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.

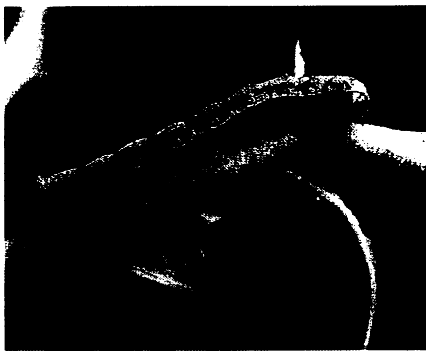
"It's a very special toxin; there are not going to be lots of others like it," Gould says. "We should not use it unwisely."

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 arteries to thicken, thus reducing blood flow to the brain. With less blood getting through, some neurons die, causing portions of the brain to die. Some researchers believe that although it may take years, such a process eventually leads to a type of dementia characterized by problems with memory, arithmetic, and spatial tasks.

On the other hand, the high pressure may simply lead to compression of the brain and swelling of the ventricles, a process that doesn't necessarily impair the brain's function, says Vladimir Hachinski of the University of Western Ontario in London.

Hachinski calls the team's findings "intriguing" but says further research must determine whether hypertension causes brain atrophy. "It was an in-depth study of a small number of patients; I'd like to see it confirmed," agrees Salerno.

Despite the small sample size, Hachinski says the study was well conducted. "I think it's a good beginning," he says.

A multicenter study of 5,000 men and women age 65 and older may soon provide scientists with more definitive data regarding hypertension's effect on the brain. Timothy J. Miller, a neuroradiologist at Johns Hopkins Hospital in Baltimore, and his colleagues will look for signs of brain atrophy and enlarged ventricles in the MRI scans taken from otherwise healthy hypertensive volunteers. Miller says he expects to get preliminary results from that study within the next two years. *—K.A. Fackelmann*

Major Japanese jolt may be on its way

A minor earthquake that struck southwest of Tokyo in 1990 may herald the arrival of a much stronger shock in the near future, report two Japanese seismologists.

Earthquake experts in Japan have long recognized the potential for a major quake emanating from the Odawara region, located 80 kilometers southwest of Tokyo. Over the last 400 years, five very strong earthquakes have rocked this area with remarkable regularity, roughly every 73 years. The last major jolt, the Great Kanto Earthquake of 1923, measured magnitude 7.9 on the Richter scale and destroyed much of nearby Tokyo and Yokohama. Simple arithmetic would suggest the next quake is due sometime around the year 1996.

Mizuho Ishida and Masayuki Kikuchi think the Earth may now be sending warnings of that impending disaster. While studying a magnitude 5.1 quake that shook the Odawara area in August 1990, they found this tremor exhibited several unusual signs previously associated with so-called preshocks.

Most noticeably, the 1990 jolt occurred in a seismically quiescent area—one that had passed 57 years free of earthquakes larger than magnitude 4.6.

Taking a closer look, Ishida and Kikuchi observed that the 1990 shock packed an unusually concentrated punch. Calculations suggest that the Odawara quake relieved much more stress than an average earthquake of similar magnitude. What's more, the 1990 shock began and finished in about one-third the average time, the researchers say. Ishida, who works at the National Research Institute for Earth Science and Disaster Prevention in Tsukuba, and Kikuchi, a researcher at Yokohama City University, discuss their data in the Aug. 21 GEOPHYSICAL RESEARCH LETTERS.

In the late 1970s, Ishida recognized similar unusual characteristics in small shocks that preceded California's 1971 San Fernando earthquake and the 1952 Kern County earthquake. In these cases, small power-packed quakes occurred in seismically quiet regions a few years prior to the large shocks. Because of the similarity in circumstances, she and Kikuchi suggest that the 1990 earthquake may foreshadow the larger Odawara quake, expected to measure magnitude 7 or stronger.

Thomas H. Heaton, a seismologist at the U.S. Geological Survey in Pasadena, Calif., cautions that the case may not be so clear. Geophysicists have not yet demonstrated that they can distinguish preshocks from ordinary earthquakes on the basis of the amount of stress they relieve, he says. *—R. Monastersky*

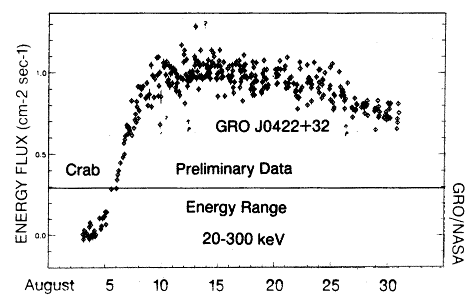
X-rays from dim space hint at a black hole

Last month an object in the constellation Perseus that had been so dim no one had ever detected it began spewing out a barrage of X-rays and gamma rays. NASA's Compton Gamma Ray Observatory (GRO) found that the puzzling source had become the most powerful radiator detected at the X-ray energy of 100,000 electron-volts.

Preliminary evidence now suggests that the object belongs to a special class of binary stars likely to contain a small black hole. Variously dubbed Nova Persei 1992 or GRO J0422+32 for its location in the sky or the observatory that discovered it, the object has X-ray and ultraviolet spectra resembling those of other candidate black holes that have literally burst on the scene in the past 20 months. Researchers reported some of their findings last week at the World Space Congress in Washington, D.C.

Nova Persei 1992 appears to belong to a subtype of a general class of X-ray-emitting stars called low-mass X-ray binaries. Low-mass binaries typically feature a dwarf star closely orbiting a highly compact object, either a neutron star or a black hole. (A black hole is a collapsed star theorized to have such a strong gravitational field that not even light can escape it.) Matter from the dwarf star falls directly onto its compact partner or onto a disk of matter surrounding that partner, emitting intense radiation in the process. Many binaries emit light continuously, masking the faint glow of the dwarf star. But some binaries, perhaps including Nova Persei 1992, emit radiation in bursts that die down after a few months, allowing researchers to observe the dim dwarf star and estimate its mass and velocity. From such data, scientists can determine if the dwarf's compact partner has more than three times the mass of the sun — the minimum value a star must have to become a black hole. Two binary stars that recently unleashed an outburst of radiation — Nova Muscae 1991 and V404 Cygni — would qualify as black hole systems on the basis of their mass (SN: 2/15/92, p.101).

If Nova Persei is also a binary, as scientists suspect, they need wait no more than a year to determine whether it harbors a black hole. But several features already hint at its character, says Rashid Sunyaev of the Space Research Institute in Moscow. He reported that observations over many wavelengths, including those made with a gamma-ray telescope aboard the Soviet satellite GRANAT, show that Nova Persei's outburst matches the pattern expected when matter falls onto a disk surrounding a black hole. In addition, GRO spectra, described by Gerald J. Fishman of NASA's Marshall Space Flight Center in Huntsville, Ala., as well as GRANAT data, show that Nova Persei's output flickers in a near-periodic fashion — a feature that could stem from instabilities in such a disk.



X-ray intensity of GRO J0422+32, as seen by the GRO. At its peak, the source emitted about three times the X-ray output of the Crab Nebula (solid line).

"I haven't any doubt that this object is a black hole," says Sunyaev. Based on recent observations, he estimates the Milky Way contains 3,000 to 5,000 binaries that harbor black holes. *—R. Cowen*