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New Hope — and an Old Hurdle — for a Terrible Disease With Terrible Treatments

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Researchers in developing countries are trying to find treatments for conditions that affect the poorest people. But the system is stacked against their therapies.



Dr. Juliana Quintero, a leishmaniasis expert, examined Maria Salomé Tilano, 7, who has scarring from the disease. Her cousin Andrés, second from left; grandfather Jesús; and mother, Mildred, have all been infected by the parasite. Federico Rios for The New York Times

Three years ago, Jesús Tilano went to a hospital in a thickly forested valley in Colombia with large open lesions on his nose, right arm and left hand. He was diagnosed with leishmaniasis, a parasitic disease that is spread in the bite of a female sand fly and which plagues poor people who work in fields or forests across developing countries.

He was prescribed a drug that required three injections a day for 20 days, each one agonizingly painful. Mr. Tilano, 85, had to make repeated expensive bus trips to town to get them. Then his kidneys started to fail, which is a common side effect of the drug, as are heart failure and liver damage.

“The cure was worse than what I had before,” Mr. Tilano said.

Leishmaniasis is a terrible disease, with terrible treatments that have hardly changed in a century. The drug Mr. Tilano took was first given 70 years ago. All the treatments are some combination of painful, toxic, expensive, or challenging to administer, requiring an inpatient hospital stay or daily visits for a month.

Among the so-called “neglected tropical diseases,” many experts believe leishmaniasis is in a class of its own in terms of the lack of progress, in the 120 years since it was first identified, to help the two million people who contract it each year.

Now, finally, that is starting to change: When Mr. Tilano's grandson Andrés Tilano, 14, contracted leishmaniasis last year, he was treated in a clinic in Medellín, with an experimental therapy that cured his infection in days.

The treatment he received is one of several being developed by the Program for the Study and Control of Tropical Diseases, known as PECET, a small research institute based at the University of Antioquia in Medellín. In its effort to hunt for new treatments for leishmaniasis, the program has partnered with the Drugs for Neglected Diseases Initiative, or DNDi, a nonprofit research and development organization based in Geneva.

All of the experimental treatments the researchers are evaluating are far less toxic, onerous or expensive than what exists now. But a big hurdle still stands in the way of getting them to the millions of people who need them.



Mr. Tilano's son Luis, a logger who has become something of a local expert on the disease, receiving a locally developed cream to treat leishmaniasis from Dr. Quintero. Federico Rios for The New York Times

None of the new treatments have been tested in a large-scale trial, or approved by Colombia's drug regulator, or adopted into the national treatment guidelines. When a drug is made by a pharmaceutical company, the firm will shepherd it through the expensive and time-consuming regulatory process.

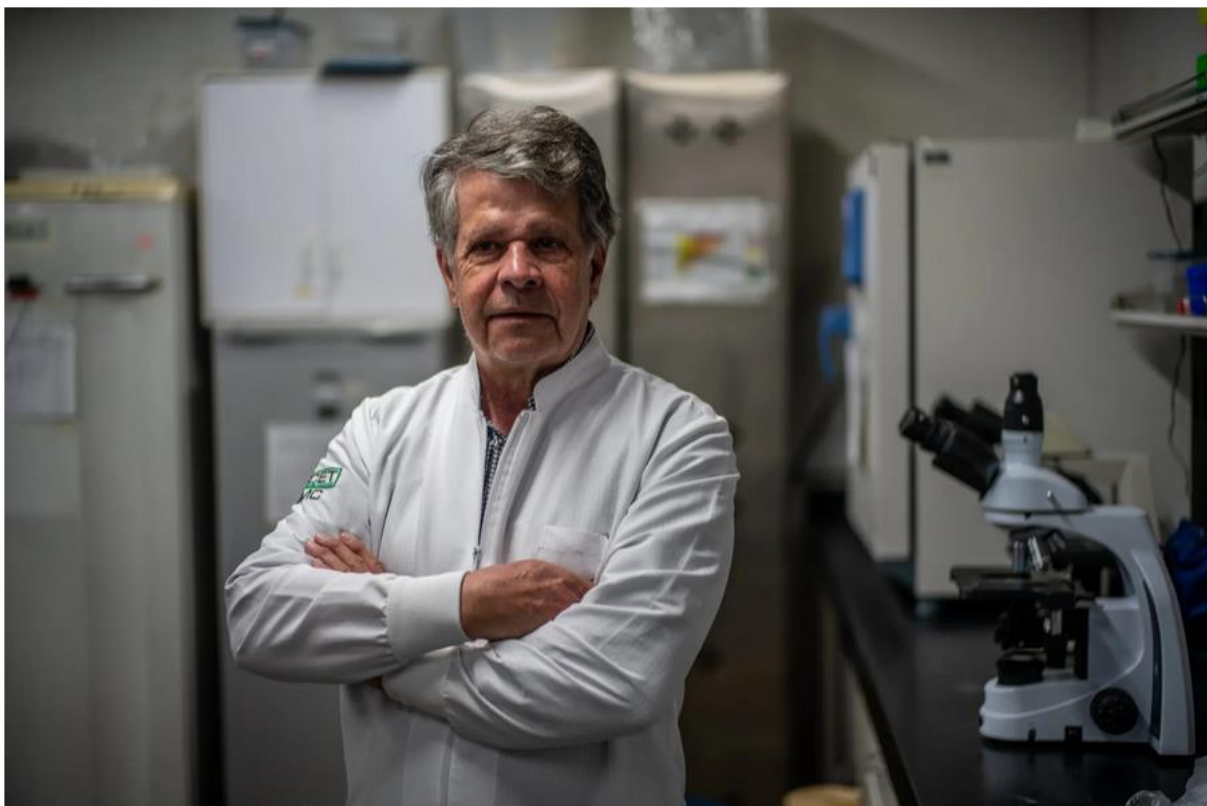
But there is no money to be made on a drug for a condition that overwhelmingly affects the poor, and academic or public health institutes rarely have the resources to push a drug through to the end of the process, said **Marcela Vieira**, a Brazilian intellectual property lawyer with an expertise in drug development and access.

The global drug development system has long favored private sector firms that can bankroll experiments and diseases that afflict people with money to pay for treatments. Increasingly, new research on diseases such as leishmaniasis is [coming from public sector and academic institutions in middle-income countries](#), particularly Brazil, South Africa, India, Cuba and China, Ms. Vieira said. The Covid-19 pandemic, during which low- and middle-income countries were shunted to the back of the line for vaccines and therapeutics, helped spur new investment into building drug development and production capacity.

“We need to do it, because no one will do it for us,” said Dr. Juliana Quintero, an expert in leishmaniasis and researcher at PECET.

The program’s research labs sit six floors up in a bulky brick building at the University of Antioquia in Medellín. On the ground floor, Dr. Quintero sees patients who arrive on buses from rural towns. She knows that few can afford to stay in the city for a month of injections; she wants a treatment she can send home with them, ideally one they can take by mouth. Because funds for drug development for leishmaniasis are so scarce, she hopes for something that will work for every one of the 22 parasites in the family that cause variations of the disease in tropical countries around the world.

The leishmaniasis researchers have taken inspiration from Indigenous people in the region: One drug they are testing, a gel applied to lesions, is derived from a plant Indigenous people use to fight the parasite. The experimental treatment that cured Andrés Tilano is called thermotherapy, and it resembles the traditional Indigenous cure of burning the lesions. In her clinic, Dr. Quintero used a hand-held device that emitted heat at 50 degrees Celsius, or 122 degrees Fahrenheit, over top of the lesion, killing the parasite deep inside.



Dr. Iván Darío Vélez-Bernal, who recently retired as the director of the Program for the Study and Control of Tropical Diseases, at the University of Antioquia in Medellín, Colombia. Federico Rios for The New York Times

Today Dr. Quintero prescribes two treatments her institute has developed and supplies them to patients under a so-called compassionate use model, since they have not yet been approved or registered by the Colombian government.

Mr. Tilano and his grandson had cutaneous leishmaniasis, which is the least severe form of the disease. It can progress to mucosal leishmaniasis, when the parasite infects tissue such as that inside of the nose. Another species of the parasite migrates to the spleen, liver or bone marrow and causes what is called visceral leishmaniasis.

Untreated, the visceral form of the disease is fatal in more than 95 percent of cases; it kills an estimated 6,000 people each year, most of them in Africa and Asia. The number of deaths has dropped significantly in the past few years mainly because of progress in finding and treating leishmaniasis in India, where it is known as kala-azar.

Because the existing treatments are so onerous and hard to get, Dr. Quintero said, few patients complete the course. That creates a newly drug-resistant parasite, which another sand fly can transmit to its family or others in their community. When Dr. Quintero went to visit Mr. Tilano at home not long ago, she met his daughter and granddaughter, who had the large circular scars of lesions that had finally healed.

Mr. Tilano's son Luis, a logger who has become something of a local expert on the disease, asked Dr. Quintero to accompany him down to the bank of the Cauca River to see a neighbor who he thought might also have leishmaniasis. After navigating a field of curious cattle and a steep river bank, she crawled through the twisted vines of a fig tree and met a group of older women panning for gold at the water's edge. The neighbor, María de las Mercedes González, 55, had large lesions on her face, and Dr. Quintero used the flashlight of her cellphone to try to determine whether the parasite had already moved into the cartilage in her nose.



María de las Mercedes González, a gold miner on the Cauca River, had her lesions inspected by Dr. Quintero. Federico Rios for The New York Times

“Imagine such a tiny animal that in one bite can cause such a problem: It’s a very irritating little creature,” Ms. González said after Dr. Quintero explained the risk she faced without treatment, and broke the news she would have to spend 10,000 pesos (about \$2.50, more than she typically earns in a day of mining) to make the daily trip to the city for treatment. The drugs, at least, would be free through Colombia’s public health system.

DNDi, the nonprofit organization, has screened more than 2.5 million compounds — a standard first step in drug development — to come up with five chemical structures that seemed, in early lab tests, like they might work against the parasite that causes leishmaniasis. But of those five, only one or two will progress to larger clinical trials, said Jadel Kratz, who runs the organization’s drug discovery work in Latin America.

Early discovery and preclinical studies cost \$10 million to \$20 million, he said, while getting through the first small clinical trials for safety and some sign of efficacy could be another \$6 million. The last phase, a large trial in patients to test whether the drug works, costs at a minimum \$20 million — far more than the public and academic research teams can fund.

“It’s a huge risk for local research if only multinational corporations can do this work,” said Dr. Iván Darío Vélez-Bernal, who recently retired as director of PECET, the research institute.

But DNDi’s focus on leishmaniasis, and the work of researchers in a network that includes India, Colombia and Brazil, is starting to pay off. Today there are five drugs in Phase 1 trials, and another in Phase 2, which is unprecedented in the history of the disease.

It is not clear when or how the drugs will get to the next phase of the process. Drugs that come out of public sector institutions tend to languish without a champion, said Ms. Vieira, who is a researcher with the Global Health Centre at the Graduate Institute of International and Development Studies in Geneva.



Mr. Tilano and his grandson, Andrés, who developed lesions last year but was treated in a clinic in Medellín with an experimental heat therapy that cured his infection in days. Federico Rios for The New York Times

Drugs that originate from public health organizations in Brazil or India are often different in key ways from ones developed by a pharmaceutical company in an industrialized country, Dr. Kratz said: The scientists creating them think about access from the start, knowing that whatever they design will have to be delivered by a low-resource health system.

In Colombia and neighboring Brazil, leishmaniasis mainly affects farmers, loggers and miners — people whose work brings them into regular contact with the sand fly. But climate change is causing the fly’s habitat to spread quickly, and Dr. Quintero finds herself more frequently treating cases from semi-urban areas. During Colombia’s long civil war, much of which was fought in jungles, the parasite also sickened soldiers, who accounted for up to half of the cases nationally. So the army was keen to find treatment, and helped test some of the experimental drugs.

The Colombian government is missing an opportunity now by not funding the Phase 3 trial for PECET’s experimental therapies, Ms. Vieira said.

“The trials are expensive but it’s much less than what they will pay for a treatment if it is developed by a for-profit company, or all the things that they already have to pay for, for people who are sick and don’t have access to the treatment,” she said.