No MORE Mosquitoes?

Scientists are hacking mosquitoes' biology in a battle against these disease-carrying pests

LAB-GROWN INSECTS
A lab facility in China raises mosquito larvae (*inset*) as part of research into reducing disease transmission.

SHUTTERSTOCK.COM (MOSQUITO); KEVIN FRAYER/GETTY IMAGES (LAB); DEAN CALMA/IAEA (LARVAE)

AS YOU READ, THINK ABOUT the pros and cons of eliminating certain types of mosquitoes from an environment.

One morning this past November, biologist Nsa Dada woke up feeling sluggish.

At first, she figured she'd stayed up too late the night before. But she quickly grew weaker and soon spiked a fever. "I couldn't stand. I couldn't eat. I couldn't do anything," she recalls.

Dada had recently visited relatives in the West African country of Nigeria. During the trip, she'd been bitten by mosquitoes—the very insects she studies. For most people in North America, mosquito bites are an itchy annoyance. But in many other parts of the world, the insects represent a deadly threat. When Dada became ill, "I knew immediately that I might have *malaria*," she says. Malaria is a serious flu-like illness caused by *Plasmodium* parasites, which are carried by certain mosquitoes. When the insects bite, they pass the parasites to people.

Malaria is one of the most dangerous diseases that mosquitoes transmit. In 2020 alone, malaria infected an estimated 241 million people across Africa, Asia, and Central and South America, and killed about 627,000. In Africa, where most cases occur, children under 5 account for three-quarters of malaria deaths. The problem is particularly bad in rural areas, where people don't have easy access to medical care.

Fortunately, Dada received medication to treat the illness and recovered. But the ordeal was a reminder of why she studies mosquitoes. She and other scientists are working to find ways to stop mosquitoes from making people sick. Some even hope to eliminate populations of the pests entirely.

BEHIND THE BITES

Not all mosquitoes are bloodsuckers. Only some adult females bite. Males and females feed mainly on plant nectar. But females of most species need protein from blood to produce eggs. They locate victims by sensing carbon dioxide gas exhaled by humans and other animals. A female mosquito can do this from 10 meters (32 feet) away, says Craig Montell, a neuroscientist who studies mosquitoes at the University of California, Santa Barbara.

Once the mosquito finds a target, the sight, smell, and heat of a person's skin help guide the bug in for a landing. The insect pierces the skin with its *proboscis*, a needle-like mouthpart, and extracts its blood meal. As it feeds, it injects saliva. The saliva contains chemicals that keep blood flowing so the mosquito can continue drinking. Our bodies react to these substances by producing itchy welts. If the mosquito carries any *pathogens*—disease-causing organisms like viruses and parasites—those can enter the victim, too.

Continued on the next page →

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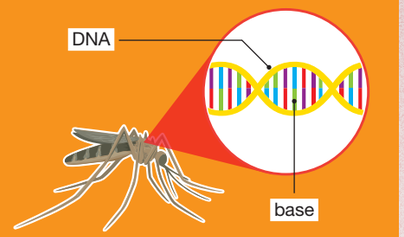
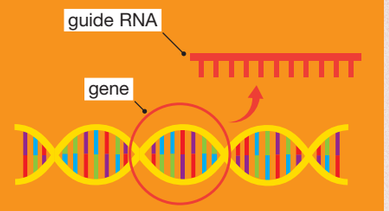
REWRITING THE CODE

Scientists have created a tool called CRISPR (pronounced "crisper") that allows them to edit the *DNA*, or hereditary material, of an organism such as a mosquito. Here's how it works.

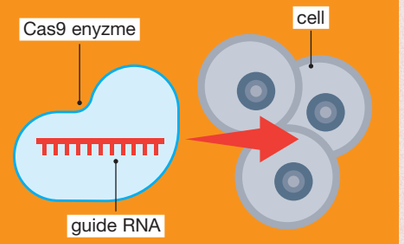
1 A mosquito's cells contain DNA. It consists of two twisted strands made up of connected molecules called *bases*. The order of these bases acts as the code that determines the mosquito's traits.



2 Scientists identify the *gene*, or section of DNA, that they want to change. They create a piece of *guide RNA*—a molecule similar to DNA but made up of a single strand—that matches the sequence of bases in that gene.



3 The scientists inject the guide RNA into mosquito eggs along with an *enzyme*—a large molecule that causes chemical changes within cells. The enzyme, called Cas9, is capable of cutting a DNA strand.



4 The enzyme binds to the guide RNA, which helps it find the target gene in the cell's DNA. The enzyme separates a portion of the DNA's two strands. The RNA holds the enzyme in place while the enzyme snips through both strands of DNA.

5 Once the DNA is cut, other molecules the scientists have injected can add or remove bases. The cell naturally repairs the cut DNA, stitching the gene back together with the new sequence in place. The mosquito will now have traits determined by the new sequence.

OFF THEY GO: In 2018, scientists used a drone to release mosquitoes unable to produce offspring in Brazil to help reduce the bug population.

FLYING FREE: A scientist releases mosquitoes as part of a field test studying ways to reduce disease transmission in Florida in 2018.

Besides malaria, mosquitoes transmit diseases including yellow fever, dengue fever, West Nile virus, and Zika virus. If a mosquito bites someone who has any of these illnesses, it can pick up the pathogens and then infect people it bites in the future. By some estimates, mosquito-borne diseases have killed nearly half of all people who have ever lived, says Montell (*see Deadly Animals, right*). "We have a lot of reasons to want to restrict the ability of mosquitoes to bite us," he says.

STOPPING THE SPREAD

For decades, people have relied on *insecticides* to control mosquitoes. These insect-killing chemicals can be sprayed in areas where mosquitoes breed or rest. Insecticides are also applied to protective netting that people can hang over their beds. Since 2000, governments and nonprofit organizations have distributed more than 1 billion treated bed nets in Africa, Asia, and South America. This has reduced the rate of malaria significantly. But over time, insecticides lose their effectiveness. Dada will soon begin work at Arizona State University, where she'll continue studying how mosquitoes develop *resistance* to these chemicals. That could help determine better approaches for managing mosquitoes.

Some scientists hope to reduce the insects' ability to transmit disease. In Australia, Brazil, and Indonesia, researchers have infected mosquitoes with *Wolbachia* bacteria, which reduces the transmission of dengue fever to people. In the wild, those infected mosquitoes pass the bacteria to their offspring, further halting the spread. In some areas, this strategy has cut cases of dengue fever by more than 75 percent. Scientists are studying whether the same bacteria can stop other mosquito-borne diseases too.

LUNCHTIME: A researcher in Australia provides a blood meal to mosquitoes—a common feeding technique in labs that raise the insects.

DEAN CALMA/IAEA (DRONE); LYNNE SLADKY/AP IMAGES (TUBE); STEVE MORTON/MONASH UNIVERSITY (LAB)

Other researchers are altering mosquitoes' *DNA*—the molecule that carries hereditary information (*see Rewriting the Code, p. 15*). Scientists have modified male mosquitoes with *mutations*, or genetic changes, that make them unable to produce offspring. Montell's lab is exploring genetic changes that disrupt mosquitoes' senses. That could make it harder for the insects to find humans. Omar Akbari, a geneticist at the University of California, San Diego, is experimenting with genes that could make mosquitoes less likely to harbor pathogens. "We're engineering the mosquitoes to do what we want," he says.

GOOD RIDDANCE?

Last year, the British company Oxitec conducted the first field test of genetically modified mosquitoes in the United States. Researchers released 750 million male mosquitoes in the Florida Keys to combat dengue and Zika. The males carried a newly introduced *gene*, or unit of hereditary material, that prevents their female offspring from hatching. Similar trials in Brazil, the Cayman Islands, Panama, and India have successfully reduced mosquito populations. Opponents argue that this approach could have unintended consequences for ecosystems. But Akbari hopes more research will make the release of modified mosquitoes a safe, accepted strategy.

Is there a downside to killing off disease-spreading mosquitoes? Akbari doesn't think so. There are more than 3,200 mosquito species, he points out, and control efforts target only the few that pose a threat to human health. Animals that eat the insects could switch to other bugs for food. But some scientists argue that ecosystems are complex, so it's difficult to predict the effects of wiping out an entire species.

In Africa, where mosquito-borne diseases are rampant, controlling the insects would make an enormous difference, says Dada. Some people in vulnerable areas restrict their activities to reduce their risk of bites. With fewer mosquitoes, "they wouldn't have to worry about getting sick when they go out to gather wood in the forest, work on their farms, or chat outside in the evening," she says. "We would have healthier, happier people."

—Mara Grunbaum

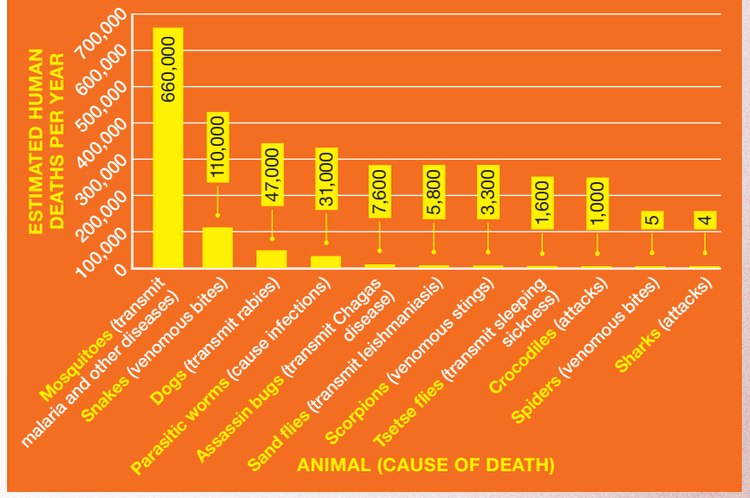
COMMUNICATING INFORMATION: Why are scientists searching for new ways to control mosquito populations?

WIDESPREAD PEST: The southern house mosquito transmits several diseases and is found in warm regions around the world, including the southern U.S.

CDC (MOSQUITO)

DEADLY ANIMALS

By transmitting malaria and other infectious diseases, mosquitoes cause more human deaths than any other animal. Here's how they compare with some other species.



SOURCES: WORLD HEALTH ORGANIZATION, PLOS NEGLECTED TROPICAL DISEASES, CROCBITE WORLDWIDE CROCODILIAN ATTACK DATABASE, UNIVERSITY OF FLORIDA