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Uganda, Infectious Diseases

Uganda: The Effects of Malaria

Imagine that you wake up tomorrow morning and instead of being in your warm comfy bed with a roof over your head, you wake up on the floor with an imprint of your hip in the dirt from how you slept, and a straw roof leaking in the foggy morning air. Instead of going to brush your teeth or take a shower, you immediately get up to start collecting what little wood you can find for a fire to cook all of your food that day. You live in fear of whether or not you will be able to provide for your family, or even yourself, and hope no one gets sick from drinking the unclean water. This is the reality that contributes to food insecurity Ugandans face every day.

One of the major factors of food insecurity is infectious disease. The most common infectious disease in Africa is malaria, with 10.3 million cases in Uganda alone. Dark skinned people are more susceptible to the disease than light skinned people, which is why it is so common in Africa. Malaria is a mosquito-borne disease caused by the bites of parasite infected mosquitoes of the Anopheles genus. (World Health Organization, 2016). Of the four different malaria-carrying species, the female mosquitoes are the only ones which can transmit the disease. The female mosquito can become a parasite host when it bites an infected person. Common malaria symptoms include high fever, shaking chills, headaches, vomiting and fatigue, which are all similar to flu symptoms. The symptoms have to be caught within 24 hours for treatments to be effective. Malaria hits developing countries hardest because they do not have the technology or funding to prevent or treat it. According to *Building with Biology: Should We Engineer the Mosquito?,* in 2015, over 400,000 people died globally from malaria infections, and nine out of every 10 cases and deaths occurred in Africa. The majority of these deaths impact children and people living in poverty. These families struggle to have enough money to carry out their daily lives, like buying food and necessities, they especially do not have enough money to treat such a severe disease. However, drug resistance has already developed in southeast Asia and there is a high probability that it will become widespread in Africa, also. Food insecure families lack enough money to treat a malaria case, and if people begin to become resistant to the drugs, treatment prices will likely rise. Finding a reasonable, feasible and efficient answer to this problem is critical. Therefore, genetically modifying the mosquito would be an ideal solution to the malaria-endemic that Africa is experiencing.

Uganda is located in Eastern Africa, bordered by South Sudan in the north, Kenya in the east, Rwanda and Tanzania in the south, and the Congo in the west. It is a little over half the size of California but holds two million more people than California. The population of Uganda is 40,853,749 people. (CIA, 2018). Kampala, the capital city of Uganda, houses the majority of the urban population. The rural population outweighs the urban population by 76.2%. Of the rural land, 71.2% is cultivated for agricultural purposes. One-third of Uganda's population is living in poverty. Most Ugandan families grow their own food; only 3.73 acres are used nationally for production and crops. Agriculture plays a crucial role in the livelihoods of many Ugandan families. Because most people grow their own food and animals on a private farm, the agriculture industry is dominated by small farmers. A farm size in Uganda can range from 2.4 acres to 13.2 acres. Their most prominent cash crops include coffee, tea, cotton, tobacco, and cocoa. Farming these crops is a vital source of income for many poor families.

A typical Ugandan family has five children. Most people fail to use modern contraception, or any at all resulting in the high fertility rate of 5.8 children per woman. Women also get married at a very early age, typically before age 18, therefore many women bear children earlier in life. After marriage, women usually move into the husband's family home. Some of their daily duties include cooking meals, taking care of the children, farming, and carrying water. The women are responsible for 70%-80% of all crop and animal production, after production they process and cook up to 90% of the food their family will consume. Boys ages 12 and up are not allowed in the kitchen, and the girls and women do all of the cooking. Cooking is done over an open fire using primarily firewood, charcoal, or manure. For families who cannot afford gas or electricity, the kitchen is separate from the main house. This hut is built to keep smoke and fumes from the fire away from the main house. On a typical day, Ugandans will eat two meals: lunch and dinner. On occasion they will have tea and porridge for breakfast. Some common foods in a typical diet include posho (polenta), beans, tomatoes, mangoes, rice, sorghum, millet, goat, and fish. The female role is vital in the home, it is critical that they remain as healthy as possible. These nutritious foods that they cook contribute to the overall health of the family.

Most job opportunities are related to agriculture, industry, or services. Minimum wage is $7.25 an hour; however, it is rare for a poor family to ever get the opportunity to have a job that pays this high. The average annual wage of one of the most common middle-class jobs, an accountant, in the capital city of Kampala is $18,178. Some of the highest paying jobs in Uganda include a pilot, engineer, doctor, construction manager, and accountant; however, these jobs could never be filled by women or poor Ugandan citizens due to the credentials these jobs require. Food insecure families and women usually have little to no education because it is difficult to have time for an education when all of a family's time has to be put into survival. Some citizens who are fortunate enough to receive an education don't finish school completely. Only 70% of the country is literate, and the men and urban populations make up the greater portion of this group.

On October 9th, 1962, Uganda gained their independence from British rule. The initial government implemented in Uganda after gaining independence consisted of monarchial districts and a central government. Uganda later adopted a republican constitution and elected a president. A republic is governed by representatives elected by the people, these officials then hold the power to make decisions beyond the electorate level. The Ugandan government system is very similar to the United States' three-part system, with an executive, legislative, and judiciary branch. There are also 121 local district governments, where Ugandan citizens have the ability to vote for a district chairperson who they think will make the decisions they want for their country. This would allow for someone to present an idea at the district level so the district chairperson could further act upon it with their fellow chairpersons.

There are several contributing factors to the widespread malaria cases lower class families face, including unclean conditions, crowded living, and tropical climate. The unclean conditions of Uganda affect many aspects of its citizen's lives. The high population, high fertility rate, and tropical climate all contribute to how quickly disease can spread. Malaria is the most common infectious disease in Africa, and it is most prominent in sub-Saharan countries. People living in close proximity to each other leads to the improper disposal of waste, therefore leading to a larger breeding ground for mosquitoes in the unclean water. Unclean water is a huge problem facing food insecure areas and families. The first step to creating and sustaining food security is having a clean source of water. Clean water is fundamental for growing food and living healthy lives. The higher the population of mosquitoes, the greater probability for someone to get bit by one that is infected with the parasite, *Plasmodium*. Malaria is not contagious, but it can be transmitted through blood transfusions, organ transplants, or sharing blood contaminated needles or

syringes (Centers for Disease, 2019). Infected women who are pregnant could also give their unborn infant malaria, this is called “congenital” malaria. This is one reason that the high fertility rate in Uganda contributes so much to the 10.3 million cases in Uganda alone. The disease is also more fatal to infants and children because their bodies are not strong enough to combat the affects that is has on their bodies, or they may be too young to take the antimalarial drugs. More than two-thirds of all malaria related fatalities occur to children under age five (World Health Organization, 2016).

Several preventatives are already in place in malaria susceptible countries, including Uganda, one example being the insecticide treated bed nets. Their purpose is to repel mosquitoes and protect people from mosquito bites while they sleep. Although these bed nets are somewhat effective while people sleep, they do not protect people from bites during the day. Some other solutions that have been implemented to prevent the spread of malaria include antimalarial drugs, usually in pill form, and spraying to kill mosquitoes. Several mosquitoes are adapting to the use of insecticides and drug therapies, resulting in stronger insecticide potency along with a greater number of mosquitoes. This poses a risk of contaminating water sources, air, land, and other organisms in the ecosystem, while also not making progress towards lowering the risk of contracting malaria. The more mosquitoes present in homes and communities put people at a higher risk of getting bit by an infected mosquito. But what if there was an efficient and inexpensive solution that could dramatically reduce malaria transmission or even completely end malaria? Scientists have developed a system called a gene drive where they use foreign DNA or the CRISPR/Cas 9 system to genetically engineer organisms.

Engineering the male mosquito was the first process to work towards decreasing the number of potentially infected mosquitoes. The male engineered mosquitoes carry a gene that means their offspring will die during development unless they are fed a necessary chemical that is only available in the lab (Building with Biology, 2016). The engineered males are released to mate with wild females, and their offspring will inherit the lethal gene. This results in the imminent death of the offspring. However, scientists found that some genes in nature have higher than a 50/50 probability of being passed on to offspring, therefore, these more prominent genes are ideal to engineer gene drive systems. A gene drive is taking an altered gene and adding another piece of the desired trait to the DNA to guarantee a 100% chance of passing it on. Genes with gene drives would be inherited through fewer generations due to having two copies of the preferred gene present rather than one. Typically, the altered gene plus the gene drive becomes effective throughout the entire population within 2-3 breeding cycles.

In this specific situation, there are two different targets to a gene drive: the mosquito or the parasite. If the gene drive targets the mosquito, the new gene written in their DNA will cause the males to become sterile, which means they will not be able to breed with the females, potentially reducing the mosquito population of that specific species. Female mosquitoes bite to provide nutrients for their growing eggs, if males cannot mate with the females, there will be no offspring to feed, resulting in less mosquito bites. This will likely permanently reduce the mosquito population, which with a small enough population, malaria cannot be transmitted (Building with Biology, 2016). Side effects of this gene drive would be how it affects other mosquito species that eat and interact with the altered species, and it could impact ecosystems and food chains. If the gene drive targets the malaria parasite that lives inside the mosquito, it would inhibit the mosquito from being able to host the malaria parasite. Targeting the malaria parasite should only affect this individual mosquito species and not any other animals. The species will also still be present in the ecosystem. However, some complications might include the malaria parasite developing a resistance to the altered gene and returning in a few years. Scientists also do not know to what extent altering the malaria parasite would affect other mosquito species, the altered gene might be inherited by mosquitoes of the same genus. Scientists have suggested that if any issues were to occur with either one of these gene drive systems, then they could release a second gene drive to reverse the results of the first

gene drive. The population would function the same as before the first gene drive, but the second gene drive would still be present in the DNA.

Mosquitoes of other species have been engineered for other mosquito-borne diseases, such as the Zika virus and yellow fever. They have been released in the Cayman Islands, Malaysia, Brazil, China along with other countries across the world. Malaria is transmitted by four different mosquito species, instead of one, which makes it more difficult to focus on all aspects of the system. However, just because the system has several areas that need close observation does not mean it is expensive or ineffective. Without the malaria preventative gene drive system, an estimated $6 billion per year is being spent on malaria control in Africa, over half of this cost is going toward vector control (US National Library of Medicine National Institutes of Health, 2018). Vector control is defined as limiting any organism which can transmit disease, in this case the vector would be the mosquito. Gene drive systems would be a very cost-efficient solution, and genetic engineering has proven to be more successful with other mosquito species than all current malaria prevention innovations. While there is no specific number as to how much using gene drive technology to combat malaria in Uganda would cost, The Defense Advanced Research Projects Agency (DARPA) has donated $100 million into the research for fighting mosquito-borne illnesses and invasive rodents. The Bill and Melinda Gates Foundation has invested $75 million in research for gene drives specifically focused on fighting malaria (Scientific American, 2019). The only requirements for genetic engineering are trained scientists, a laboratory, mosquitoes, and the correct tools. The modifying of the genes actually takes place within the DNA, different strands and processes happening inside the cells are being edited until the desired trait is produced. Implementing this biological solution, which has already been tested and proven successful in other countries, on mosquitoes in Uganda is necessary to ending the spread of malaria.

Oxitec is a global biotech company that focuses on saving lives and improving livelihoods by developing safe, highly effective biologically-engineered solutions to control disease-transmitting and crop-destroying insects globally. (Oxitec, 2018) Their team of scientists, engineers, public health and agricultural experts, entrepreneurs, community engagement experts, along with others have launched several successful technologies that can be applied in the fields of public health and food security (Oxitec, 2018). Oxitec is a branch of the Intrexon Corporation, who also works to better DNA. They have already engineered what they call *Friendly Mosquitoes*, which target the *Aedes aegypti* mosquito, the primary transmitter of viral diseases dengue, Zika, chikungunya and yellow fever. (Oxitec, 2018). In order to monitor the progress, they are making within countries where the *Friendly Mosquitoes* have been released, Oxitec has implanted a fluorescent marker gene. They use the information collected to make modifications to the location and rate of releases (Oxitec, 2018). Oxitec is currently working on the technology for their *2nd Friendly Mosquito*, which targets malaria transmitting species. Oxitec's global connections would allow them to release mosquitoes in any country where the technology is needed, as long as the government provides. Their work has been published across several distinguished social media and news platforms, therefore, making Oxitec a great contender for controlling the release of genetically modified mosquitoes in Uganda. They understand how much of an impact disease has on a food insecure family and the community in which they live. If the *2nd Friendly Mosquito* were to be released in Uganda, Oxitec could use the techniques they have developed with the *Friendly Mosquitoes*, for example, implanting a fluorescent marker gene, to track the mosquitoes breeding and measure the effectiveness of the release. Uganda is surrounded by numerous countries that are also battling the malaria endemic. If any of the mosquitoes released in Uganda were to mate with mosquitoes from any adjacent country, that would potentially be spreading the altered genes to other countries, creating a greater coverage area.

There are also several nonprofit groups active in Africa advocating for the fight against malaria, including Malaria No More and Freedom From Hunger. These charities work towards helping families with prevention, providing drugs, and educating them about the effects of malaria. If these nonprofit organizations could also work to educate citizens about the benefits of gene drives, then citizens might be more open to the idea. Ordinary citizens could then be advocates for the idea of introducing biotechnology into the fight against malaria in Uganda.

Uganda would be an ideal country to release malaria preventing, genetically modified mosquitoes. Communities in developing countries need cost-efficient solutions most because they are the poorest places in the world. A solution that does not have a high start-up cost and is not expensive to maintain is imperative for their current situation. Gene drive technology is some of the most advanced biotechnology; even though continued funding will be required to implement this solution is Uganda, the extremely high success rate of gene drives makes it the most viable and credible solution. Uganda's presidential republic government system poses no barriers and would allow this solution to be implemented very easily. A citizen or interest group could propose this idea to be voted on to their district representative. No family wants to spend all of their money on health expenses, especially if that family is struggling to support themselves. Less mosquitoes means less breeding, resulting in cleaner facilities; less mosquitoes put less people at risk of being bitten, which reduces the chances of malaria. This combination multiplies exponentially, advancing the objective of this gene drive, to reduce or exterminate malaria transmitting mosquitoes and aid in the food security and overall health of Ugandan citizens.

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