Podcast Interview: Scott O’Neill

PNAS: I’m your host, Ann Griswold, and welcome to Science Sessions. In tropical and subtropical countries, a mosquito can be more than a minor annoyance. Mosquitoes transmit a number of diseases to humans, from malaria and encephalitis to a debilitating illness known as dengue fever. Treatments for dengue remain limited despite years of research and subsequent infections can prove fatal. Residents of dengue-infested areas must contend with heavy insecticide exposure—or risk recurring infections. In the tropical north of Australia, pest control teams swoop down on the neighborhoods of infected people, spraying under beds and around porches—and not just at the infected house, but at surrounding houses, too. Medical entomologist Scott O’Neill, dean of science at Monash University in Melbourne, published a 2011 paper in PNAS about the debilitating disease and an interesting approach to curbing its spread.

O’Neill: So dengue is a virus that is transmitted between people by one particular mosquito called *Aedes aegypti*. It causes huge amounts of problems around the world for people from a human health perspective. It’s estimated that 2.5 billion people are at risk of infection every year. Maybe 50- to 100-million cases. At the present time, there is no vaccine available; there is no treatment. So most controls focus on the mosquito.

PNAS: So O’Neill explored ways to limit Dengue transmission. His search led him to an intracellular bacterium called *Wolbachia*.

O’Neill: We got interested in the potential of using them because of the effects in *Drosophila* where the effects of a particular strain of *Wolbachia* shortened the lifespan, and so we thought well we can just transfer this bacterium into *Aedes aegypti*, where it doesn’t occur. Maybe we can shorten the lifespan of the insect.

PNAS: But it wasn’t easy to transfer the bacteria into the mosquito. Different people in O’Neill’s lab tried different techniques with little success. The process took years. Finally, something clicked.

O’Neill: And so when we got the strain in, that was a fantastic event. We were really happy at that point. We wanted to look and see if it shortened the lifespan and it did. And then something happened that was quite unexpected. We did a series of experiments in the lab and what we found to our surprise is that when we put the dengue in by injecting it into the mosquito, it didn’t grow. The *Wolbachia* was there. And that was huge for us. We’d been thinking for years about shortening the lifespan and then all of a sudden lifespan didn’t really matter.

PNAS: So the group chose one strain of *Wolbachia* for further study. Mosquitoes infected with the strain had a typical lifespan but couldn’t sustain dengue virus infection. To see if the bacteria could invade a wild mosquito population and establish a persistent infection, the group built contained cages in a remote area of North Queensland. The cages housed a realistic urban environment to mimic the mosquito’s natural surroundings. A garden path in the cage led to a raised porch area with light levels similar to under a mango tree. Attracted to the scent of sweaty towels from a local
fitness center, mosquitoes gathered beneath the boards of the artificial front porch and fed on human volunteers who entered the cages for 15 minutes every day. After showing that the strain of *Wolbachia* could in fact invade and establish in wild mosquito populations, the researchers faced an even more daunting challenge.

**O’Neill:** Our experiment would only work if members of the community were willing to have our mosquitoes, which were carrying this foreign bacterium inside them, be able to bite them, and their children, and members of the community. We explained what we wanted to do, and then we asked the communities how they wanted to be engaged and what did they think was required of us in order to demonstrate to them that it would be ok to proceed.

**PNAS:** It seemed a difficult proposition. When O’Neill polled an audience of several thousand scientists during his opening talk at the American Society for Microbiology conference in San Francisco, few seemed willing to support the release of *Wolbachia*-infected mosquitoes in their neighborhoods. But O’Neill says his team got a very different response.

**O’Neill:** If you live in a place where dengue’s a big problem, there’s a sense of fear of how to prevent yourself from getting dengue. So as a result, people are much more accepting of something like this.

**PNAS:** I asked O’Neill what’s next for his group.

**O’Neill:** So we’re establishing trial sites now in areas with much stronger dengue transmission; in three countries: Indonesia, Vietnam, and Brazil. And over the next few years, doing large set of trials to demonstrate the effect that we can get by reducing dengue transmission using this method. We’ve released a relatively small number of mosquitoes that carry the *Wolbachia*. Those mosquitoes go and mate with the wild mosquitoes and the *Wolbachia* infection then gets passed into the wild population. And then we’ve been tracking that population now for around 18 months, and over that 18 month period the *Wolbachia* is maintaining itself at 100% levels. So in those areas where the *Wolbachia* has become established, it is essentially dengue-proofed. And that dengue proofing should essentially sustain itself going into the future.

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