axons, was an especially tempting subject. Foreign researchers set up shop at the coastal town of Montemar, where the University of Chile had a laboratory, and they were soon joined by Chileans, among them Mario Luxoro, who had been a graduate student at the Massachusetts Institute of Technology. Luxoro went on to establish biophysics as an indigenous field of research.

This first generation of Chilean channel researchers "made very excellent contributions," says University of Pennsylvania biophysicist Clay Armstrong. Luxoro and his student Eduardo Rojas, for example, were among the first to suggest that proteins, later identified as individual ion channels, played a role in transmitting electrical signals across the cell membrane. And during the 1960s a stream of visitors, including Armstrong and scientists from the U.S. National Institutes of Health, made Montemar into a sort of Woods Hole Marine Biological Laboratory in the Southern Hemisphere. The lab "was like a little window through which we were able to look at the world," says Latorre, who earned his doctorate under Rojas.

The contacts he and others made at Montemar served them well in the early 1970s, when those golden years ended. First the squid vanished from Chilean waters, for reasons that are still debated. Then came the 1973 military coup. By the mid-70s all but a few researchers in the field had left, many winding up in Europe or in Boston. Those who attempted to return in the 1970s found working conditions impossible. By then half the university faculty had been fired and "there was absolutely no support from above," recalls Francisco Bezanilla, now at the University of California, Los Angeles.

A turning point came in 1984, when conditions under Pinochet had become somewhat more tolerable. Latorre came back from Harvard to head the biophysics section of the Centro de Estudios Científicos de Santiago (CECS), a private institute being founded by physicist Claudio Teitelboim. There he worked to lure back other expatriates. CECS provided returnees with temporary salaries and funds to start up labs at the universities, circumventing the academic bureaucracy. As a result, more biophysicists trickled back each year. "We were very much aware that by coming back, we would make a big difference," says Cecilia Hidalgo, who returned to Chile from the Boston Biomedical Research Institute.

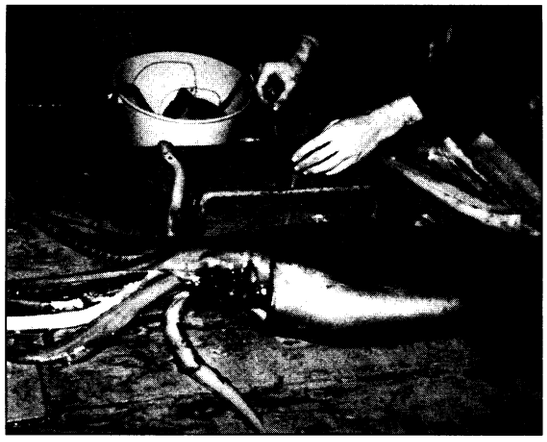
And Latorre's recruits, working mostly at the University of Chile, have continued to do internationally competitive research. For example, Hidalgo and others at the Faculty of Medicine have gained new insights into the biochemistry of calcium release in muscle, the cellular event that triggers contraction; they have also established muscle cell lines in which that process is defective, which will aid in studying muscular dystrophy. At the Faculty of Sciences, a team led by Pedro Labarca has identified a potassium channel that may explain an inherited learning defect in *Drosophila*. And Latorre's own lab, notes MacKinnon, has made "very nice advances" into the workings of calcium-activated potassium channels.

Some of this work has been done in collaboration with labs in the United States—in part because of the logistical and funding difficulties that still plague work in Chile. Know-how and equipment obtained through these foreign ties have also helped Chilean researchers expand their own labs. In 1991, for example, Latorre and Labarca set up a molecular biology lab so they could clone channel proteins themselves instead of getting them from abroad. Returning postdocs are also building up the molecular biology infrastructure by bringing expertise in such areas as protein structure determination.

Because of the difficulties of working in Chile, many of the best Chilean biophysicists still remain abroad. But some of their colleagues in Chile believe the climate for basic science may soon become more favorable. Suarez-Isla says that the Faculty of Medicine's new government hopes to add 40 new positions for researchers, some in basic science, in the next few years. Chile's government is also considering taking steps to strengthen basic research, such as offering large grants to leading investigators.

Putting more money into science is not unreasonable, even in a country where basic economic needs are still pressing, Luxoro argues. "You see," he says, "underdevelopment is a question of mind rather than anything else."

–Jocelyn Kaiser



E. ROJAS/NIDDK/NIH

What a nerve. The squid *Dosidicus gigas*, whose outsized axons drew foreign biophysicists to Chile in the 1960s.

Jocelyn Kaiser, a former Science *intern, is an intern at* Science News.

MEXICO

A Stubborn Amoeba Takes Center Stage

MEXICO CITY—Amebiasis, the diarrheal disease caused by *Entamoeba histolytica*, is one of those serious diseases that tend to get short shrift from funding agencies in rich countries like the United States. But not in Mexico. For more than 20 years, Mexico has produced some of the world's leading researchers studying *E. histolytica*, a protozoan that afflicts millions of people with diarrhea and, in extreme cases, causes liver abscesses. All told, the organism accounts for an estimated 100,000 deaths a year. "The largest center for doing work on amebiasis in the world is Mexico," says Louis Diamond, who studied amebiasis for 35 years at the U.S. National Institutes of Health (NIH).

Diamond, who retired last year, had the only lab on the NIH campus studying the disease. In contrast, Mexico City's Center for Research and Advanced Studies (CINVESTAV) alone has three prominent amebiasis research groups. "In the long term, [Mexican researchers have] made some of the really pivotal observations," says Sharon Reed, an amebiasis researcher at the University of California, San Diego. "They were pioneers in the field, and they're still in there." Their work touches on almost every aspect of the disease: how prevalent it is, how *E. histolytica* destroys cells, how to detect it, and what proteins it contains. Mexican investigators have also been key players in a debate about whether or not there is a benign strain of *Entamoeba* as well as the disease-causing one—a debate whose outcome will shape future public-health strategies (see box).

Mexico's commitment to amebiasis research stems from its high rate of the disease: A recent survey of nearly 70,000 Mexican blood samples revealed that 8.4% showed evidence of prior infection with a disease-causing strain of the amoeba. Mexican researchers hope their work will lead to new treatment and vaccine strategies. There is certainly a need for new approaches: Although the drug metronidazole is effective against acute amebiasis, the disease still causes over 1200 deaths annually in Mexico alone. And because it can be difficult for a clinician to be sure that a patient's diarrhea is caused by amebiasis and not another disease (such as bacterial dysentery or inflammatory bowel disease), researchers are also working on new diagnostic tests, some based on cutting-edge technologies such as the polymerase chain reaction.

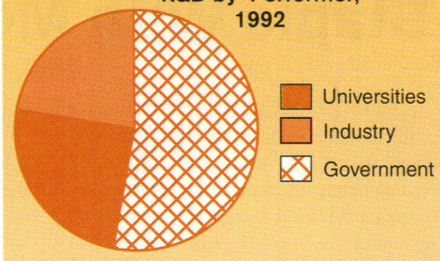
Thanks to the work of the now-deceased amebiasis researcher Bernardo Sepúlveda Gutiérrez, the Mexican government long ago decided that tackling these problems was a priority. "Sepúlveda built the whole thing up," says Diamond, noting that his former colleague also launched an international seminar about the disease that for more than two decades has remained the best attended amebiasis meeting in the world.

The senior statesperson of Mexican amebiasis research today is Adolfo Martínez-Palomo, the head experimental pathologist at CINVESTAV. Martínez-Palomo is renowned for his stunning scanning electron micrographs (EMs) of *E. histolytica*, which have helped detail its morphology and pathogenesis. "He's made beautiful EMs of amoebas invading the intestinal epithelium," says William Petri, a microbiologist at the University of Virginia who studies the pathogenesis of amebiasis. Petri notes that Martínez-Palomo offered some of the first evidence that the organism has to contact cells to kill them.

Just how the amoeba causes disease is also a specialty of CINVESTAV's Esther Orozco, one of Martínez-Palomo's former graduate students. Orozco, a Howard Hughes Medical Institute international research scholar (a recipient of a 5-year grant but not, unlike Hughes investigators in the United States,

MEXICO AT A GLANCE

R&D by Performer, 1992



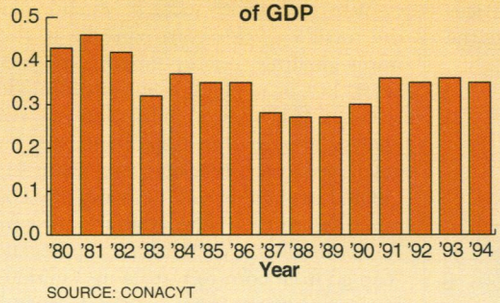
SOURCE: CONACYT

The Big Picture

Population, 1994:	92.2 million
GDP, 1993 (est.):	$348.7 billion
Federal R&D Spending, 1993:	$1.244 billion
Scientists and Engineers, 1991:	22,600

SOURCES: GDP, R&D, Scientists and Engineers: CONACYT; Population: 1994 CIA World Fact Book

Federal R&D as Percent of GDP



SOURCE: CONACYT

In 1993, Mexico spent more than 40% of its R&D budget on the National Council for Science and Technology (CONACYT)—which funds individual research projects—26 national research centers, and the National Autonomous University of Mexico. Other institutions receiving substantial chunks of the R&D budget were the Mexican Petroleum Institute, the National Institute for Agricultural and Forestry Research, and the Center for Research and Advanced Studies. The government's National System of Researchers also awards fellowships to Mexico's most active scientists.

The Amebiasis Organism: A Jekyll-and-Hyde Parasite?

Clinicians have long puzzled over the fact that only about 10% of the 500 million people infected with *Entamoeba histolytica* develop dysentery and liver abscesses—the hallmarks of amebiasis. During the past few years, however, most amebiasis researchers have settled on an explanation: There are two strains of the protozoan—the disease-causing *E. histolytica* and a benign strain called *E. dispar*. But one leading Mexican investigator, Esther Orozco of the Center for Research and Advanced Studies (CINVESTAV) in Mexico City, isn't convinced. She thinks that there's only one form of the protozoan; in symptomless infections, it's just lying low.

"We differ from most people," Orozco acknowledges. Indeed, other than Orozco and David Mirelman from Israel's Weizmann Institute of Science, nearly every major amebiasis investigator now firmly backs the two-strain hypothesis. But the debate, now several years old, continues to trouble the field because it has profound clinical implications, says CINVESTAV's senior amebiasis investigator, Adolfo Martínez-Palomo. If there is only one strain, everybody who is infected would need treatment, he explains. But if the vast majority of infected people harbor the benign *dispar* strain, then only those who have the *histolytica* strain would require treatment. Moreover, any vaccine should be tailored to *E. histolytica*, not *E. dispar*.

One clue to the existence of two strains surfaced in 1973, when Martínez-Palomo and his co-workers showed that in the test tube, *E. histolytica* derived from people with dysentery behaved differently from organisms isolated from healthy carriers. Five years later, Peter Sargeaunt and his colleagues at the London School of Hygiene and Tropical Medicine bolstered the two-strain theory by showing that pathogenic amoebas had different enzymes.

J. COHEN

Dissenter. Esther Orozco doubts that the amoeba has a benign strain.

Still more evidence has come from molecular biologists, such as Graham Clark of the U.S. National Institute of Allergy and Infectious Diseases (NIAID) and Egbert Tannich of the Bernhard Nocht Institute in Hamburg, who recently found that the genes of pathogenic and nonpathogenic amoebas differ significantly. Concludes Louis Diamond, a veteran amebiasis researcher who recently retired from NIAID, "There are two species. It's settled."

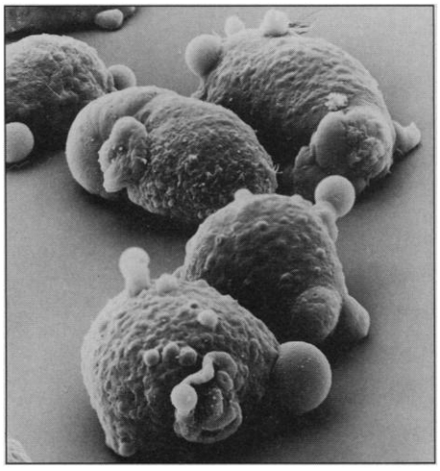
Not as far as Orozco is concerned. "We think *Entamoeba histolytica* may be a single species that's able to modulate the virulence," she says. She notes that her lab and Mirelman's have found that altering the conditions in which *E. histolytica* is growing can, by some still-unknown mechanism, transform the protozoan from pathogenic to nonpathogenic. Orozco has also shown that she can take a single *E. histolytica*, clone it, and end up with a less virulent "sister clone." The organism "is very, very plastic," says Orozco. "I think it's a big mistake of the scientific community to be too passionate about one hypothesis or the other. We need to do more research."

–J.C.

an institute staff member), has shown that after latching onto a host's cells, virulent *E. histolytica* strains can destroy them by phagocytosis—simply gobbling them up. The key evidence comes from landmark 1983 work in which Orozco took bacteria that had a gene making them sensitive to light and fed them to a pathogenic strain of *E. histolytica*. She then illuminated her samples, a treatment that selectively killed bacteria-filled amoebas. The amoebas that survived were those that had engulfed fewer bacteria because of a decreased rate of phagocytosis. When tested in cell cultures, they turned out to be dramatically less virulent.

Isaura Meza, who heads the cell biology department at CINVESTAV, is studying the molecular mechanisms behind *E. histolytica*'s cell-killing ability. Meza's specialty is the cytoskeleton of *E. histolytica* and, in particular, the role of actin, a protein that helps the amoeba move. As Meza, her co-workers, and others have shown, actin is a lead actor in the process by which *E. histolytica* binds to a host's cells and lyses them, a cell-killing mechanism that is separate from phagocytosis. Meza also helped identify a surface protein of *E. histolytica* found mainly in people who have symptomatic disease. If the amoeba does indeed have two strains, she says, this protein may be a key to distinguishing between people who are infected with pathogenic and nonpathogenic strains.

ADOLFO MARTÍNEZ-PALOMO



Tough customers. *Entamoeba histolytica*, the organism that causes amebiasis.

Besides these three CINVESTAV researchers and their co-workers, half a dozen other Mexican research groups at other institutions have shed much light on amebiasis. And all of these groups are continuing to train a new generation of amebiasis researchers. "This is one of the few fields in science where Mexico is a leader," Martínez-Palomo says, and if the efforts by him and his colleagues pay off, Mexican researchers are likely to remain at the top for years to come.

–Jon Cohen

MEXICO

Project Refines an Ancient Staple With Modern Science

SALTILLO, MEXICO—Build a better tortilla-making machine, and the world will beat a path to your door. At least that's what scientists in this sleepy town in northeastern Mexico hope. Two years ago, this group of physicists, biochemists, cereal chemists, and mechanical engineers launched the Tortilla Project to improve the making of the tortilla, an ancient Aztec delicacy that is a staple at tables throughout Mexico and Central America.

Why tinker with success? Much loved as the tortilla is, this corn pancake is also a water-guzzling, energy-sapping, polluting beast. But by applying the tools of modern science, from x-ray diffraction to stress analysis, the Tortilla Project scientists have developed a prototype machine, about 4 feet tall and five-and-a-half feet long, that could tame the tortilla. The contraption, which Rube Goldberg would have appreciated, "can go from corn to tortilla in 5 minutes," explains physicist Jesús González Hernández, who heads the Tortilla Project and is director of the Center for Research and Advanced Studies (CINVESTAV) branch in Saltillo. "In commercial plants, this takes 8 to 18 hours." González adds that the new tortilla machine is also energy-efficient, wastes no water, creates no pollutants, and produces a product that is more nutritious than the traditional tortilla.

The project has had top-level government support. Indeed, it was dreamed up by Feliciano Sánchez Sinencio, a physicist who until last month headed the entire CINVESTAV, a network of government-funded research and development centers with headquarters in Mexico City. And research officials point to the project as a prime example of applying the tools of modern science to tackle social problems that are important to Mexico and do high-quality research at the same time. Says Sánchez: "If you work on tortillas, you can do as good work as if you were working on fullerenes, superconductivity, or magnets."

Sánchez cites statistics to show why the government has been so keen on the Tortilla Project: Mexico consumes more than 10 million tons of tortillas each year. For each ton, 10,000 liters of water are used to soak and wash the corn. Not only is water a precious resource in much of Mexico, but the discarded water also contains high concentrations of lime—calcium hydroxide—which is one ingredient in tortilla making. "We're producing 800 million tortillas a day, and that means there are rivers of water with lime that are contaminating Mexican fields," says Sánchez.

The cooking process is just as wasteful. While more than 40% of Mexicans still make their own tortillas from scratch, many others buy their daily tortillas at tortillerías, small shops that are as common as convenience stores are in the United States. Tortillerías are equipped with gas-fired tortilla makers, which make and cook fresh tortillas from industrially prepared dough, called masa, or from corn flour. The energy inefficiency of these machines is evident in almost any tortillería, which are famous for being sweatboxes.

The challenge facing the Tortilla Project team—which includes physicists Elías López Cruz and José Martínez and cereal chemists Fernando Martínez Bustos and Juan Figueroa—was to understand how the traditional steps of tortilla making affect the product, then develop more efficient substitutes. The first step, traditionally, is to mix corn kernels with water and lime, then boil them for 45 minutes. Afterward, most people let the mixture soak overnight, although industrial makers cut soaking time down to as little as 4 hours. The lime-contaminated water is then dumped, and the corn is repeatedly washed, eliminating excess lime—along with nutritious parts of the corn kernel. This "nixtamalized" corn is ground into masa, which can be shaped into tortillas and cooked or dried and ground again into flour for later use.

Because the purpose of this process is to give the lime and water a chance to interact with corn starch and gelatinize it, the CINVESTAV workers reasoned, why not grind the corn to begin with? That should make it easier for the water and lime to mix with the starch, speeding the process and reducing waste. Using the known diffusion coefficients of water and lime in starch, they then calculated the optimal size for the corn particles at 150 microns.

Next, they calculated the precise amount of lime needed to make a tortilla that tastes as good as the traditional one and has similar physical properties. Using x-ray diffraction, they studied how different lime concentrations lead to different degrees of cross-linking between the corn sugar and the water molecules, a key factor determining the plasticity of the tortilla. They also examined how various lime concentrations affected tortilla firmness with a Universal