Lab insect thwarts potent natural toxins

Often touted as one of the most effective weapons in biological pest control, bacteria called *Bacillus thuringiensis* (Bt) may have met their match.

Bt strains produce at least nine proteins that can kill moth and butterfly caterpillars. For years, organic farmers have sprayed Bt formulations on their crops. Unlike most chemical insecticides, Bt toxins quickly break down in soil, so insects do not develop resistance to them as fast. And when they do, that resistance tends to thwart only one protein in Bt's chemical arsenal, says Fred Gould, an entomologist at North Carolina State University in Raleigh.

But Gould and his colleagues have now bred a caterpillar that seems to totally disarm these mighty microbes. Their findings may complicate efforts by genetic engineers to make plants pest-proof with Bt toxins, Gould says.

Molecular biologists have focused on inserting Bt-toxin genes in plants for several reasons, says Gould. Because genes code directly for these proteins, the genetic alteration is more straightforward than for other natural insecticides, which require genes encoding several enzymes that then produce the toxins. Also, unlike most proteins, Bt toxins do not disintegrate in the gut and so maintain their potency. And these proteins affect only the pest insects.

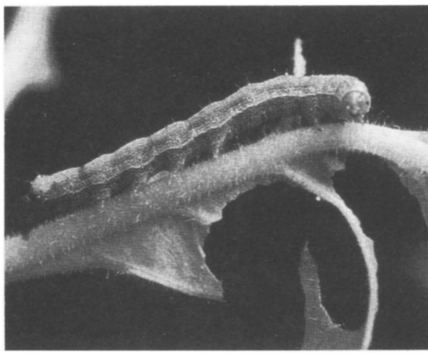
"It's a very special toxin; there are not going to be lots of others like it," Gould says. "We should not use it unwisely."

In 1988, as part of their efforts to determine the best way to use Bt, Gould and his colleagues collected eggs produced by *Heliothis virescens,* a cotton, soybean, tobacco, and tomato pest sometimes called the tobacco budworm. As the researchers raised successive generations, they fed the insects enough of one Bt toxin to kill 75 percent of that generation. By the 17th generation, the researchers needed to use at least 50 percent more toxin, they report in the Sept. 1 Proceedings of the National Academy of Sciences.

Previous research done elsewhere on different insects had led Gould to expect these caterpillars to develop resistance against that toxin. The toxin works by binding to receptors in the insect's gut and disrupting the gut lining. Typically, resistant insects change the receptor so that the toxin cannot attach.

But these insects were also resistant to other Bt toxins, including one very different one. "Not only was [this toxin] unrelated in terms of its amino acid sequence, but recent work shows that its mode of toxicity was different," says Gould. "And that level of resistance was as high as or higher than [the resistance to] the original [toxic] compound."

Some researchers had thought that by switching to different Bt toxins or engineering two toxins into a crop, farmers could stay one step ahead of resistant strains and maintain the effectiveness of this insecticide. "Now they will have to combine that strategy with other measures in the field to combat resistance," says Pamela G. Marrone, an entomologist with Novo Nordisk Entotech, Inc., in Davis, Calif. For example, she says, if farmers were to grow patches of unaltered varieties in with the genetically engineered crops, some pests would stay vulnerable and, by mating with resistant individuals, would slow overall resistance.


Karl Suiter/NCSU

Heliothis virescens *caterpillar.*

At the Monsanto facility in Chesterfield, Mo., researchers are working on varieties of corn, potato, and cotton that make their own Bt toxins. While the company says it depends on scientists such as Gould for guidance, "[this report] will probably not make too much impact in the way we view resistance management," says Monsanto entomologist Steven R. Sims. "This is only one laboratory experiment, which may not necessarily correlate well to what happens in the field."

Both he and Marrone have conducted experiments like Gould's, and their results highlight the need to know more about how Bt works and how insects counter it. "What we're seeing is that there is a lot more variation [in types of resistance] than we expected when we started," says Sims. *— E. Pennisi*

Chronic hypertension may shrink the brain

High blood pressure, even if well controlled by medication, may cause the brain to shrink, according to a new report. The significance of brain atrophy remains unclear; however, researchers worry that long-standing hypertension could lead to cognitive difficulties.

"We think these healthy males with hypertension have brains that are aging at an accelerated rate," says Declan G.M. Murphy, co-author of the report in the September issue of Hypertension and a researcher at the National Institute on Aging in Bethesda, Md. "The question is how much more brain tissue they need to lose before they become affected clinically."

This is not the first time scientists have demonstrated changes in the brains of people with hypertension. A 1984 study by a team of Japanese researchers showed that older men with hypertension had more brain atrophy than controls. However, that study relied on a technology called computerized tomography to obtain images of the brain. To get a sharper picture, Murphy and his colleagues used a newer technique called magnetic resonance imaging (MRI).

The U.S. researchers wanted to find very early changes in brain structure, so they recruited 18 otherwise healthy men age 51 to 80 who had suffered from hypertension for at least a decade, says study co-author Judith A. Salerno, also at the National Institute on Aging. The team recruited 17 healthy men within the same age range without hypertension to serve as controls.

MRI was used to obtain three-dimensional brain images of each participant. Next, the researchers used a mathematical method to calculate the percentage of brain matter and of fluid in the ventricles, large spaces in the brain that act as "gutters" to drain cerebrospinal fluid, Murphy says.

The group discovered that men with hypertension had smaller brains than the controls. Their analysis also revealed that men with hypertension had enlarged ventricles, a sign of brain atrophy, Salerno adds.

Most of the men with hypertension had extensive medical records dating back to the time of their diagnosis, Salerno notes. In addition, most took medication to keep their blood pressure under control.

The MRI data don't pinpoint the brain region most affected by chronic hypertension. However, Murphy thinks that high blood pressure may injure the so-called wiring portion of the brain known as white matter. The white matter consists of neurons, or nerve cells, that connect the brain's computers (gray matter) to each other and to the rest of the body, Murphy says.

The volunteers in this study showed no sign of cognitive problems. All scored normal on tests of cognitive function, Salerno notes. However, the researchers believe the MRI picks up changes in the brain at an early stage, before cognitive difficulties show up. Even so, Salerno said she was surprised that some of the more severely affected men showed no symptoms of cognitive problems.

Nobody knows the mechanism by which hypertension might lead to brain atrophy. One theory holds that high pressure causes the muscle lining the brain