

Engineered Mosquitoes

- So far, genetic engineering of mosquitoes has focused on the species of mosquito that transmits another mosquito-borne disease called dengue fever, because it is only transmitted by one species. Malaria is more difficult because it is transmitted by four different species.
- Oxitec, a British biotech company, has engineered the dengue-transmitting mosquito, causing the offspring of engineered mosquitoes to die before adulthood. Oxitec releases millions of engineered male mosquitoes to breed with wild females.
- Bites from engineered females have not affected lab animals any differently than bites from wild females.
- Genes in nature are sometimes more likely to be passed on to offspring than the expected 50/50 chance. Scientists have figured out a way to use this feature to make something called a *gene drive*, which could pass on engineered traits in mosquitoes that would then spread quickly through the population.
- When an organism inherits a gene drive from only one parent, it can force the cell to copy the gene drive to the other chromosome.
- Engineered mosquitoes have been released in the Cayman Islands (2009), Malaysia and Brazil (2011), Panama (2013), and China (2015).



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Dengue fever is only transmitted by one species of mosquito

Gene Drives

Most genes have a 50% chance of being inherited, but some genes in nature have evolved ways to beat the odds. By using elements of these genes, engineers have developed gene drives. Genes with gene drives spread through the population over several generations, even if they are not helpful for the organism.

One type of gene drive copies itself onto chromosomes that don't already have the gene drive. When an organism inherits this gene drive from one parent, it cuts the chromosome from the other parent, forcing the cell to copy the gene drive and any adjacent genes when it repairs the damage.

Previous Releases of GE Mosquitoes

1. Oxitec released GE mosquitoes in 2009 on Grand Cayman Island, killing 80% of the mosquitoes that transmit dengue fever. These mosquitoes have since been released in Malaysia,

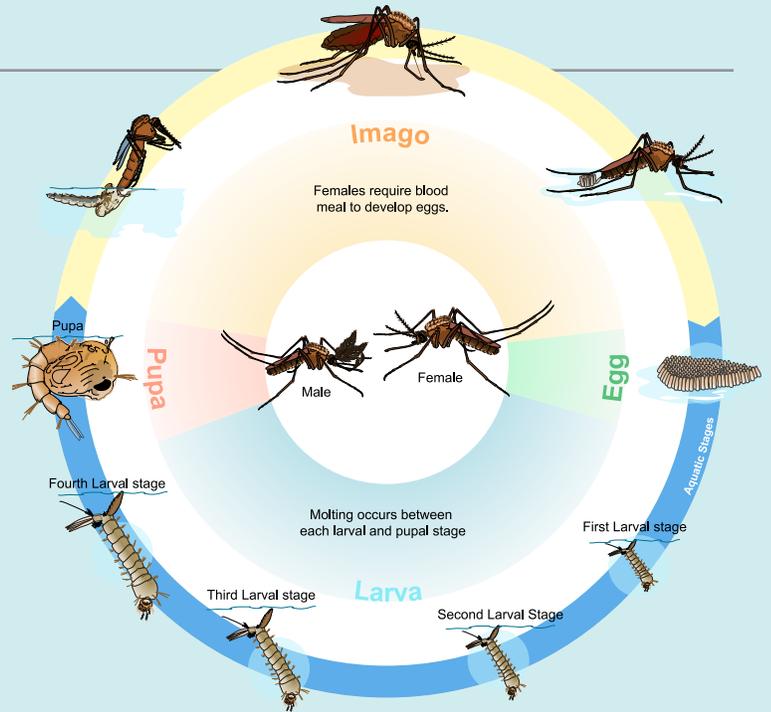
Brazil, and Panama, and there are plans to release them in Florida. The Caymans and Brazil have ordered larger-scale projects. As of spring 2016, Florida has delayed the release due to ethical, environmental, and social concerns. By early 2015, Oxitec had released 70 million engineered mosquitoes around the world with no reports of negative human impacts.

2. In 2011, a group at the University of California, Irvine, engineered female mosquitoes to be flightless. The female adults hatch on water and cannot fly away. Males fly away, mate with wild females, and pass on the engineered genes. This method was ineffective in cage-based testing in Mexico because the males were not good enough at mating.

3. Starting in 2015, China began releasing 1 million modified mosquitoes into the environment every week, after a record-high number of cases of dengue fever were reported in 2014, reducing the mosquito population by 90% on an island trial.

Mosquito Information and Life Cycle

- Mosquitoes transmit many deadly diseases, including malaria.
- Only a small percentage of species of mosquitoes bite humans.
- Some mosquitoes may serve an important purpose in the ecosystem.
- Only female mosquitoes bite humans and need to eat blood to produce eggs. Males never bite humans.
- The mosquito goes through 4 stages in its life cycle: egg, larva, pupa, and adult. Males live for a week in the adult stage, while females can live up to a month.
- To mate, males form swarms around dusk and females fly into the swarms.



Mosquitoes lay eggs on water

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Mosquitoes and Disease

Mosquitoes are the deadliest animal on the planet. Mosquitoes carry malaria, yellow fever, dengue fever, Japanese encephalitis, Rift Valley fever, Chikungunya virus, Zika virus and West Nile virus.

There are 3,500 known species of mosquito, but only a few hundred species bite or bother humans. Four of these species transmit malaria.

Mosquitoes live in all types of habitats and may serve important roles in those ecosystems. All species require water for their life cycle.

Most *Anopheles* mosquitoes (the species that transmits malaria) are crepuscular (active at dusk or dawn) or nocturnal (active at night).

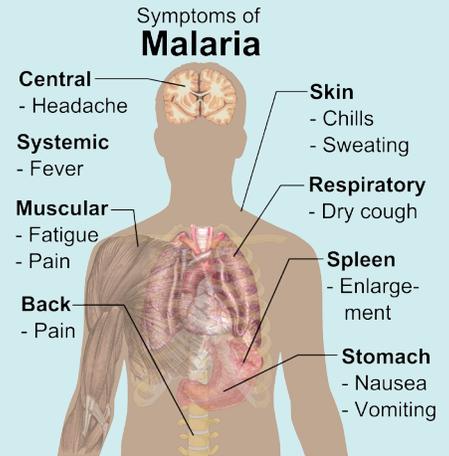
Life Cycle Details

Generally, both males and females are pollinators and consume nectar. Males live for about a week and never bite humans. Only female mosquitoes bite humans, because they need a blood meal to produce eggs.

After eating a blood meal, the female rests for a few days and digests the blood while the eggs develop. This process usually takes 2-3 days. Once the eggs are fully developed, the female lays them and looks for another meal. The cycle repeats itself until the female dies. Females can survive up to a month but usually do not live longer than 1-2 weeks.

Malaria and Traditional Control Methods

- Mosquito control is the main way to reduce malaria transmission, including insecticide-treated bed nets and insecticide spraying.
- Malaria is transmitted by female *Anopheles* mosquitoes. Females need blood meals to produce eggs. Unlike humans, the mosquito does not suffer from the presence of the parasites.
- A study of the main species that transmits malaria found that no other species depends on this species of mosquito, but it is unclear how eliminating a species of mosquito would affect the environment.
- Mosquitoes are developing resistance to insecticides and may be adapting to bite earlier in the evening, when people are not protected by bed nets.
- Drug therapies are effective against the most common malaria parasite, but the parasite is developing resistance to the drugs.
- Children under five are particularly susceptible to malaria.
- Malaria during pregnancy carries risks for the mother and child.



Malaria affects many parts of the body



Traditionally, bed nets are used to protect against mosquito bites

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Mosquitoes and the Environment

In general, mosquitoes might be important in ecosystems, but the only study of the main species that transmits malaria found that no other species depended on this species of mosquito. Eliminating one mosquito species might have little impact on the food chain and environment.

Traditional Control Methods and Insecticide Resistance

Insecticide-based control measures (indoor spraying with insecticides and bed nets) are the principal way to kill mosquitoes that bite indoors. DDT application and insecticide-treated bed nets have been used to suppress malaria by reducing the mosquito population.

After generations of exposure to insecticides, mosquitoes may develop resistance, meaning insecticides won't kill them. Since mosquitoes have many generations per year, resistance can arise quickly. Insecticide resistance has been documented

within a few years after introduction, including in Kenya. Mosquito nets work because malaria-carrying mosquitoes feed inside at night, but mosquitoes are adapting to eat earlier and outdoors.

Malaria and Drug Resistance

Drugs are highly effective against the most common malaria parasite. However, the rapid spread of drug resistance threatens progress in malaria control. Already, parasite resistance to the best medicines has been detected in 5 countries in Asia.

Young children are particularly susceptible. In 2015, malaria killed an estimated 306,000 children under age five.



Three out of 4 malaria deaths occur in children under five

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