THE CHRONICLE of Higher Education

Global

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February 26, 2012

Border-Crossing Research Lessens the Sting

By Steven Ambrus

Cuernavaca, Mexico

Arizona, home to the dangerous bark scorpion, was about to exhaust the United States' last supplies of scorpion antivenom, and Leslie Boyer was out of options. She knew that if a young child were stung and had no access to the antidote, he could suffer a loss of nerve and muscle control, asphyxiate, and die within as little as an hour.

Around that time, Dr. Boyer, a pediatrician and toxicologist at the University of Arizona College of Medicine, traveled to Cuernavaca to meet with one of the world's leading scorpion experts as part of a National Geographic documentary on venomous creatures.

She remembers the experience at his laboratory at the National Autonomous University of Mexico, commonly known as UNAM, with awe.

A mouse had just been injected with scorpion venom. It lay on its side, blue, twitching and frothing, only moments from death. Then, Lourival Possani, the scorpion expert, pulled out a vial and injected the animal with an antivenom developed in Mexico. Within 15 minutes, the mouse had revived. It was pink, happily drinking water, even grooming itself.

"It was phenomenal," Dr. Boyer recalled of that 1999 resurrection. "I told them, 'I don't know what's in that vial. But whatever it is, I want to take it home. I want to inject it into children.'"

Last August, Dr. Boyer got her wish. After a 12-year combined effort, a team including UNAM and University of Arizona scientists and the Bioclon Institute, a Mexican pharmaceutical company, won approval from the Food and Drug Administration for an antivenom called Anascorp.

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Laura Segall for The Chronicle

Leslie Boyer, a toxicologist at the U. of Arizona who helped develop an antivenom for the U.S. market, studies a scorpion she found in her house.

It is the first antiscorpion drug proved effective under clinical trials, far more potent and much safer than the crude, unlicensed one once produced in Arizona.

Created from antibodies that horses produce when injected with the scorpion venom, Anascorp can alleviate the most severe symptoms of a scorpion sting in just 30 minutes. And it is safer because it employs a modern technology that involves clipping off the part of the antibody that creates allergic reactions.

To top that, Anascorp is the first drug fully developed in Latin America to get FDA approval.

"It is an excellent drug," said Michelle Ruha, a medical toxicologist at Banner Good Samaritan Medical Center, in Phoenix. "It has the best safety profile of any antivenom I've seen."

But getting there wasn't easy. UNAM and Bioclon had already developed a scorpion antivenom before Dr. Boyer arrived at the UNAM laboratory in Cuernavaca. Indeed, that drug, first marketed in Mexico in 1995 and now administered to 300,000 people a year throughout that country, has helped reduce annual scorpion sting deaths from 300 in 1994 to fewer than 15 in 2010.

The big hurdle was getting the drug approved in the United States, where the FDA has a well-earned reputation as the toughest regulatory agency in the world. To do so, some adjustments had to be made to improve quality control, and the drug had to be tested using the rigorous protocols demanded in the United States, with clinical trials, designed by Dr. Boyer, encompassing some 28 hospitals in Arizona and Nevada, and 2,000 patients.

Along the way, the team hit some spectacular snags. Because of mix-ups at the border with labeling and translating information, for example, the white-powdered drug was repeatedly returned to Mexico, costing months in lost work. High-ranking officials of UNAM were pulled over on the highway so authorities could check their immigration status, and the president of Bioclon, Juan López de Silanes, was detained at Miami International Airport because his name resembled that of someone on the Department of Homeland Security's terrorist watch list.

"I called Juan Silanes one day and said, 'Won't you please buy a

truck, write the word 'Cocaine' on it in five-foot letters, and crash it through the border fence. Because even if you are arrested and have to hire a lawyer, it will be a faster, cheaper, and less bureaucratic way of getting the drug to me," recalled Dr. Boyer.

A New Model

Still, for all the mishaps, the collaboration between scientists at the two universities and the Mexican pharmaceutical company suggests a new model. Its success was made possible in part by what Dr. Boyer describes as the brilliance of well-trained UNAM biochemists and their ability to do what she calls "old-fashioned brain-and-hand bench chemistry," involving deep thinking about problems and innovation rather than "simply relying on machines that go ping," as many U.S. biochemists, with their high technology, seem to do.

"When I was a medical student at Harvard, the conceit was that Americans invent drugs and then test them in the third world. But this drug was developed in Mexico and the testing was done in the U.S. It turned out that that equation, with old-fashioned biochemistry on one side and the rigorous testing and U.S. bureaucracy on the other, worked out pretty well."

Mexican biotechnology has always included a roster of internationally recognized scientists, including Francisco Bolivar, who participated in the 1970s in the development of the first genetically engineered human protein, and Luis Herrera-Estrella, who worked on the first gene-transfer techniques for plants.

Today, scientists at academic research centers at UNAM, the National Polytechnic Institute, and other Mexican universities continue doing acclaimed work employing microorganisms to degrade environmental contaminants, developing biologically obtained insecticides, and improving genetically modified organisms.

But those experiences are not the norm. Because of the lack of cultural emphasis on patenting and product commercialization, the skill of Mexican biotechnology has often gone unrecognized. And because of the low level of government support for biotech research and development—$46.5-million in 2012, versus billions in the United States—many of the most promising young scientists leave the country for their postdoctoral studies and end up doing their best work abroad.

Laura Segall for The Chronicle

Leslie Boyer was amazed by an antivenom she saw demonstrated at the National Autonomous U. of Mexico in 1999. Determined to bring the drug to the United States, she worked for 12 years with her Mexican partners to get FDA approval.

In that context, the success of Anascorp may have given Mexican biotechnology a much-need injection of confidence, just as Mexican universities are creating offices to help researchers patent their products and find collaborators in the private sector, or even, as at UNAM, encouraging some scientists to start their own spinoff companies.

"I have had scientists come up to me since Anascorp was approved by the FDA and tell me that they now know it can be done," said Alejandro Alagón, the antivenom researcher at UNAM's Institute of Biotechnology who did the critical work in applied science that made the drug possible. "I think more scientists at Mexican universities will be now reaching out to collaborate with partners in the U.S."

Saving Lives

On a recent morning, Dr. Alagón, whose twinkling brown eyes seem full of wonder, was inspecting a room full of scary creatures at the Institute of Biotechnology, now widely considered one of the premier research centers for antivenoms in the world. There were poisonous black widows with fiery red markings; long-limbed, hairy tarantulas; and a black-backed scorpion that shot a stream of venom down Dr. Alagón's shirt when he picked it up with tweezers. Another room held poisonous snakes.

Back at his office, Dr. Alagón discussed projects under way. The institute's staff of 30 to 35, along with Dr. Boyer, is working with Bioclon to bring antivenoms for rattlesnakes and coral snakes to the U.S. market. The same team is working to develop an antivenom for North African scorpions, and the institute is also working with the Rocky Mountain Poison and Drug Center, in Denver, to develop an antivenom for black widows.

Thousands of people will ultimately be helped. For example, an antivenom developed over the last six years by the Mexican team, along with researchers in France and at the University of Benin, is now being sold in Congo, Benin, and Senegal to treat bites from 85 percent of the poisonous snakes in sub-Saharan Africa.

"We have the opportunity to help people around the world, as we work to increase the volumes of antivenoms we've already developed, comply with regulations in different countries, and

Dominic Bracco II, Prime

Alejandro Alagón, a scientist at the National Autonomous U. of Mexico, is responsible for much of the science behind the antivenom Anascorp.

develop new antivenoms for other regions of the world, like Asia," Dr. Alagón said. "We want to increase the number of people we can reach."

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