

This disease kills half the people it infects. So why isn't more being done?

February 20 2018, by Carrie Arnold

Every morning, Prasart Songsorn used to wake before dawn to head out to the fields before the tropical sun and oppressive humidity made it impossible to work. Prasart, who spent all his 56 years on his family's small rice farm in north-eastern Thailand, worked barefoot in the warm mud. Boots amplified the heat and humidity, and he didn't want to buy something that would only add to his misery.

Although diagnosed with diabetes in his mid-40s, Prasart seemed healthy and never missed a day of work. So when he started having difficulty breathing and ran a high fever in early June 2017, he tried to push through it. When he couldn't, he travelled a few miles to a local community hospital, where he was diagnosed with kidney [disease](#) due to his untreated diabetes. He was so ill by then that the doctors transferred him to Sappasithiprasong Hospital in the city of Ubon Ratchathani, nearly two hours away.

His younger sister, Aroon, didn't trust the diagnosis. "If you cannot breathe, how could that be a problem with your kidneys?" she thought. But she figured the more experienced physicians in the city would soon figure out what was wrong. They didn't.

For more than a week, Prasart suffered without really knowing what was wrong. Only after her brother had died did Aroon learn that he'd actually had an infection called melioidosis. Although it's one of the leading causes of pneumonia in this part of Thailand, especially during the rainy season, it remains a mystery to most people.

"We had never heard of melioidosis," says Prasart's brother, Sompurn. "After he died, we got a brochure about how it came from the soil and how to protect yourself."

Since 2002, when he began researching melioidosis at the Mahidol Oxford Tropical Medicine Research Unit (MORU) in Bangkok, Direk Limmathurotsakul has found official recognition of the disease to be similarly low. "Melioidosis is so neglected that the World Health Organization doesn't even list it as a neglected tropical disease," he said at the 2017 'Biothreats' conference in Washington, DC.

Melioidosis is a bacterial infection that can cause a range of symptoms, including fever, muscle aches, abscesses and cough, leading researchers to call it "the great mimicker". It's hard to diagnose, requiring a skilful process that can take more than a week – time that patients like Prasart often don't have.

This, coupled with a general lack of awareness, meant that no one knew how many [cases](#) of melioidosis there were in Thailand – or anywhere else around the world. Limmathurotsakul made it his life's mission to change that and get melioidosis recognised as one of the world's more important neglected tropical diseases.

His greatest battle proved not to be against the disease itself, but a much more formidable enemy: the stasis and indifference of government bureaucracies. He knew melioidosis was a big problem; the question was whether he could get anyone to take notice.

In the 1910s, British physician Alfred Whitmore and assistant surgeon C S Krishnaswami noticed a gruesome trend among the patients at Rangoon General Hospital in Burma (in what is now the city of Yangon in Myanmar). A steady stream of young men, either dead or nearly so, were showing up with blistering fevers, malnutrition and track marks

from injecting opium. Initially, Whitmore suspected the opium was the cause of their illness, but the speed of their decline and the location of abscesses far from injection sites caused him to rethink.

When they grew bacteria from the men's abscesses, they discovered that "cultures from both lungs and spleen gave luxuriant growths in pure culture of the bacillus under investigation". They named this bacteria *Bacillus pseudomallei*, but without antibiotics there was little to be done for these malnourished, sickly and vulnerable patients.

Not much changed in the 80 years between Whitmore and Krishnaswami's discovery and Limmathurotsakul's graduation from medical school. The disease had been formally named melioidosis in 1932, and scientists had discovered the bacteria (renamed *Burkholderia pseudomallei* in 1992) in soil and water throughout South-east Asia, although the disease was found mainly in Thailand, Myanmar, Cambodia and Laos.

Learning to treat melioidosis was a trial by fire. Limmathurotsakul had read about it in textbooks, but had never treated a patient until he arrived at Sappasithiprasong Hospital in Ubon Ratchathani. Although he now had antibiotics at his disposal, few worked against this disease. And by the time his patients arrived, some were too ill for antibiotics to be of use. "About half the patients I treated died. It was like a coin toss," he says.

During the rainy season, from July to October, torrential downpours stir up the bacteria living in water and soil. Scientists still don't know exactly why – one idea is that the rain aerosolises the bacteria, which are then inhaled. This season is also when rice farmers like the Songsorns spend long days in the fields, their bare limbs immersed in melioidosis-laden soil and water. The result is a surge in disease that leaves the melioidosis wards in Ubon Ratchathani overflowing.

During his first rainy season, Limmathurotsakul's days in the sweltering melioidosis ward took on a grim routine. "You walk around and you see melioidosis, melioidosis, melioidosis, melioidosis. Within two or three days, each dies," he says. New patients quickly replaced those who didn't make it.

That year, more than 100 people died of melioidosis at Sappasithiprasong alone. Despite the drudgery, Limmathurotsakul knew those under his care had a major advantage over most other melioidosis patients, because they had sought treatment at a hospital that could diagnose and treat them.

The illness's array of symptoms makes it difficult to diagnose. The same bacteria can cause pneumonia in one person, septicaemia in another, an abscess in the elbow for another. In one small hospital study, over half the children with melioidosis had come in with local infections, many in the parotid glands (salivary glands in front of the ear), whereas in Australia, where melioidosis often turns up in isolated areas of the Northern Territory, older men are disproportionately likely to have prostate abscesses.

As in Whitmore's day, diagnosing melioidosis involves culturing bacteria from abscesses, urine, sputum, blood or wherever else a physician thinks the disease might be found, explains Vanaporn Wuthiekanun, a soft-spoken microbiologist who has worked with melioidosis at Sappasithiprasong for more than 30 years.

"It's easy if you have experience, but it's challenging for those who don't do it much," she says. It's also time-consuming, and like Prasart Songsorn's family, many people don't know what has affected their relative until after they have died, if they ever find out at all.

Even knowing what it is in time doesn't make treating melioidosis easy.

The bacteria's waxy outer membrane makes it resistant to most antibiotics. Drugs like gentamicin, used to treat pneumonia and sepsis, don't work on melioidosis. Instead, treating the disease requires two to four weeks of intravenous ceftazidime in hospital, followed by three to five months of oral antibiotics as an outpatient.

The sooner doctors can start this regimen the better, says Wuthiekanun, but prompt treatment is still no guarantee. Mortality rates for melioidosis in Thailand hovered at 50 per cent when Limmathurotsakul began his work and haven't budged much since. In northern Australia, at least 10 to 20 per cent of patients die.

By most infectious disease standards, explains Patrick Harris, an infectious disease physician in Australia, that number is astronomical. Compare it to other, better-known neglected tropical diseases: malaria (mortality rate 0.2 per cent), dengue (1 per cent, higher in severe cases), Chagas disease (less than 5 per cent) and leptospirosis (5–15 per cent).

"On a global scale, the disease burden is still quite dramatic, probably because people present late. They can't get to a hospital quickly. It's very often more prevalent in poor communities, rural farmers, people who may be a long way away from a big city or a major hospital. There's a lot of other societal factors," Harris says.

Limmathurotsakul knew that the parade of patients coming through his melioidosis ward could only be a small fraction of the country's total melioidosis burden. Plenty of patients died before they could get to the hospital; others sought care from a hodgepodge of community health providers, who prescribed everything from penicillin to herbal remedies to massage. Thailand, he realised, had a major melioidosis problem. If he was seeing 100 melioidosis deaths in a single hospital in just the [rainy season](#), tens of thousands of people must be dying each year.

Yet ever since 1947, when Thailand reported its first case of melioidosis, the official annual number has been tiny – even in the mid-2000s, it was approximately one case of melioidosis per 100,000 people. Laos didn't document any melioidosis cases until 1999. The only cases from Burma/Myanmar since 1945 have been in travellers. The poor data created a circular problem: funding agencies wouldn't give money to do research on a disease that didn't appear to be present, but Limmathurotsakul couldn't get data to show it was present without money.

"The major question that everyone tries to ask is how many die of the disease, because if we cannot tell, the policy makers don't move," he says.

The fever started in February. Pailat Ganjanarak found it increasingly difficult to ignore the fatigue, chills and vomiting, so he went for a massage, a common cure-all for mild illnesses in this part of Thailand. It didn't help. Then, the 55-year-old, who owns a small grocery store off the main road running south from Ubon Ratchathani, went to the doctor, who diagnosed an inflammatory problem and prescribed steroids. After a week, Ganjanarak was sicker than ever. Twelve days of antibiotics didn't help, either. He just kept getting worse.

"I was so sick, I couldn't even walk," he says.

His wife drove him to Sappasithiprasong Hospital, hoping that doctors there could identify her husband's mysterious ailment. It took until mid-March, more than a month after Ganjanarak first became ill, for the blood cultures to return the answer. Despite living nearly all his life in the part of the world where it is most prevalent, Ganjanarak had never heard of melioidosis. Neither had most of his friends. "Most people didn't believe me because they had never heard of it," he says.

Everyone knows about leptospirosis – a bacterial infection that can cause kidney disease – meningitis and pneumonia, but it's rare for someone to know about melioidosis, says Pornpan Suntornsut, a microbiologist at the MORU–Sappasithiprasong melioidosis research unit. She reckons that only about 2 per cent of people in Ubon Ratchathani know what it is. Physicians aren't always more knowledgeable, either.

To Suntornsut, this reflects the official attitude towards melioidosis. Patients don't know to ask about melioidosis, doctors can't give a quick diagnosis and the government doesn't have enough data – or enough political will – to do anything about it.

Another problem is the disease-reporting system in Thailand. After World War II, Limmathurotsakul says, the government wanted a method to discover and contain cholera outbreaks. At first, all it took was a phone call to the Ministry of Public Health to have people sent to investigate.

Over the next 60 years, however, more and more diseases were added to the list – the current total is 78. But in most of Thailand's hospitals, including 1,000-bed hospitals that might treat upwards of 200,000 patients each year, there's still only one person who is responsible for reporting all these diseases, according to Limmathurotsakul.

He says this makes the system susceptible to shifts in priorities: "This year, we are in a panic of dengue, so the Ministry of Health says report dengue. We will report. We need the data to tell the people in the country. Whether panic of influenza, panic of bird flu, Ebola, cholera... whatever panic of this year, they will say, OK, this year this is the priority."

Melioidosis isn't a disease that causes large outbreaks or pandemics, and it doesn't capture media headlines or government attention – it just

causes infections at a steady rate. It's not usually spread from person to person, either, which decreases its priority level further. It also tends to affect poor, rural rice farmers in Thailand, another strike against it in terms of getting official attention.

Across the border in Laos and Cambodia, there are similar challenges. At the Angkor Hospital for Children in Siem Reap, Paul Turner sees around 40 to 50 diagnosed cases of melioidosis each year. He estimates Cambodia must have thousands of cases each year, but the disease's endemic nature means the government doesn't require reporting for it.

The ultimate outcome is that melioidosis is vastly underreported, both in South-east Asia and elsewhere around the world. Physicians have reported cases in Brazil and across Africa – cases not linked to travel, which means the sick person must have picked it up in their own backyard. Limmathurotsakul and David Dance, a British doctor working on melioidosis in Laos, suspect this represents only a fraction of the disease burden, since melioidosis looks like so many other tropical diseases and remains difficult to diagnose. And the burden looks set to increase due to two factors in particular: climate change and diabetes.

Across the Indian Ocean in Sri Lanka, infectious disease physician Enoke Corea put a call out to her colleagues to be on the lookout for melioidosis cases a decade ago. For the first few years, they found only a case or two. Now, the trickle has become a steady stream.

"We suddenly found that we were seeing maybe 10 cases a year, then you went up to 23, then to 65, then to a hundred and something. This year we are already three-quarters of the year through and we are almost on 60, 70 cases already," Corea says. She expects the number to keep rising, thanks to climate change bringing more extreme weather events that will aerosolise more bacteria from the soil, as well as increasing the areas of the world where *B. pseudomallei* can thrive.

The effects of climate change are already beginning to be felt in Australia. Climate models predict that more parts of the country will become hospitable for melioidosis. Rising numbers of people with diabetes will likely push the melioidosis numbers even higher. Although no one knows exactly why, diabetes increases the risk of developing melioidosis, and seems to make it more likely that someone will develop more serious forms of the illness, such as sepsis or pneumonia, that increase the chance of dying from it.

"Both [diabetes and climate change] will almost certainly lead to increased incidence in the future," Dance says.

Even as his colleagues were predicting rises in melioidosis cases, Limmathurotsakul was struggling to convince his own government to document the current disease burden. Everywhere he went, he found a different type of resistance. At the bottom level, they lacked time and resources, or feared that their higher-ups would think they had made a mistake by not reporting all these cases sooner. Upper management, however, didn't want to cause a panic and didn't believe the data was that important.

"I had to fix every stage," he says. The process involved years of meetings with government officials, from the staffs of small community hospitals to the head of the Ministry of Public Health.

At the same time, Limmathurotsakul and his team began to gather data and develop computer models to estimate the true disease burden. In 2016, they published the first ever global estimate of melioidosis prevalence, and the numbers were far higher than anyone anticipated. Their work showed that approximately 165,000 people develop melioidosis each year and 89,000 of them die as a result. Importantly, their work revealed overlooked melioidosis hotspots outside of South-east Asia, including India and Sri Lanka.

"That paper was the beginning of it, really," says Dance. "To try and raise awareness of the disease and raise awareness of the fact that if the predictions from that modelling are correct then it's a much bigger killer of humans than some other diseases that are much better known."

Combined with Limmathurotsakul's years of tireless groundwork convincing government officials to improve disease reporting, this high-profile report has led to changes to the official attitude towards melioidosis. In Ubon Ratchathani province alone, estimates of melioidosis prevalence surged from 4.4 cases per 100,000 people in the early 1990s to 21.0 cases per 100,000 in 2016, thanks to improved reporting. As more hospitals report more cases, Limmathurotsakul hopes it will encourage other hospitals to step up their game, too. He also hopes the data will spur new research.

Stopping melioidosis will require more than just data. While others have their eyes on the long-term development of a vaccine or the construction of new health facilities, Limmathurotsakul says less splashy initiatives are needed, like providing safe drinking water. In Ubon Ratchathani, Pornpan Suntornsut and her team are trying possibly the simplest approach of all.

Across the region's lush rice paddies, people stoop over to tend their fields, muddy brown water up to their mid-calves as they tend their crops. Most work barefoot. Arriving in the midday tropical heat, I quickly understand why.

Sweat instantly begins oozing from my pores. In less than five minutes, I am drenched, my hair plastered to my forehead. Even in sandals, my feet feel absurdly hot. The thought of putting on boots seems laughable. But boots are exactly what the MORU team have come to advise.

Long hours working barefoot in the soil is a major path of melioidosis

transmission. But the brutal heat means that protective rubber boots are a tough sell. With few official cases of [melioidosis](#), the hassle of working in boots just didn't seem worth it to most people, Suntornsut says. But now that the disease is gaining recognition, they are here to provide information and talk about the importance of wearing boots and boiling drinking water to kill bacteria. Although it's still too early to have conclusive data, Suntornsut feels the team's efforts are paying off.

Limmathurotsakul may have changed the government's attitude about disease reporting, but his battle is far from over. Sitting behind his desk back in Ubon Ratchathani, he pauses after nearly two hours of rapid-fire chatter and leans back.

"You just need to keep pushing," he says. "Because if you don't, and you just disappear, no one else will push. You cannot hope that someone will do the work for you."

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