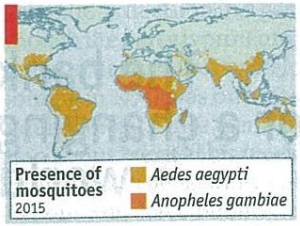
Extinctions to order

Gene-ocide

The promise and peril of "gene drives"



IN A competition to find the world's least-loved animal, the mosquito would be hard to beat. Only a few species of the insect carry the parasites that cause human diseases such as West Nile virus, dengue and yellow fever, but the harm they cause is enormous. Malaria kills more than 400,000 people, mostly children, every year. Zika has spread to dozens of countries (see page 69). If species such as *Anopheles gambiae* and *Aedes aegypti* could be eradicated, the world would surely be a better place.

Genetic engineers have already taken some steps in that direction: male *A. aegypti* mosquitoes that have been modified to become sterile have been released in Brazil, for example. Such approaches, controversial though they are among some greens, are limited in their impact and geographical range. A nascent technique called a "gene drive", which could make it far easier to wipe out species, raises harder questions.

The term refers to the engineering of genes so that they are almost guaranteed to be inherited by offspring (the conventional laws of inheritance predict that offspring have only a 50% chance of inheriting a specific gene). You might, say, be able to engineer *A. gambiae* to produce only male offspring, release the modified bug into the wild and extirpate the entire ▸▸

▸ species.

The use of gene drives in the wild is not imminent. But the research is proceeding rapidly, thanks to new gene-editing technology and to some lavish funding: this month the Bill and Melinda Gates Foundation said it would increase its investment in gene drives to $75m. Mosquito species are the main targets, but need not be the only ones. Some wonder if gene drives could be used on the ticks that carry Lyme disease, or to change the genetic makeup of bats, a reservoir of infectious diseases. As interest grows, however, so do the concerns.

Dodos and don'ts

Some take an absolutist stance: it is morally wrong to take a deliberate decision to eliminate any species, however unpleasant. Try explaining that piece of armchair ethics to the people who still suffer from horrors such as bilharzia and Guinea worm. The eradication of smallpox in 1980 was a monumental advance in public health. The removal of the malaria parasite would be bigger. If *A. gambiae* has to go with it, then tough.

There are other, more powerful causes for concern. One is that the impact of getting rid of a species is hard to predict. The mosquito that just fed on a person's arm may go on to feed a swallow. The absence of one bug might lead another to thrive. However carefully scientists model the impact of gene drives, the risk of unintended consequences looms large in complex ecological systems. Another worry is that gene drives could be used for evil: a mosquito could just as well be engineered to be more suited to carrying deadly diseases, for example.

That argues for two guiding principles in the use of the technology: reversibility and consent. Reversibility means that no species should be driven extinct in the wild without the means to reconstitute it. Colonies of unaltered organisms must always be retained, so that they can be reintroduced.

The second principle concerns consent. The presumption behind the regulation of genetically modified organisms is that their spread can be contained. The Cartagena Protocol on Biosafety allows a country to refuse entry to a GM crop, for example. Such rules will not contain gene drives, which will spread across borders without permits. A decision by one nation, or one group, to release them might eventually affect every country where the species exists. Governance arrangements must be international from the start.

The power of gene drives demands proper debate. Ensuring that the technology can be thrown into reverse, and that its use is subject to international monitoring and co-ordination, would make it easier to unlock its vast potential for good. ■

The next article has the latest stuff on ZIKA written in a "common dog" style – i.e. it is readable and understandable

The Zika virus

A mystery no more

Scientists have learned a great deal about Zika since the outbreak began. Now for the task of stopping it

A YEAR ago, most people would have drawn a blank if asked about Zika. Since then, an outbreak of the mosquito-borne virus that began in early 2015 in Brazil has spread to more than 60 countries in the Americas, Africa, Asia and the Pacific islands (see chart on next page). A study published on September 1st in the *Lancet* estimates that 2.6 billion people live in areas to which Zika could eventually spread.

At first, scientists knew little more than anyone else. Zika is not new; the virus was first isolated in Africa in 1947. But it was obscure, and therefore little studied. Only during the present outbreak did it become clear that infection among pregnant women was associated with birth defects and neurological problems in babies. But there has been much progress, and scientists now know far more about the disease than they did when the outbreak began.

Start with transmission. The vast majority of Zika infections occur through the bite of *Aedes aegypti*, a mosquito common in tropical climates and especially in cities. Another species, *A. albopictus*, which thrives in cooler climes, may also be able to transmit the bug, though possibly not as efficiently. Unusually for a mosquito-borne virus, Zika can also be transmitted sexually (the first case of transmission in the United States occurred this way). Studies are under way to find out how long after infection that remains possible, but traces of the virus's genetic code have been found in semen six months after the onset of symptoms. Infection through blood transfusion has been confirmed as well. The virus has also turned up in urine, tears and saliva, though that does not necessarily mean that it can spread through them.

The health effects of the virus are becoming clearer too. Something like four in five Zika infections cause no symptoms. The rest usually pass with only mild discomfort, including a rash and red eyes. Occasionally, infected people develop Guillain-Barré syndrome, a condition in which the immune system goes awry, causing weakened muscles and temporary paralysis. Death is rare, but some sufferers spend weeks hooked to a breathing machine.

Infection is also dangerous if it occurs during pregnancy: in perhaps 1-2% of cases the virus attacks the brain tissue of the fetus. That causes microcephaly, a condition characterised by an abnormally small head, a result of the skull collapsing around the shrunken brain. Babies who escape that fate may suffer other Zika-related damage, including eyesight and hearing loss. Scans of apparently healthy babies born to infected mothers sometimes show brain abnormalities, though it is too early to know whether these will lead to developmental problems later in life. And there are worries, as yet unresolved, about the neurological implications in adults, too.

Then there is the question of tracking and diagnosis. Working out just how far

that are then recognised by the immune system. DNA is much easier to handle than weakened or dead viruses; and by focusing on genetic sequences common to different variants, a vaccine may offer protection against several strains of the virus. If all goes well, large-scale trials could begin early next year, with results by mid-2018.

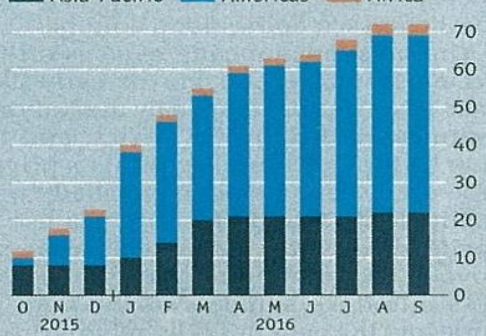
By contrast, efforts to cull mosquitoes have been less successful. *Aedes aegypti* is a hardy creature, happy to breed in water pools as tiny as a bottle cap; it has also learned to live indoors, in nooks where outdoor spraying cannot reach it.

So the hunt is on for other ways to limit mosquito numbers. One is to unleash mosquitoes pre-infected with *Wolbachia*, a bacterium that impairs their ability to transmit Zika, and makes males sterile. The hope is those males will mate with wild females but produce no offspring, shrinking the size of the next generation. An alternative is to release mosquitoes sterilised with radiation, though this may make them less appealing suitors. Oxitec, a British firm, has developed genetically modified *Aedes aegypti* whose offspring die before reaching adulthood; in trials, releasing them into the wild has cut mosquito counts by 90%.

The trouble with such ideas is that they give evolution a powerful incentive to select its way around the problem. Over time, that could make them less effective. One option that might avoid that problem is a "gene drive", a new technique that tweaks genomes in a way that ensures that the modified, damaging traits are inherited by all of a mosquito's offspring. Gene drives are highly controversial: if they work, they could give humans the power to wipe out—with minimal effort—any species that engages in sexual reproduction. They are also experimental and confined to labs; no one knows how effective they would be in the wild. Last week the Bill and Melinda Gates Foundation, a charity, announced it would boost its funding of gene-drive research to $75m. That will speed up the work—and the debate about deliberately wiping out a species. ■

The flies have it

Number of countries and territories reporting mosquito-borne Zika transmission, cumulative



Source: World Health Organisation

Also in this section

70 Similarities in language
70 Precision agriculture
71 Food and illness
72 An AI autopilot

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Zika has spread within a country is tricky. A common test works by testing for antibodies, specialised proteins produced by the immune system that are designed to disable the virus. But it cannot distinguish easily between antibodies for Zika and those for dengue fever, another mosquito-borne illness, which is related to Zika and often occurs in the same sorts of places. That may turn out to be a good thing: antibodies against dengue may provide some defence against Zika. But it muddles attempts to track the disease, and to predict how it might spread.

Two open questions are whether a Zika infection confers lasting immunity to the virus, and how strains from the two known lineages—one African and one Asian—might interact. There are reasons to worry: an initial infection with one of the four strains of dengue is usually harmless, but subsequent infection with another strain can be fatal.

An ounce of prevention

Official advice continues to evolve with the stream of new findings. Preventing mosquito bites is the main line of defence. The World Health Organisation prescribes condoms or sexual abstinence for at least six months for those returning from areas where Zika is spreading. Several countries have begun screening blood donors.

The most encouraging news is on the vaccine front. Several are in early-stage trials. Two—one developed by the National Institutes of Health in America, and the other by Inovio Pharmaceuticals, a private firm—use a new technology called "DNA vaccination". Traditional vaccines use either dead viruses or weakened live ones to provoke an immune response. DNA vaccines introduce snippets of the viral genome into the patient's cells, relying on the cells themselves to produce viral proteins ▸▸