Commentary

Male mosquitoes make waves in paradise

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Invited Commentary on 'Open release of male mosquitoes infected with a Wolbachia biopesticide: field performance and infection containment', O'Connor et al.

While the 'neglected' mosquito-borne tropical diseases dengue and chikungunya often dominate attention, lymphatic filariasis continues to be a threat to over a billion people. The obvious subdivision provided by islands of the south Pacific provide what is arguably low-hanging fruit for a progressive mass-drug-administration program to eliminate this endemic disease, but this has met with surprising difficulty.¹

The usual hurdles of ensuring compliance and consistent program implementation contribute, but these are exacerbated by what is apparently a very efficient vector, even at low densities, *Aedes polynesiensis*. Often hiding in crab holes and rat-gnawed coconut shells, *Ae. polynesiensis* is protected from exposure to insecticides, so unconventional approaches to control are being considered including methoprene-impregnated baits that the crabs 'auto-disseminate' to their burrows² and fabric resting targets.³

Isolated island mosquito populations have traditionally been favorite targets for genetic control strategies, so the combination of a stubborn vector, a significant disease and hundreds of islands makes the south Pacific a perfect target. Stephen Dobson's lab at the University of Kentucky has exploited this opportunity to explore sexual sterility for control by infecting *Ae. polynesiensis* with particular *Wolbachia* endosymbionts. Unlike the population replacement goal of the Australia *Ae. aegypti* *Wolbachia* program,⁴ Dobson's lab is using *Wolbachia* solely for the male sterility that occurs when infected males mate with uninfected wild females. A similar approach has been used previously, most dramatically against *Culex quinquefasciatus*.⁵

O'Connor *et al.*⁶ have now reported the results of a field release of male *Ae. polynesiensis* infected (via introgression) with an *Ae. riversi* *Wolbachia*. This endosymbiont causes bidirectional sexual sterility when mated to wild *Ae. polynesiensis*. By releasing

approximately 100 000 carefully selected males, they were able to demonstrate population suppression on Toamaro atoll (French Polynesia) relative to two control sites. They also demonstrated that the likelihood of males transferring *Wolbachia* to *Ae. polynesiensis*, *Ae. Aegypti*, or *Ae. albopictus* is, at best, extremely low.

Essential to this approach is that females cannot be released (at least in large numbers) since they can cause population replacement rather than elimination. On the scale of production of this experiment, they were able to accomplish this and argue that replacement is not likely regardless. All results were good preliminary demonstrations of safety and efficaciousness.

In spite of arguments that population replacement is not likely, stringent removal of females will continue to be necessary until their inability to establish is demonstrated to be a fact. Considering this requirement, the main advantage of bi-directional sexual incompatibility over classical irradiation-based sterile male release may be good mating competitiveness: this was demonstrated.

This project revives an approach whose performance must compete head-to-head with other options for producing similar sterile-male effects: classical sterile insect technique and transgenesis. Critical to further development of the technology is the ability to successfully eliminate females on a large scale during production, a technology that is not yet available. However, continued development of such methods as this team has demonstrated should move ahead until their potential in area-wide programs is soundly assessed.

References

- 1 PacELF. The PacELF Way: towards the elimination of lymphatic filariasis from the Pacific: 1999–2005. Geneva: World Health Organization; 2006.
- 2 Lardeux F, Séchan Y, Faarua M. Evaluation of insecticide impregnated baits for control of mosquito larvae in land crab burrows on French Polynesian atolls. *J Med Entomol.* 2002;39:658–61.
- 3 Chambers EW, Bossin HC, Ritchie SA, Russell RC, Dobson SL. Landing response of *Aedes* (Stegomyia) *polynesiensis* mosquitoes to coloured targets. *Med Veterin Entomol.* 2013; doi: 10.1111/j.1365-2915.2012.01065.x.
- 4 Hoffmann AA, Montgomery BL, Popovici J, Iturbe-Ormaetxe I, Johnson PH, Muzzi F, *et al.* Successful establishment of *Wolbachia* in *Aedes* populations to suppress dengue transmission. *Nature.* 2011;476:454–7.
- 5 Laven H. Eradication of *Culex pipiens fatigans* through Cytoplasmic Incompatibility. *Nature.* 1967;216:383–4.
- 6 O'Connor L, Plichart C, Sang AC, Brelsfoard CL, Bossin HC, Dobson SL. Open release of male mosquitoes infected with a *Wolbachia* biopesticide: field performance and infection containment. *PLoS Negl Trop Dis.* 2012;6:e1797.

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