MEETING BRIEFS

# New Clues for Two Toxicological Mysteries

**CINCINNATI**—Record floods on the Ohio River didn't keep more than 4000 scientists from gathering here last month for the annual meeting of the Society of Toxicology. Topics ranged from the possible synergistic effects of endocrine disrupters (*Science*, 28 March, p. 1879) to toxins produced by marine microorganisms and how pesticides may affect the development of the eye.

## Toxin's M.O. Identified

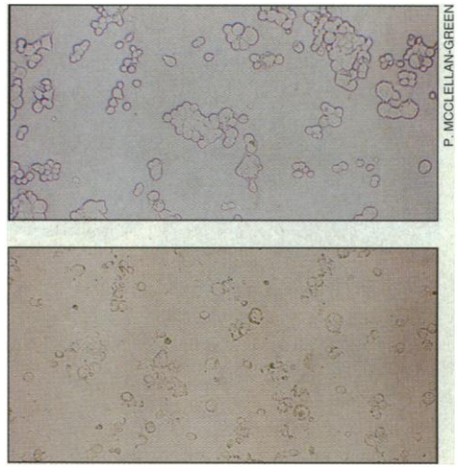
Many years ago, the movie *Jaws* scared a lot of people right out of the water. Nowadays, the latest findings from marine science labs are apt to play a similar role. In 1993, a marine microbe called *Pfiesteria piscicida* that secretes potent toxins gained notoriety by apparently poisoning two scientists who were studying it. And at the meeting in Cincinnati, other researchers reported that *Pfiesteria*, one of a broad class of microorganisms that lurk in red tides and other algal blooms, can damage cultured neural and gut cells and cause learning problems in rats.

*Pfiesteria*, which has been found from the Delaware Bay to the Gulf of Mexico, is a shifty character that can assume at least two dozen forms. When threatened by a protozoan, for instance, it slips into a predator-engulfing, amoebalike guise, and when fish appear, it takes on a deadly dinoflagellate form. In 1988, botanists JoAnn Burkholder and Howard Glasgow at North Carolina State University in Raleigh identified this dinoflagellate as a major cause of fish kills in coastal waters.

Researchers became acutely aware of the organism's ability to attack the nervous system in 1993 after Burkholder and Glasgow were poisoned when they inhaled *Pfiesteria* toxins wafting out of laboratory fish tanks. In addition to experiencing nausea and a burning sensation in the eyes, they suffered from loss of short-term memory, difficulty reading, and disorientation.

To get a better understanding of *Pfiesteria*'s possible effects on mental processes, a team led by environmental toxicologist Edward Levin of Duke University Medical Center in Durham, North Carolina, gave rats a learning task. The researchers trained rats to walk down eight planks radiating from a platform like spokes on a wheel to reach a reward—a piece of Froot Loop cereal. The rats soon learned that once they had fetched their reward, there was no point in venturing down a particular plank again, and they remembered this lesson even after being injected with *Pfiesteria* cells. But when rats were injected before training, they learned the lesson much more slowly. "We've nailed it down primarily to learning," not memory, says Levin, adding that this may explain why the researchers had trouble picking up new information like telephone numbers.

But while scientists may have homed in on the organism's modus operandi, they have not yet identified its weapon. "We just need to find the active ingredient"—the toxin secreted by *Pfiesteria*—and probe its mechanism, says U.S. Environmental Protection Agency neurotoxicologist Hugh Tilson. As a first step, a team led by North Carolina State toxicologist Patricia McClellan-Green is studying a partially purified extract that contains the poisons. As they reported at the meeting, this extract proved "extremely toxic" when they applied it to cultured human gut cells and mouse neural cells, causing the cells to lyse at a concentration as low as mere femtograms per milliliter. Fortunately for fish eaters, says McClellan-Green, the toxin's potency appeared to fade within a few hours. If true, that could mean only the freshest fish would pose a threat to human health.



P. MCCLELLAN-GREEN

**Shifty killer.** An extract with *Pfiesteria* toxins added to healthy neural cells *(top)* quickly lyses the cells *(above)*.

## A Pesticide-Myopia Link?

Add one more possible health effect to the long list of hazards associated with overexposure to pesticides: eye and vision problems. In Cincinnati, researchers described data suggesting that one widely used insecticide, chlorpyrifos, can alter eye development in young chickens.

The impetus for the work, led by William Boyes at the U.S. Environmental Protection Agency (EPA) in Research Triangle Park, North Carolina, was an intriguing entry in the annals of medicine: reports of an epidemic of nearsightedness among Japanese schoolchildren in the late 1950s through the early 1970s. The rise in reported myopia coincided with widespread use of certain insecticides, called organophosphates (OPs), that kill insects by inhibiting the enzyme acetylcholinesterase, which also is found in humans. Although no definitive experiments were done, some Japanese researchers claimed the pesticides caused the myopia.

Boyes's group thought the hypothesis merited a closer look. So, together with collaborators at Duke University and the University of North Carolina, Chapel Hill, the researchers studied pesticide effects in chickens. These animals provide a useful model for investigating the impact of neurotoxins on vision because their nervous system is highly vulnerable to damage from toxicants, and they can develop vision problems like those of humans. For example, researchers can induce myopia in a chick's eye by covering it with a translucent plastic goggle. The developing eye adapts to exposure to blurred images by growing longer, resulting in extreme myopia, says Andrew Geller, the postdoc at EPA who performed the experiments. The researchers hypothesized that if pesticides, in fact, interfered with eye development, a goggled chick dosed with the chemicals would have trouble adjusting to the goggle.

When the researchers fed the chicks moderate doses of the OP insecticide chlorpyrifos for 1 week, they found that the chicks' goggled eyes did not adapt as much as is typical: The eyes were significantly less elongated. Further, when the team examined the unblocked eyes of chicks dosed for 2 or 3 weeks, they found that the pesticide caused the eyes to grow slightly longer, suggesting that, in this case, the pesticide was making the eye myopic. "This is one of the first visual-testing models to show an OP might affect visual regulation," says toxicologist Carey Pope of Northeast Louisiana University in Monroe.

Geller says that more work needs to be done, including studies with mammals and with different doses: "We can't say what we're finding accounts for the Japanese data, but it may be we're starting down the road to understanding what happened."

–Jocelyn Kaiser