Fighting mosquito-spread viruses from the inside-out

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Credit: Monash University

The Aedes aegypti mosquito is a city dweller that breeds in puddles and stagnant drains – the female likes to feast on human flesh. In the tropics it regularly spreads disease, then is blasted with insecticides, only to reappear with the monsoons.

Since 2011, Aedes aegypti has also been recruited to eradicate the viruses it spreads. Mosquitoes that carry Wolbachia, a naturally occurring bacteria, don't transmit illnesses such as dengue, chikungunya and the Zika virus. The beauty of this method of disease prevention is that the mosquitoes themselves spread the Wolbachia down the generations; insecticides aren't necessary.

Gordonvale, south of Cairns in North Queensland, was the first place Wolbachia-implanted Aedes aegypti mosquitoes were let loose to breed with wild mosquitoes. The released mosquitoes have since gone on to breed generations of mosquitoes that also carry Wolbachia.

Professor Scott O'Neill is the scientist who discovered the good that Wolbachia can do. He now heads the not-for-profit World Mosquito Program (WMP) that has its headquarters at Monash University. He's reluctant to say his program has ended the threat of dengue in North Queensland – he'll wait on "a classic epidemiological trial" before making that claim. But he will say that as far as he's aware, local dengue transmission hasn't occurred in north Queensland in areas where Wolbachia has been deployed for the past five years.

On March 20, the Mexican city of La Paz, in Baja California Sur, announced it would be the first Mexican city to implement the self-sustaining program, taking the total number of WMP project sites to 12. Earlier in March, New Caledonia also signed up, joining Australia, Brazil, Colombia, Indonesia, Vietnam, Sri Lanka, Fiji, Vanuatu and Kiribati. The program is also working with the Indian Council of Medical Research in Puducherry to prepare for the release of Wolbachia-implanted mosquitoes in India – the country is believed to have more cases of dengue than anywhere else in the world.

In two years, the program aims to operate in 20 countries. The task ahead is enormous. About 390 million people are infected by dengue each year, and 84 countries are affected by the Zika virus. Since its debut in Gordonvale, the World Mosquito Program is close to reaching two million people. "It is going to take a lot of effort, and more people than just us to roll out this intervention globally," Professor O'Neill says.

Gaining community acceptance

He still feels a debt of gratitude to the North Queenslanders who were willing to embrace the new approach. "You could imagine the people there would be a little suspicious of scientists releasing things into the environment," he says. "Not only that, but the mosquitoes were going to bite people … The release required a lot of trust in the community to accept what at first might seem to be this counter-intuitive intervention that scientists were talking about."

He explained his method at "town hall-type meetings" with local people whom he describes as "amazingly unselfish". "Their motivation for being part of the program was quite altruistic. It was not only to protect themselves from dengue, but to help people in other countries."

Community support has been important to the program from its inception. "It felt right," Professor O'Neill says. "We have always, in all our work, indicated that if communities are not accepting of it, then we will not push it on to people."

This means that about a quarter of the WMP's budget "or more" is spent on community engagement, he says. "If you're starting from the premise that you will only do work if the community accepts it, then the onus is on you to engage the community and get the acceptance."

As far as he can recall, Yogyakarta, Indonesia, is the only city where a small number of people organised to reject the program. (Indonesia was the third country where Wolbachia-implanted mosquitoes were released.) Yogyakarta has 38 universities, and an "amazing number of students and academics", he says. "So, people there are maybe more questioning than in other communities. One university academic was fairly critical of what we were doing … so we didn't release our mosquitoes in one area. Interestingly, some years later, the community has asked us to come back and do the releases. The opposition was fairly short-lived."

As the program progresses, its successes become more evident, and the roll-out more efficient. The program not only consults with local communities, but works with local health authorities to disseminate the Wolbachia-infected mosquitoes. The aim is for the program to cost $US1 per person for its approach.

The program already has the backing of philanthropic organisations including the Bill and Melinda Gates Foundation, the Wellcome Trust, the Tahija Foundation in Indonesia, the International Community Foundation – Candeo Fund, the Gillespie Family Foundation, the Rotary Foundation and local clubs. It's also supported by the governments of Australia, Brazil and the UK, and USAID and the Foundation for the National Institutes of Health in the US.

Professor O'Neill has been working with Wolbachia since he was a Ph.D. student at the University of Queensland. "I knew nothing about Wolbachia," he recalls. "My professor was interested in the evolutionary biology of mosquitoes, not about Wolbachia in disease control."

Explainer: the World Mosquito Program's Wolbachia method

Professor O'Neill went on work at the University of Illinois as a post-doctoral researcher, where he continued to work on Wolbachia. From Illinois, he spent a decade at Yale, where he was "fascinated by the potential of Wolbachia's ability to spread into insect populations".

"At that time, lots of people were talking about how we could genetically engineer, or intervene with mosquitoes, to stop them transmitting disease agents," he recalls. Malaria was his focus in those days, because it's responsible for more childhood mortality than any other mosquito-borne disease. "The idea was that we could put a genetically engineered cargo inside Wolbachia like a Trojan horse, which, once it had spread into the mosquito population, could stop them transmitting the disease."

While he was at Yale considering mosquitoes, Seymour Benzer at Caltech was researching fruit flies. Benzer was a celebrated molecular biologist and behavioural geneticist. In his later years, he became interested in the science of ageing and longevity, and as part of his research was investigating fruit flies with particularly short lifespans. Benzer's lab discovered that fruit flies who died young carried Wolbachia.

At Yale, Professor O'Neill read Benzer's research and thought "Whoa, there is something here he hasn't realised". A mosquito's lifespan is "really critical for how effective it is in transmitting malaria, or dengue, or other disease. If Wolbachia could shorten the lifespan, that could be enough to stop disease transmission. So, we could throw out the whole genetic engineering thing. If we could get this strain of Wolbachia into the mosquito, we were on to something."

The breakthrough

Professor O'Neill returned to the University of Queensland. By this stage his research focus had switched from malaria to dengue fever, for the pragmatic reason that he believed he was more likely to "get results" with dengue. While at Queensland, his talented research student, Conor McMenamin (the brother of Wallabies rugby player Hugh McMenamin and Diamonds netballer Clare McMenamin), became the first person to successfully microinject life-shortening Wolbachia into the eggs of a female mosquito.

"We had to make glass needles to do it," Professor O'Neill recalls. "And we had to take those needles with the Wolbachia preparation and get the needle into the egg before the egg is more than an hour old, before it has formed cells … If you can imagine taking a really coarse knitting needle and putting it into a balloon full of water, and then pulling it out without the balloon breaking, that will give you a sense of the technical difficulty."

Professor O'Neill says he's not a big believer of 'Eureka' moments in science, but Dr. McMenamin's success with the glass needle was one of the turning points in his Wolbachia research. "The way it happens in science is that you're working on something for months and years and everything is always failing, and sometimes you get a positive result," he says. "You don't believe it. And then you repeat it. And then you repeat it again after a month's time, and you still don't believe it. And then it has to be repeated a third time, and that takes another month …"

There's always the possibility the Wolbachia method may not suppress dengue and Zika forever – it's impossible to predict how long it will work. But the method is certainly working now – it's saving lives and will continue to ease the amount of suffering in the world into the future.

"As a scientist interested in applied outcomes, 80 per cent of what everybody does fails," Professor O'Neill says. "I think I've been incredibly fortunate to be at the right time, in the right place, asking the right questions, to stumble onto something that can have a very large impact. And even more lucky to be able to position myself to follow it through."

Provided by Monash University