

Can America cope with a resurgence of tropical disease?

August 11 2015, by Carrie Arnold

One rainy Friday morning in March 2015, Dr Laila Woc-Colburn saw two patients with neurocysticercosis (a parasitic infection of the brain) and one with Chagas disease, which is transmitted by insects nicknamed 'kissing bugs'. Having attended medical school in her native Guatemala, she was used to treating these kinds of diseases. But she was not in Guatemala any more – this was Houston, Texas.

For half a day each week, one wing of the Smith Clinic's third floor in Houston is transformed into a tropical medicine clinic, treating all manner of infectious diseases for anyone who walks through the door. Since it opened in 2011, Woc-Colburn and her colleagues have treated everything from dengue and chikungunya to river blindness and cutaneous leishmaniasis. Their patients are not globetrotting travellers, bringing exotic diseases back home. The Smith Clinic is a safety net provider, the last resort for healthcare for people on low incomes and without insurance. Many of their patients haven't left the Houston area for years.

This suggests that what Woc-Colburn sees in the clinic may be just the leading edge of a gathering crisis. Diseases once associated with 'elsewhere' are increasingly being found in the southern states of the USA. Infectious disease physician Peter Hotez was so concerned that he founded a school of tropical medicine at the Baylor College of Medicine in Houston, well within the territory that Hotez argues is one of the world's ten hotspots for so-called neglected tropical diseases.

"While we were calling them neglected tropical diseases, the 'tropical' part is probably a misnomer," says Hotez. "Most of the world's neglected tropical diseases are in wealthy countries. It's the poor living among the wealthy."

Poverty is a critical factor. But the American South's hot and humid climate, the influx of insects that carry diseases, and the ever-increasing movement of humans have combined with the region's high poverty levels to create a perfect storm of disease. While we might already have seen some of the storm's effects, the worst has yet to arrive.

Tropical diseases have been affecting people in the American South as long as humans have been living there. In 2003, archaeologists discovered that mummified remains in the Rio Grande Valley from more than 1,000 years ago showed signs of Chagas disease. Transatlantic trade brought the mosquito *Aedes aegypti* over from Africa, and it thrived in the long, humid summers south of the Mason-Dixon Line. Human travellers brought pathogens that could be transmitted by imported and native mosquitoes. As a result, European settlers in North America were cut down by repeated epidemics of malaria, yellow fever and dengue.

Drainage and sanitation projects in the 19th century eliminated many mosquito breeding grounds, but epidemics continued. The last yellow fever outbreak in the USA hit New Orleans in 1905, killing nearly 1,000 people. Malaria was even more difficult to eradicate, stubbornly remaining in pockets of the South into the 1940s and 1950s. The Centers for Disease Control and Prevention was founded in 1946 specifically to combat this problem, which is why their headquarters are in Atlanta: it was then the heart of malaria country.

Once aggressive government-funded eradication programmes finally halted local malaria transmission, the optimism of the 1950s and early

1960s – combined with the advent of life-saving antibiotics and anti-parasitic drugs – made infectious diseases seem like ancient relics.

"People thought that specialising in [infectious diseases](#) would be a waste of time because they would soon be history," says Lucas Blanton, an infectious disease physician at the University of Texas Medical Branch.

And so the number of physicians specialising in infectious disease and parasitology dwindled, as did government investment in the public health infrastructure geared to fight them.

As tropical diseases faded from medical consciousness in the rich countries of the world, they also vanished from public awareness. By the dawn of the millennium, most tropical diseases had become profoundly neglected, although many of them were still rife in low-income countries. Perhaps this entrenched the idea that they were distant problems: if Americans thought about them at all, it was as diseases of other countries far away, not something to be found in their own backyards. Although travellers and immigrants occasionally needed treating, tropical disease was essentially a thing of the past for the USA.

For those in the know, there were warning signs. Not enough to set alarm bells ringing, but indications nevertheless that something serious was in the offing.

Paediatrician Morven Edwards, a soft-spoken petite woman in her 60s, is an infectious disease consultant at Texas Children's Hospital in Houston. She's the doctor other doctors call when they can't figure out what's going on with their patients. In 2010, she took a call from a local paediatrician whose 17-year-old patient had tested positive for Chagas disease after donating blood for her high school blood drive.

Edwards knows a few things about Chagas: it is caused by the parasite

Trypanosoma cruzi and spread by a group of insects called Triatoma, or 'kissing bugs' (because they like to bite near the mouth). Most people with Chagas don't know they've been infected but that doesn't mean damage isn't occurring. Over time, the T. cruzi parasite can chew through cardiac muscle and cause heart failure. Chagas is a major problem in Latin America, where an estimated 8 million people are infected. It's also one of the leading causes of heart failure in the region and causes an estimated 11,000 deaths each year.

Edwards' new patient, however, had never been to Latin America. She had never even left the USA. She was, Edwards explains, "your All-American girl", hardly a candidate for a disease that mainly infected poor, rural populations in Central and South America. Edwards repeated the blood test, just to be sure. Again it turned up positive for Chagas. Given the girl's young age and the high risk for heart failure if the disease is untreated, Edwards decided to treat her with anti-parasitic drugs.

The case has stayed with Edwards for several reasons, the main one being the mystery of how the girl became infected if she'd never left the country. But south Texas is home to the same kissing bugs that transmit Chagas. The answer, then, had to be this: she had been infected with Chagas in Texas. And she was unlikely to be the only one.

At the time, Chagas was not a reportable disease in Texas – which meant public health officials had no idea how many cases there were in the state, explains Susan Montgomery, leader of the Epidemiology Team in the Parasitic Diseases Branch at the CDC. "The numbers we have are all estimates; it's hard to get a handle on the real number of cases," she says.

Like mosquitoes, [triatomine bugs](#) drink blood from a variety of vertebrates, including humans. However, triatomine bugs don't spread the Chagas parasite directly through their bite. After they finish feeding,

some bugs might defecate, leaving parasite-laden faeces on their host's skin. Scratching the bite can cause microscopic tears in the skin, through which the parasite can enter. In other cases, touching the bite can transfer the parasite to the fingers, which then spread it to the eyes and nose. The disease can also be transmitted from mother to fetus during pregnancy and through blood transfusions.

Most triatomine bugs feed at night, which is why many people don't know they have been bitten. And while some have flu-like symptoms several days after they were infected, or develop a swelling near the eye called a chagoma, many people have no symptoms at all.

Results from studies that tested donated blood for Chagas support the idea that it is a major problem in Texas. A 2014 study showed that one out of every 6,500 people who donated blood screened positive for Chagas – almost 50 times more than the CDC's estimate that one in 300,000 Americans was infected. Although the results can't prove where someone was infected, interviews by Baylor College of Medicine epidemiologist Melissa Nolan Garcia revealed that a substantial portion had no known risk factors for Chagas disease and had never spent an extended time in another area where Chagas was known to be present.

In 2010, disease ecologist Sahotra Sarkar at the University of Texas published some of the first work showing that much of southern Texas was indeed at "very, very high risk" for Chagas disease. A physicist and philosopher by training, Sarkar transferred his skills to modelling disease risk across geographic areas. He teamed up with Edward Wozniak at the Texas Department of State Health Services to determine the distribution and density of triatomine bugs across the state and the proportion of them that were infected by *T. cruzi*, the Chagas parasite.

A trio of studies published beginning in the early 2000s had suggested that more than half of the triatomine bugs in Texas were infected with *T.*

cruzi. Sarkar's work used this infection rate, along with the population density of both triatomine bugs and humans, to create a Chagas disease risk map for Texas. The southeastern tip of the state, curved in a 'C' shape and bordered by the Rio Grande in the south and the Gulf of Mexico to the east, was at the highest risk for Chagas. Other areas, such as the bayous of Louisiana and San Antonio, Texas, also saw unusually high risk.

To Sarkar, the message was clear: the mixture of parasite-infected bugs and lots of people meant that Chagas disease was endemic in Texas. But, he says, "the response from physicians was almost complete silence because they didn't even know this disease could be a serious issue in Texas."

Head northeast from downtown Houston on San Jacinto Street. As you cross the I-10, the roads begin to change. Smooth pavement gives way to ruts and potholes. Dilapidated housing and convenience stores replace skyscrapers and cute boutiques as you journey into the heart of Houston's Fifth Ward. In the Fifth Ward, the city's poorest neighbourhood, the rate of HIV infections is twice as high as it is in the rest of Houston and there are three times as many sexually transmitted diseases. Its poverty levels are also reflected in the housing. Stagnant water collects in streets, sidewalks and yards, providing the perfect breeding ground for mosquitoes. Ripped and missing window screens provide plenty of opportunities for mosquitoes and other vectors to bite humans. Stray dogs roam the streets.

"It looks like the global health movies you show to first-year Masters of Public Health students," says Hotez.

Conditions like these foster the spread of tropical diseases, whether in the USA or anywhere else. In 2005, an outbreak of dengue (a virus carried by mosquitoes that causes headache, fever and severe joint pain)

affected two cities on either side of the US–Mexico border: Brownsville in Texas and Matamoros. Although the mosquito that spread the virus was present in roughly equal numbers in both cities, the infection rate in Matamoros was nearly double that of Brownsville's. The reason? Better housing and a higher standard of living in Brownsville meant the widespread use of air conditioning, which deters mosquitoes. Poverty matters, and it matters a lot.

"There's been a gradual rise in the economies of all nations...but it's leaving behind a bottom segment of society, and that bottom segment of society is who gets the neglected tropical diseases," Hotez says.

The American South has always been a land of contrasts. Spend just a few hours in the car and you can move from the muggy humidity of the Gulf Coast to the arid furnace of the Texas hills. The mountains of Appalachia flatten out and become the lowlands of Louisiana. But perhaps the most striking contrast in the region is in its wealth and inequality.

An estimated 45 million Americans live in poverty, including more than one in five children. Approximately 1.65 million live in extreme poverty, defined as living on less than \$2 per day. Economists estimate that the disparity between rich and poor Americans now is greater than at any time since the Great Depression, and this includes the South.

"Poverty is seldom evenly distributed across the country. Poverty clusters in pockets. It clusters in northeastern Brazil, it clusters in northern Argentina, it clusters in southern Mexico, it clusters in southwestern China," Hotez says. "Well, it's the same thing in the USA. Poverty is clustered in the American South."

Although there's no single cause for this, it has deep historical roots. The Civil War might have legally freed the slaves, but Jim Crow laws and

centuries of prejudice meant that many black people remained in a state of abject poverty. Today, poverty is still a much bigger problem for black people than white people in the South.

Economists believe that a combination of low-paying jobs, inadequate social safety nets and systemic racism all contribute, while disease – as well as being a consequence of inequality – might also turn out to be a significant factor.

Diseases of poverty include more than those spread by insects. Parasitic diseases like hookworm disease and cysticercosis, which are both caused by worms that infect the gut, are also in the USA. In the low-income, mainly African-American counties around Montgomery, Alabama, scientists in the 1930s showed that around 41 per cent were infected with hookworm, which can cause anaemia and malnutrition. A follow-up study in the 1950s revealed that infection rates had dropped significantly, but roughly 15 per cent of people remained infected. After that, we don't know: for the next 60 years, the subject was confined to dusty medical libraries as a historical artefact.

In 2014, Baylor tropical medicine physician Rojelio Mejia travelled to Montgomery to test his suspicion that hookworm remained a significant problem. He wanted to recruit 100 people for a small pilot study that would test them for hookworm and provide treatment where needed. His first trip netted just 11 participants.

"They have a lot of mistrust of a tall, bald white man coming to see them," he says.

Partnering with a local civic organisation and church led to more volunteers, and his final study had 56 participants. Mejia and colleagues also went to the volunteers' homes to sample the environment. In contrast to the urban poverty of Houston's Fifth Ward, these were poor

rural areas. The region's fertile black soils can't filter waste effectively, but most residents can't afford the expensive septic systems required to solve the problem cleanly. Instead, they simply buy as much pipe as they can afford and run it from their toilet to the back of their yards, where the waste collects. The hilly terrain means that rain and flooding spread the waste over the ground – perfect conditions for spreading hookworm. Mejia has now finished collecting samples, but he hasn't yet finished his analysis.

Mejia and Hotez believe that parasitic infections like hookworm contribute to a vicious cycle of poverty. Hotez points to a little-known parasitic disease called toxocariasis (caused by roundworm) as another example: he estimates it infects 2.8 million African Americans, most of them living in urban poverty. The disease can cause asthma and wheezing, as well as cognitive delays and behaviour problems. In 2014, Hotez proposed that some of the educational and economic disparities experienced by poor African Americans might be partially due to toxocariasis. These difficulties, in turn, make it harder for people to find steady employment and well-paying jobs as adults. This means their children are also likely to grow up poor, continuing the cycle for another generation.

"So many of these neglected tropical diseases are not acute infections like...the flu or common cold," Hotez says. "Many are chronic, debilitating conditions that mimic non-communicable diseases... If somebody has epilepsy, they don't think of cysticercosis... If a child tests poorly in school, the paediatrician or nurse practitioner won't think of toxocariasis."

Of course, suspecting that a tropical disease might be the problem is only useful if a physician can easily diagnose and then treat it. Despite tremendous advances in other types of illness in recent decades, [tropical medicine](#) remains stubbornly stuck in the 1950s, leaving the USA as

unprepared as low-income nations to treat any significant number of cases.

The letter that changed Maira Gutierrez's life almost got tossed with the junk mail. Gutierrez, a then 24-year-old Californian, regularly donated blood at her employer's blood drives and thought the Red Cross was just asking for donations. But when she ripped open that letter in 1997, she learned that she had been banned from ever donating blood again. Her blood had been tested as part of a pilot programme to screen donated blood for Chagas disease, and she had tested positive.

"At the beginning, I was just confused. What are they talking about? What is this? I had never heard of it. How did I get it?" Gutierrez says.

Her doctor didn't know much more, either. He told her she had probably picked up the parasite that causes Chagas as a child in her native El Salvador. Frustrated with a lack of answers, Gutierrez turned to an infectious disease specialist. He told her (incorrectly) that there weren't any treatments and she would just have to cross her fingers and hope she wasn't among the roughly one-third of victims whose infections progressed to heart failure. Gutierrez went back and forth between doctors looking for answers and treatment for more than a year before she finally gave up.

"I had my physical. I was fine. I didn't see anything, I didn't feel anything. So I just assumed that if my physical was fine and everything was coming up fine, that I was fine. So I stopped trying," she says.

Life went on. She got married and had two kids. Her career at Universal Studios advanced. As the diagnosis retreated further into the past, it seemed more and more like a bad dream. Then, in 2008, her sister called, hysterical. "Put on channel 11," she said. "There's a story about Chagas."

By the time Gutierrez had flipped on the TV, the segment was over, but her sister had managed to copy down the phone number of Sheba Meymandi, the director of the Center of Excellence for Chagas Disease in Los Angeles. The next week, Gutierrez was in Meymandi's office. Finally, she got answers – and treatment.

Gutierrez had almost certainly been infected with the Chagas parasite before she fled El Salvador's civil war in 1981 at age eight. For nearly 20 years, the parasite had lurked silently in her body. Like nearly all people with Chagas, she had had no idea she was infected and had missed any opportunity for prompt treatment.

To Mejia, cases like this emphasise the need for better education and diagnostics for tropical diseases. Diagnosing someone with a parasite generally involves testing for antibodies against the organism or looking under the microscope to see the parasite in action, both of which are time-consuming and inexact. In comparison to other areas of infectious disease, which have largely moved to DNA-based diagnosis, work on most tropical diseases hasn't kept pace. Mejia and Hotez hope to change that by creating cheap, easy-to-use diagnostic tools. Mejia spent three years building new tests from the ground up; a pilot study in Ecuador revealed that his tests were five times more sensitive than traditional microscopy at detecting *Giardia* parasites, which cause an infection called giardiasis.

Treatments, too, need to advance – something that Gutierrez, like many other Chagas sufferers, knows all too well. As soon as Meymandi confirmed her diagnosis, she started a three-month course of nifurtimox, one of the two available anti-parasitic drugs that can treat Chagas. Both cause serious side-effects, such as headaches, nausea, appetite loss, rashes and psychiatric symptoms. In her three months taking nifurtimox, Gutierrez lost 25 pounds.

She was fortunate that Meymandi knew how to get the drug in the first place. Drug manufacturers don't believe the market for Chagas treatments is great enough to justify jumping through the regulatory hoops to obtain FDA approval, which means the agency hasn't made them available by prescription, despite the fact that these medications are used safely around the world. This means that physicians can only obtain the drugs from the CDC via a special research protocol.

"Most physicians have a hard enough time...dealing with the preauthorisations that they need to get drugs from the insurance companies, let alone having to do all of this paperwork to treat one patient," Meymandi says. Patients must also be monitored closely, which requires extra appointments for patients and extra paperwork for physicians.

Even then, the drugs aren't always effective. Cure rates are almost 100 per cent if given soon after infection, but Gutierrez had been infected for at least 30 years and the drugs had no effect on the number of parasites in her body. "The CDC considers me a complete fail," she says, and there is no other treatment to try.

She has now begun to develop early signs of [heart failure](#). Although the only symptom so far is palpitations, Meymandi can see the channels in Gutierrez's heart muscle where the parasites have eaten holes in her heart. Since no other treatments for Chagas disease are available, Gutierrez must live with the knowledge that she could die of a heart attack any day.

It is the nature of these diseases – neglected diseases, diseases of poverty, call them what you like – that they can go unnoticed for years, chewing away at the health of individuals and communities. As poverty, geography, climate and social factors combine to bring tropical diseases out of hiding once again in the US South, physicians, politicians and the

general public have to take the warning signs seriously and recognise that the tools available for tackling [tropical diseases](#) are sorely lacking. With diseases like Chagas now known to be prevalent and transmissible within the USA, better awareness, better tests and better treatments are all urgently required. Otherwise, as Hotez says, the number of people affected and infected will only continue to rise as this perfect storm grows ever stronger.

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