

Stevens James USGR

From: Stevens James USGR
Sent: Thursday, January 04, 2001 9:53 AM
To: Pastoor Tim USGR
Subject: FW: pesticides/Parkinson's disease

The paraquat battle will start a new! Jim

-----Original Message-----

From: ACQUAVELLA, JOHN F [AG/1000]
[mailto:john.f.acquavella@monsanto.com]
Sent: Thursday, January 04, 2001 9:16 AM
To: ACQUAVELLA, JOHN; Bartels, Mike; Burns, Carol; Duggan, Angelina; Kreckmann, Kim; Leonard, Robin; Lunchick, Curt; Reape, Marty; Stevens James USGR; Tobia, Abe
Cc: 'Ott, Jerry'; 'Yarborough, Chuck'
Subject: pesticides/Parkinson's disease

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John

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<<...OLE_Obj...>>
</cgi/users/toc>FOR IMMEDIATE RELEASE: 3 JANUARY 2001
Contact: Tom Rickey
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Combination of two widely used pesticides linked to Parkinson's

disease

Scientists have shown that the combination of two widely used agricultural pesticides-but neither one alone-creates in mice the exact pattern of brain damage that doctors see in patients with Parkinson's disease. The research offers the most compelling evidence yet that everyday environmental factors may play a role in the development of the disease.

The latest findings of the team led by Deborah Cory-Slechta, Ph.D., professor of environmental medicine and dean for research at the University of Rochester School of Medicine and Dentistry, appear in the Dec. 15 issue of the Journal of Neuroscience. The scientists caution that more studies are necessary to explain the link, since it's probable that many factors contribute to a complex disease like Parkinson's, and they say it's unlikely that the pesticides on their own actually cause the disease.

Cory-Slechta's team studied the effects of a mixture of two very common agrichemicals, the herbicide paraquat and the fungicide maneb. Each is used by farmers on millions of acres in the United States alone: Maneb is applied widely on such crops as potatoes, tomatoes, lettuce and corn, and paraquat is used on corn, soybeans, cotton, fruit, and a variety of other products. In the experiment, mice exposed to either one had little or no brain damage, but mice exposed to both share a significant trait with people in the very early stages of the disease: Though they appear healthy, key brain cells known as dopamine neurons are dying. The mice exposed to the mixture carried nearly all of the molecular hallmarks of Parkinson's disease as seen in humans.

"The environmental reality is that several of these chemicals are used on the same crops and in the same geographical locations. You've got to get rid of the weeds. Then the insects. Then funguses. These are different chemicals that do different things, but they're often applied in the same fields," says Cory-Slechta, who was joined in the research by graduate student Mona Thiruchelvam and faculty members Eric Richfield, Raymond Baggs, and A. William Tank.

The study is one of the first to examine the effects of such chemicals in tandem. Cory-Slechta notes that current regulations and determinations of safety levels are usually based on the effects of single chemicals. "In the real world, we're exposed to mixtures of chemicals every

day. There are thousands upon thousands of combinations; I think what we have found is the tip of the iceberg," she says. "There are a dozen different fungicides related to maneb alone. I don't think we just happened to pick the right chemicals to see such an effect."

Maneb, paraquat, and many other pesticides are used in the same agriculture-rich areas of the country, including the Midwest, California, Florida and the Northeast. The map of their use mirrors areas of the country where people are more likely to die of Parkinson's disease.

Several epidemiological studies have hinted at a role for pesticides in the development of the disease. Studies have found that farmers, people who live in rural areas, and people who drink well water are more likely to have the disease than people who don't. In addition, just last month, scientists at Emory University presented evidence that rats given a steady dose of the natural pesticide rotenone, used on home-grown fruits and vegetables, develop Parkinson's-like symptoms. Cory-Slechta's study, which used much lower levels of chemicals than the Emory research, is the first to link a combination of more widely used pesticides to the disease.

"No one has looked at the effects of studying together some of these compounds that, taken by themselves, have little effect," says Cory-Slechta. "This has enormous implications."

Currently scientists have little understanding of what causes Parkinson's, where a tiny group of dopamine-producing neurons deep within an area of the brain known as the substantia nigra die. This cell death leads to a shortage of the neurotransmitter dopamine and to the tremors, rigidity, and slow movement that mark the disease as it progresses slowly over a period of years or decades. Parkinson's affects about 1 million people in North America.

There is a growing consensus among scientists that both genetic predisposition and environmental agents may play a role in the disease. Doctors see a similar effect in heart disease, where a patient might have both a family history and a sedentary lifestyle, or in cancer, where certain genes may make one prone to develop colon cancer and a poor diet makes the disease even more likely.

Cory-Slechta thinks it's unlikely that exposures to such chemicals actually cause Parkinson's on their own, but they may contribute to the development of the disease. "This is the first time that truly environmental risk factors for Parkinson's disease have been identified," she says.

Cory-Slechta heads a research center funded by the National Institute of Environmental Health Sciences where researchers study the effects of environmental agents like cigarette smoke, air pollution, and metals like mercury and lead on human health. She believes scientists must do more research on the effects of exposure to multiple chemicals. "It's a huge problem to start thinking about a nearly infinite array of mixtures of chemicals, instead of the risk that a single chemical might pose," she says.

She also says more work must be done to see how much of these chemicals people are actually exposed to. Usually it's not clear exactly how much of a pesticide remains on crops by the time they reach the dinner table. Maneb frequently shows up as a slight residue, she says, while paraquat usually shows up just in trace amounts; exposures can also occur via other routes. Oftentimes the two are used at different stages of the growing cycle. "The real issue is what happens when they hit humans in the food chain. If they're both present, then you are exposed to the combination."

In the Journal of Neuroscience paper, and in an earlier paper in Brain Research, the scientists showed how mice injected with both maneb and paraquat differed from normal mice in many ways. Most obviously, the mice moved around much less; immediately after the last of 12 injections over six weeks, the mice ran around their cages just one-tenth as much as their normal counterparts. More importantly, the mice that received both chemicals showed brain damage in exactly the same way as humans with Parkinson's:

* The amount of a key molecular marker, tyrosine hydroxylase, that is one measure of the health of the dopamine system was lower by about 15 percent in the mice, in the exact same areas of the brain that are damaged by the disease. Other closely related areas of the brain were spared, as in humans.

* The mice had nearly four times as many "reactive astrocytes," structures which indicate brain damage, compared to the control mice, in areas affected by Parkinson's disease.

* The mice had about 15 percent fewer dopamine neurons and ultimately produced about 15 percent less dopamine than normal mice.

The team is currently pursuing several new avenues of research, with funding from NIEHS. For instance, preliminary findings indicate that the Parkinson's-like effects on mice may be permanent, and that older mice may be more sensitive to the combination than younger mice. The team is also studying the effects of exposure to the mixture early in life, and they've shown that mice with the same genetic abnormality that causes some people to develop Parkinson's are specially vulnerable to the mixture.

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