Tagged. Radio chips have helped reveal how many bees lose their way after pesticide exposure.

Pesticides Under Fire For Risks to Pollinators

As the European Union moves to ban a popular type of pesticide, researchers struggle to assess exactly how dangerous the chemicals are to honey bees and other pollinators

IN APRIL 2008, SOMETHING WENT TERRIBLY wrong with beehives in southern Bavaria and the Upper Rhine Valley of Germany. Confused honey bees huddled trembling outside their hives rather than taking off for their morning flights. Many dropped dead. Over the next 2 weeks, the bodies piled up and more than 11,500 colonies were hit by the mysterious affliction. "It was a catastrophe," recalls Peter Rosenkranz, who studies bee health at the University of Hohenheim in Stuttgart.

Researchers quickly discovered the culprit: dust from seed corn that had been treated with a pesticide called clothianidin, one of the most toxic agrochemicals for honey bees. A seed company had neglected to use an adhesive to bind the pesticide to the seeds, so the farmers' planting equipment had been spewing dust that was extremely toxic to bees. Even though it was a rare mishap, the German government banned companies from coating corn and certain other seeds with clothianidin and two related pesticides.

The event brightened the spotlight on the potential dangers of a family of pesticides called neonicotinoids. In 1999, France had banned one neonicotinoid, barring the use of imidacloprid on sunflower seeds after beekeepers suspected that it had killed a third of their colonies. Now, citing evidence from laboratory and field studies that neonicotinoids threaten honey bees and other pollinators, the European Union is poised to ban the use of three of the most common neonicotinoids in several crops by the end of the year.

Clearing the air. Planting pesticide-coated seeds can release toxic dust that kills bees. A collaboration is working to reduce the amount released.

In the United States, beekeepers and environmental advocates are demanding that the government suspend its approval of two of these pesticides, and recently they sued the Environmental Protection Agency (EPA), alleging that the agency hasn't adequately evaluated the chemicals.

Even as European regulators act, however, scientists are divided on whether pollinators are exposed to enough of the pesticides to pose a grave threat to their colonies, in part because of a paucity of data and the challenges of doing rigorous field trials. Pesticide and seed companies maintain that their products are safe when used properly. And many scientists remain unconvinced that chronic exposure to doses typically encountered in farm fields is a leading cause of pollinator declines. "The jury is still out," says Marla Spivak of the University of Minnesota, Twin Cities.

There's also debate about just how vital the seed treatments are for agriculture. The pesticide industry has warned that restricting neonicotinoids will jeopardize food security and farm incomes. Some researchers, however, are underwhelmed by that claim (see sidebar, p. 675) and note that some data suggest that neonicotinoid use may offer little boost to yields.

Dust-up

Developed in the 1980s, neonicotinoids are a major new class of insecticides. The compounds mimic the toxic effects of nicotine, which tobacco plants use as a natural insecticide. Neonicotinoids block receptors for the neurotransmitter acetylcholine; high doses cause paralysis and death in insects. Because neonicotinoids bind more tightly to the insect version of the receptor, low doses are relatively safe for other animals, including mammals.

EPA approved the use of a neonicotinoid called imidacloprid in 1994, and it has since become the most widespread insecticide in the world. Approved for use in about 140 crops and numerous garden and horticultural products, sales topped $1 billion in 2009. Clothianidin and several other neonicotinoids have been commercialized over the past decade.

The most common use in agriculture is to coat seeds to protect them from soil pests. As the seed grows, it readily incorporates the compounds so that tender young plants are guarded as well.

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That means less pesticide is applied than if it was sprayed onto the plants. "It's a much more environmentally friendly way to apply a chemical," says David Fischer, director of environmental toxicology and risk assessment at Bayer CropScience in Research Triangle Park, North Carolina, a major manufacturer of neonicotinoids.

As use of neonicotinoids has grown, however, researchers have become concerned about their potential to harm birds, earthworms, aquatic insects, and especially bees. They have found traces of clothianidin and other seed-based pesticides in a large fraction of samples of dead honey bees from commercial beekeeping operations. "That's pretty astonishing" and "suggestive that the pesticides are related to the deaths," says Reed Johnson, an entomologist at Ohio State University's Agricultural Research and Development Center, Wooster. Honey bees and other pollinators can pick up the chemicals by feeding on nectar and pollen, or sipping on drops of liquid, called guttation, exuded by corn and other plants. The compounds are eventually fed to young bees back at the hive.

There's no debate that high doses of neonicotinoids kill pollinators, and studies suggest that chronic or intermittent exposure to low doses can also cause trouble. Over the past 5 years, for example, a host of findings have indicated that low doses can trigger behavioral effects in honey bees, such as memory and learning, which could affect foraging. The big question facing researchers is how to extrapolate from lab studies on individual bees to evaluate the impact on entire colonies, which are quite resilient. "You can lose a lot of bees and the colony is able to maintain itself," says Dennis vanEngelsdorp of the University of Maryland, College Park.

To study colony impacts, researchers have fed neonicotinoids to bees in colonies. But determining realistic doses experienced by bees is a sticky problem. Scientists don't know how much soil residue levels rise as fields are repeatedly planted with treated seeds. And homeowners can apply the pesticides at rates up to 120 times higher than farmers. "The actual exposure is likely higher than we think," Spivak says. New data could come soon: The United Kingdom's Department for Environment, Food & Rural Affairs (DEFRA) has funded David Goulson of the University of Stirling to measure pesticide concentrations more widely in the landscape, including soils, crops, flowers, and hedgerows.

Smaller hives

Some scientists have started to focus on bumblebees, suspecting that they may be more vulnerable than honey bees because their colonies are much smaller. "You can have quite a dramatic effect compared to honey bee colonies," Rosenkranz says. In a high-profile study, Goulson and colleagues fed bumblebees pollen and sugar water containing imidacloprid. After the bees foraged in the open for 6 weeks, the team found 85% fewer new queens in the colonies that had been exposed to the pesticide, they reported in *Science* (20 April 2012, p. 351). "To me, the evidence is pretty close to overwhelming" that exposure has big impacts, Goulson says.

Scientists with DEFRA, however, objected. Goulson's doses were unrealistically high and thus "biased towards showing a deleterious

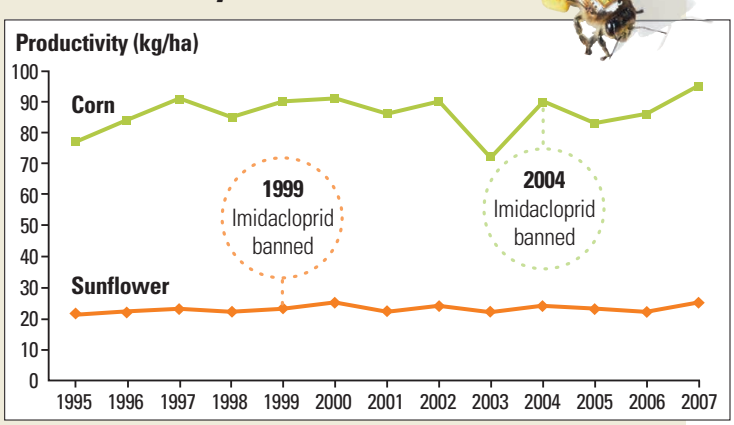
How Big a Role Should Neonicotinoids Play in Food Security?

Proponents of neonicotinoid-treated seeds claim that the chemicals offer many benefits besides killing pests, including improved plant vigor and higher yields. The business itself has certainly boomed. Almost all the corn and about one-half of the soybeans in the United States are grown from insecticide-treated seeds. "The companies are marketing them aggressively," says Paul Mitchell, an agricultural economist who studies pest management at the University of Wisconsin, Madison.

But how important are neonicotinoid seed treatments for agriculture? Agronomist Palle Pedersen, technology manager for seed care at Syngenta, says that treated corn seed produces an extra 9 bushels an acre above a national average of about 160. "We've seen a dramatic yield increase," he says. But researchers studying soybeans and other major crops have found treated seeds can come up short.

A 2-year trial of treated soybeans in South Dakota, for example, found no yield benefit. Insecticide concentration in the plants was too low by the time the major pest, aphids, arrived, according to a study published last year in the *Journal of Pest Science* by Jonathan Lundgren of the U.S. Department of Agriculture in Brookings, South Dakota. He says that his findings mirror those of other trials. A worrying postscript: The neonicotinoids also harmed predators of the aphids, such as omnivorous pirate bugs (which feed on the soybean plant itself as well as aphids). Pedersen isn't convinced. "It's such a small data set, we can't draw a conclusion out of that."

Companies say that they have copious data to prove the efficacy of treated seeds. "Admittedly, they do not increase yield all of the time, but the larger body of data says that they do provide an increase in yield a high percentage of time," says William Hairston, director of product development for seed growth at Bayer CropScience in Research Triangle Park, North Carolina. Few of these data are peer-reviewed, however, and some scientists are skeptical, saying that the trials often combine insecticide with fungicides, which are known to help prevent losses from disease.



Steady. Farmers kept yields after France banned neonicotinoid-treated seeds.

Another reason that some scientists debate the overall value of the seed treatments is that the pests they target—such as wireworms, Japanese beetles, and seed corn maggots—are rarely major problems, or are already resisted by genetically modified crops. Still, with sky-high commodity prices, farmers don't want to risk lower yields, and want to guard against any potential pests. "The price of corn is so high, it's peace of mind," says entomologist Reed Johnson of Ohio State University's Agricultural Research and Development Center, Wooster.

Entomologist Christian Krupke of Purdue University in West Lafayette, Indiana, says that neonicotinoids are good tools, but overused. "They do not need to be on virtually every annual crop seed, every year," he says. "Our pest pressures do not justify the practice in fields that I and others have examined." **–E. S.**

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Diverse. Neonicotinoid-treated seeds are used in many crops, including soybeans, cotton, rice, and peanuts. Color serves as a warning.

effect," they wrote in a review paper posted on the DEFRA Web site in March. Helen Thompson of DEFRA and others tried to resolve the question with a field study of 20 bumblebee colonies, some placed in fields of canola planted from treated seeds and others in fields of untreated canola. Unfortunately, the control failed; the bumblebees put into untreated canola had collected just as much clothianidin or imidacloprid in their nests, probably by flying to other fields. Nevertheless, DEFRA concluded in March that the neonicotinoids did not have any major effect on the hives. To James Cresswell of the University of Exeter, the bottom line is that it's difficult to conduct a rigorous field trial.

Still, others are trying. One of the largest field studies, a $950,000 effort funded by Bayer CropScience, started last summer in Ontario. A team led by Cynthia Scott-Dupree of the University of Guelph and Chris Cutler of Dalhousie University placed 20 colonies of honey bees in fields of blooming canola that had been planted with seed treated with the maximum approved dosage of clothianidin. Another 20 colonies were put in fields without treated seed, at least 10 km away. "This was our most complicated bee study to date," says Fischer, adding that, so far, there are no significant differences between the colonies.

Complex mixtures

These results are unlikely to exonerate neonicotinoids once and for all, others say. One limitation is that the farms of southern Ontario are smaller and more diverse than in places such as the midwestern United States, where bees have fewer alternatives to neonicotinoid-treated crops. Another complication is that the effect of neonicotinoids may be exacerbated by additional threats. For example, Jeffery Pettis of the U.S. Department of Agriculture (USDA) Bee Research Laboratory and others have recently shown that neonicotinoids increase the risk that honey bees will contract viruses and a deadly microbial disease.

In addition, honey bees are exposed to many other chemicals. In a report released last week, EPA and USDA noted that insecticides called pyrethroids may pose a threefold greater hazard than systemic neonicotinoids. And those aren't all. James Frazier of Pennsylvania State University, University Park, has studied commercial colonies that are trucked around the country to pollinate various crops. He found an average of more than six pesticides in pollen samples from the hives, with some containing as many as 30 chemicals. The situation may worsen over time because honey bee combs accumulate pesticides, which, according to a 2011 study, can hinder larval development. The highest concentrations were of pesticides called acaricides that beekeepers use to fight a parasitic mite called *Varroa destructor*, which scientists say is the biggest threat to honey bee colonies. The dilemma is that without acaricides, mites will usually destroy colonies.

Not much is known about the impact of these pesticide mixtures, but they appear to spell trouble. A study online in *Nature* in October found a cumulative impact from a neonicotinoid and a pyrethroid. Ohio State's Johnson and colleagues reported in *PLOS ONE* in January that certain acaricides and fungicides were more toxic to adult worker bees in combination, probably because fungicides inhibit the detoxifying enzyme cytochrome P450.

Another factor that may worsen the impact of pesticides is the way that people manage commercial beehives. Beekeepers often feed their insects high-fructose corn syrup to boost their activity. But that may hinder their ability to cope with pesticides, May Berenbaum of the University of Illinois, Urbana-Champaign, and colleagues reported last month in the *Proceedings of the National Academy of Sciences*. She found that honey (but not sucrose or corn syrup) contains naturally occurring compounds that up-regulate genes for detoxification. Adding one such compound, *p*-coumaric acid, to the sugar water fed to bees increased the bee's breakdown of a common acaricide by about 60%.

One of the biggest unknowns facing neonicotinoid researchers is the impact on solitary bees, hiveless insects which are the least well-known kind of bee. North America has some 4000 species, which typically nest in the ground and are therefore likely exposed to pesticide residues in soil as well as in nectar and pollen. The bees have short lives and many are impossible to breed in the lab. "It is incredibly difficult to do research on solitary bees," Rosenkranz says.

Europe acts

Despite such uncertainties, Europe is moving quickly to further tighten its regulations. After the European Food Safety Authority (EFSA) released a report in January concluding that neonicotinoids posed "high acute risks" to pollinators, some governments proposed a partial ban in the European Union. The bid failed, however, in a vote of member nations. But as a result of parliamentary procedures, the European Commission was free to act on its own. It decreed that, starting in December, farmers won't be able to plant seeds treated with clothianidin, imidacloprid, or thiamethoxam, nor spray the chemicals on crops preferred by bees. There will be exceptions for use in greenhouses and on fields after flowering.

The EFSA review underpinning that decision was "hurried, incomplete and failed to take into account years of field monitoring, mitigation efforts, real-life applications and sound scientific studies," complained Syngenta, which makes thiamethoxam, in a statement.

In the United States, EPA is slowly changing its process for evaluating neonicotinoids based on recommendations from a scientific advisory panel. The agency says that it is asking companies for new field studies and toxicity tests of honey bee larvae; some studies must now include measurements of residues over several years. But the pace is measured. "While EPA's risk assessment framework for pollinators provides a roadmap that will eventually result in agency-approved guideline studies for pollinators, the work is very challenging," the agency said in a statement to *Science*. Another reason for patience: EPA won't complete its regular review of all the neonicotinoids until 2019.

In the meantime, industry scientists and academics are working to reduce the amount of neonicotinoid dust released by planting coated seeds. Bayer CropScience has commissioned researchers at three universities to test a seed mixture with a better lubricant that appears to reduce planting dust by 90%, says William Hairston, a director of product development in Research Triangle Park. The new formulation should be available to farmers next year.

And researchers continue to try to understand how the increasingly widespread chemicals are affecting ecosystems. "It's been likened to living in a house with asbestos or drinking water from lead pipes" says Christian Krupke of Purdue University in West Lafayette, Indiana. Neonicotinoids, he says, "deserve the scrutiny they're getting."

–ERIK STOKSTAD

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