Let’s say we can force the mosquito into extinction — should we do it?

Not many people like mosquitoes. So why not eliminate them?

Newer techniques like CRISPR/Cas9 gene editing may make this possible. A new study by researchers at Imperial College London showed how CRISPR/Cas9 can generate a mutant gene that renders female mosquitos infertile, while males can spread the same mutation to offspring. Using a genetic tweak called gene drive, the scientists found they could extend the mutation in subsequent offspring at high enough rates to offset the effects of normal versions of the gene. This essentially wiped out the test population of Anopheles gambiae, a species of mosquito responsible for spreading malaria.

Malaria’s probably the last infectious scourge on earth that’s still unchecked by human efforts, killing about a half million people annually. The Imperial College study is not the first to try to eliminate the species, but so far seems to be the most effective.

That fact raises the question—if we can eliminate a species, should we?

The issue has jumped to the forefront this week at the United Nations biodiversity meeting in Sharm El-Sheikh, Egypt. Scientists supported by the Bill & Melinda Gates Foundation — which wants to use gene drives against mosquitos — warned about an effort to enact a global ban on field tests. In a Nov. 14 letter, they said:

> Closing the door on research by creating arbitrary barriers, high uncertainty, and open-ended delays will significantly limit our ability to provide answers to the questions policy-makers, regulators and the public are asking. The moratorium suggested at CBD on field releases would prevent the full evaluation of the potential uses of gene drive. Instead, the feasibility and modalities of any field evaluation should be assessed on a case-by-case basis.

We have been trying to use genetics to rid ourselves of pathogen-carrying pests since the 1940s. Some have been somewhat successful, but many not. In the mid-1960s, the screwworm fly, which killed cattle, was eradicated in the United States (and later Mexico and Central America). The eradication worked by raising hundreds of millions of sterile screwworms. The males were rendered sterile by irradiation that damaged germ line chromosomes. This became known as the SIT approach, short for sterile insect technique, and it worked in California and Florida on the Mediterranean fruit fly, and in some parts of Africa, the tsetse fly, which is a vector for sleeping sickness. But breaking chromosomes was a rather crude way to introduce species-killing traits to offspring.

Now, more precise techniques like Zinc Finger Nucleases, TALENS and of course the much simpler-to-use CRISPR have opened the door to more possibilities to eliminate species.

Yet even CRISPR has run into problems. Scientists quickly discovered that evolution could thwart attempts using CRISPR, through ordinary genetic variation, new mutations, and DNA repair, ultimately resisting efforts to edit the genome. The Imperial College team’s efforts were remarkable, however,

because they focused on a gene called *doublesex*, which determines a mosquito's sex and doesn't mutate in nature very much. So, when the team used CRISPR techniques to break the gene sequences in *doublesex*, little to no resistance arose and entire populations died by the eighth generation.

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Opposition to this new wave of species selection and forced extinction has arisen since CRISPR entered the gene drive arsenal. Even the developer of gene drives (in our modern sense), Harvard scientist Kevin Esvelt, has expressed reservations about using them in germ cells, or even conducting some research without public consultation — something that rarely plays a role in designing experiments.

A number of conservation groups, most notably Friends of the Earth and ETC, openly called for a moratorium on gene drive work. In 2016, 30 groups published a letter asking for such a moratorium:

> We believe that a powerful and potentially dangerous technology such as gene drives, which has not been tested for unintended consequences nor fully evaluated for its ethical and social impacts, should not be promoted as a conservation tool.

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The groups also have appealed to the United Nations Convention on Biological Diversity, which so far has not backed a moratorium, but is scheduled to meet on the subject in December.

Many scientists counter these objections. One defense against the objections is the deadliness of malaria itself. The disease has few effective treatments, and kills more than 400,000 people in sub-Saharan Africa and India (mainly) each year. Advocates also argue that gene drives will really work only in organisms with fast reproductive cycles, limiting it to fast-breeding invertebrates and unicellular organisms, not mammals (or people). Jonathan Pugh, a philosopher/ethicist at Oxford University, wrote in the *British Medical Journal* recently that:

> The first objection invokes the concept of the 'sanctity of life' in order to claim that we should not drive an animal to extinction. In response, I follow Peter Singer in raising doubts about general appeals to the sanctity of life and argue that neither individual mosquitoes nor mosquitoes species considered holistically are appropriately described as bearing a significant degree of moral status.
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> The second objection claims that seeking to eradicate mosquitoes amounts to displaying unacceptable degrees of hubris. Although I argue that this objection also fails, I conclude by claiming that it raises the important point that we need to acquire more empirical data about, inter alia, the likely effects of mosquito eradication on the ecosystem, and the likelihood of gene-drive technology successfully eradicating the intended mosquito species, in order to adequately inform our moral analysis of gene-drive technologies in this context.

One of the concerns about gene drives, even among scientists stems from the fact that once a gene drive is inserted in an organism, it's almost possible to stop using current techniques. To address this, Esvelt developed what's been called the Daisy Drive. Esvelt's Daisy Drive might be self-limiting enough to avoid perpetuation problems with current gene drive. With the Daisy Drive, the various components necessary for CRISPR-based perpetuation (aka, "gene drive"), isn't in one place on the genome. Instead, the CRISPR- altered length of DNA, and guide lengths are in different places and need to be copied separately. This provides greater control than conventional gene drives. Another group, at the universities of Cardiff and Bath, also found a technique that could put brakes on gene drives, when necessary. In this case, the Cas9 protein part of CRISPR/Cas9 depends on the existence of another protein, called BOC. By controlling the presence of BOC, gene drives can also be controlled.

Which helps relieve much of the scientific doubt.

Yet the case of whether or not to eradicate an entire species of mosquito (or a species we actually like) has not yet been convincingly made.

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