientific evidence now demonstrates these sorts of hazards are very real for neonics—and are made even more concerning by the fact that neonic exposure is chronic and widespread across the country. While more research is critically needed, here is a summary of the research raising alarms:

Human Studies: Potential Elevated Risk of Birth Defects in Prenatally Exposed Children

A systematic review of publicly available literature on unintentional human exposures to neonics reported a link between neonic exposures and malformations of the developing heart and brain, as well as a cluster of symptoms including memory loss and finger tremors (Cimino

et al. 2017). The review highlights three epidemiologic studies of U.S. populations that report a suggestive association between prenatal exposure to neonic pesticides and birth defects:

Autism like symptoms - A study by NIH-funded researchers from UNC Chapel Hill and UC Davis reported that frequent exposure (self-reported by parents) to imidacloprid applied as flea and tick treatments for pets (Advantage by Bayer) during pregnancy was associated with a 2-fold elevated risk of autism spectrum disorder in prenatally-exposed children (odds ratio 2.0, 95% confidence interval 1.0-3.9 based on 407 children with confirmed autism spectrum disorder) (Keil et al. 2014).

Birth defects of the heart - A study of infants born with heart defects born to mothers in California's San Joaquin valley reported a statistically significant association between living close to agriculture areas that use imidacloprid and having a baby born with a rare heart defect called the teratology of Fallot (adjusted odds ratio 2.4, 95% confidence interval 1.1-5.4 based on 101 cases of heart defects) (Carmichael et al. 2014).

Birth defects of the brain - A study of the same population of mothers in California's San Joaquin valley reported a suggestive association between living near agriculture areas that use imidacloprid and an almost 3-fold elevated risk of having a baby born with anencephaly, lacking parts of the brain and skull (adjusted odds ratio 2.9, 95% confidence interval 1.0, 8.2 based on 73 cases of anencephaly) (Yang et al. 2014).

While these studies are limited by small numbers of study subjects, they are well-conducted, the exposures are well-characterized, and the statistical analysis is appropriate. They also have all been peer-reviewed and published in respected scientific journals. These studies are considered by the authors to largely be "hypothesis generating studies" that raise red flags and signal the need for more additional studies.

Animal Studies: Poor Sperm Quality and Quantity

Several rat studies report adverse effects of acetamiprid on sperm, including dose-dependent decreases sperm concentration and testosterone levels associated with a 90-day neonic exposure (Arican et al. 2020), increases in abnormal sperm and low sperm count (Mosbah et al. 2018), and a guinea pig study showing acetamiprid caused cell membrane degradation in the testis (Guiekep et al. 2019).

Likewise, imidacloprid rat studies also report effects on male reproductive system, including decreased sperm count, sperm motility, and live sperm, and decreased testosterone (Lonare et

al. 2016; Bal, Naziroglu et al. 2012; Bal, Turk et al. 2012; Najafi et al. 2010). Additional studies reported on increased sperm abnormalities in rats (Hafez et al. 2016) and mice (Bagri et al. 2015).

This is relevant to humans, given that roughly one-third of all infertility is due to the male, with the most common cause being deficiencies in sperm quality and sperm count.

Animal Studies: Developmental Neurotoxicity

A number of animal studies show that prenatal exposure to neonics increases the risk of neurodevelopmental abnormalities and birth defects. In addition to published scientific studies these also include laboratory animal studies submitted by pesticide manufacturers to EPA support regulatory approval for neonics.

Based in large part on the above studies, the Endocrine Society submitted comments to EPA citing the "substantial and increasing body of literature linking exposure to neonicotinoid pesticides and developmental thyroid toxicity in wildlife." As thyroid functioning is critical to brain development, and "[neonic] chemicals may have effects at extremely low doses," the comments warn "there may in fact be no 'safe' level for these chemicals."

Harms found to animals that raise human health concerns include:

Reduced thyroid function in deer - Developmental abnormalities in white-tailed deer exposed to real-world levels of imidacloprid in their water had a higher risk of hypothyroidism and lethargy, decreased body and organ weight, decreased jawbone length, and higher mortality rates for fawns. (Berheim et al. 2019).

Thinning of some brain areas and under-activity in rats - An unpublished Bayer-sponsored rat study reported imidacloprid exposure during pregnancy produced an overall reduced activity in the offspring, and a statistically significant 2% decrease in the thickness of two areas of the brain involved in regulating movement (caudate and putamen) in the high dose female rats. (see EPA DER 2002; study MRID 45537501).

Thinning of some brain areas, altered reflexes, delayed sexual development - An unpublished Syngenta-sponsored rat study reported that exposure to the neonic thiamethoxam during pregnancy produced statistically significant adverse effects in offspring in many of the low (4.3 mg/kg) and middle dose (34.5 mg/kg) groups and all of the high dose (298.7 mg/kg) groups. These included a thinner brain cortex, altered auditory startle reflexes, delayed reproductive

development (delayed preputial separation) in males, and an increase in stillbirths (EPA DER 2005; study MRID 47034201, 46028202).

Sensorimotor deficits in rats – One study found neurobehavioral impairments in rodents exposed prenatally to a single high sublethal injection of imidacloprid (337 mg/kg at day 9 of pregnancy). Effects included sensorimotor deficits like reduced beam walking time and reduced forepaw grip time (from about 3.5 seconds in control animals, to below 1 second in imidacloprid-exposed rats. (Abou-Donia et al. 2008).

EPA's Regulatory Failure

The EPA Pesticide Office has had access to the growing body of evidence on neonics' neurotoxicity for years, but has failed to take protective action—or even honestly acknowledge the risks—proposing only minimal restrictions in its recent review of neonics. EPA's proposal not only continues to leave bees and other wildlife exposed to the widespread, wasteful neonic use decimating their populations (see NRDC's comments here), it violates the Food Quality Protection Act (FQPA), passed unanimously by Congress in 1996 to protect human health (see NRDC's 2020 petition).

The FQPA requires EPA to consider potential pesticide exposures from all sources during the entire span of human development, using a "risk cup" approach. Where those exposures exceed EPA's maximum acceptable limit (again, the Population Adjusted Dose, or "PAD"), the risk cup overflows. EPA must then cancel or restrict uses so that the total exposures no longer spill out of the cup, i.e. do not exceed the PAD. In order to protect children and other sensitive populations, the FQPA requires that EPA multiply the risk by 10 (the "Child Safety Factor") in absence of reliable evidence justifying a lower margin of safety. It must also consider the cumulative risk of all pesticides sharing a common mechanism of toxicity (i.e., that cause harm in the same way) together in the same risk cup.

For neonics, EPA discarded the Child Safety Factor for each of the five registered neonics (that is, reduced it to 1X), despite considerable evidence of neonics' risks to early life stages of neurodevelopment and no justification for removing the legally required protection for children. It also ignored neonics' common mechanism of toxicity (all target the nACh receptor), considering the risks from each neonic chemical separately, not cumulatively (i.e., splitting the risk into five cups instead of one, so that none would overflow) when real-world evidence demonstrates that many Americans are routinely exposed more than one neonic at once.

Despite EPA's questionable and illegal math (again, see NRDC's 2020 petition for all the details), the agency was still compelled by law to propose canceling certain imidacloprid lawn products to protect human health. That means that if EPA actually followed the law (i.e., assessed all the risk cumulatively in the same "cup" with the required 10X FQPA Child Safety Factor), EPA would have to cancel or severely restrict many more neonic uses.

Health-Protective Action Needed

The serious health concerns raised by laboratory and epidemiologic studies demand greater protections for people from neonic exposures—especially from widespread and wasteful neonic uses—while further research is conducted. While we hope that 2021 is the year that EPA sets the record straight on the neonics and puts the health and safety of our families and our environment first, the agency's pesticide office has a long and troubled history of failing to protect consumers and farmworkers from the damages of toxic pesticides.

Consumers can put a dent in neonic and other toxic pesticide pollution by avoiding insecticides and herbicides on home lawns and gardens, purchasing organic produce when feasible, avoiding neonic-based pet flea and tick products, and supporting local initiatives to keep pesticides off public spaces like parks and playgrounds.

Protective actions by states and local jurisdictions will continue to be critical for protecting their residents for some time. You can TAKE ACTION to support our work to protect New Jersey, California, and New York's people and wildlife from neonics.