Holland Professional Club
December 6, 2019
Charlie Vander Broek

Introduction

The idea of presenting on the mosquito came to me while walking in a very dense path on Monkey Beach in Panang, Malaysia last winter. My daughter was pregnant at the time and the Zika virus was very prevalent in areas of the tropics. There had been a lot of news about the birth defects and infant mortality caused by this newly emerging, mostly tropical disease. I have a picture of a warning in the Kuala Lampur airport. So, I did some reading on Zika, Dengue, chikungunya, and other strange mosquito borne viruses. I also did some research on how to prevent infections and protect ourselves from these diseases while we were in South East Asia. I began reading about vaccines, bed nets, using deet and other insecticides, where to travel, when to go out, etc.). On

certain days in Panang, we would see the mosquito “fogging” that occurred around our apartment building. I wondered what was more dangerous, the mosquitos or the prevention? When my interest in mosquitos was only getting more interesting, I decided to do some more in depth research on the mosquito and make it the topic of my Professional Club paper.

Information about Dengue and Zika at Kuala Lumpur airport (Malaysia)

This story is more relevant, and more complex, than I even thought when I began thinking about it a year ago. Since then a major book by Timothy Winegard, "The mosquito: a human history of our deadliest predator", has been published. In addition, over the last few months there has been a heightened concern about deaths and illness in Western Michigan caused by the Eastern Equine Encephalitis spread by our friend the mosquito. Schools moved football games to end before dusk, and aerial mosquito spray was administered in many of the counties around Holland. Several deaths and many serious illnesses were reported in several key counties.

The Mosquito – the deadliest animal on earth

> It has been one of the most aggravating sounds on earth for more than 100 million years — the humming buzz of a mosquito."
>
> Tim Weingard -New Yorker, September 2019

Currently an estimated 100 trillion or more mosquitoes occupy nearly every inch of the globe, killing about 725,000 people annually. Researchers assert that mosquitoes may have killed nearly half of the 108 billion humans who have ever lived across our 200,000-year or more existence.

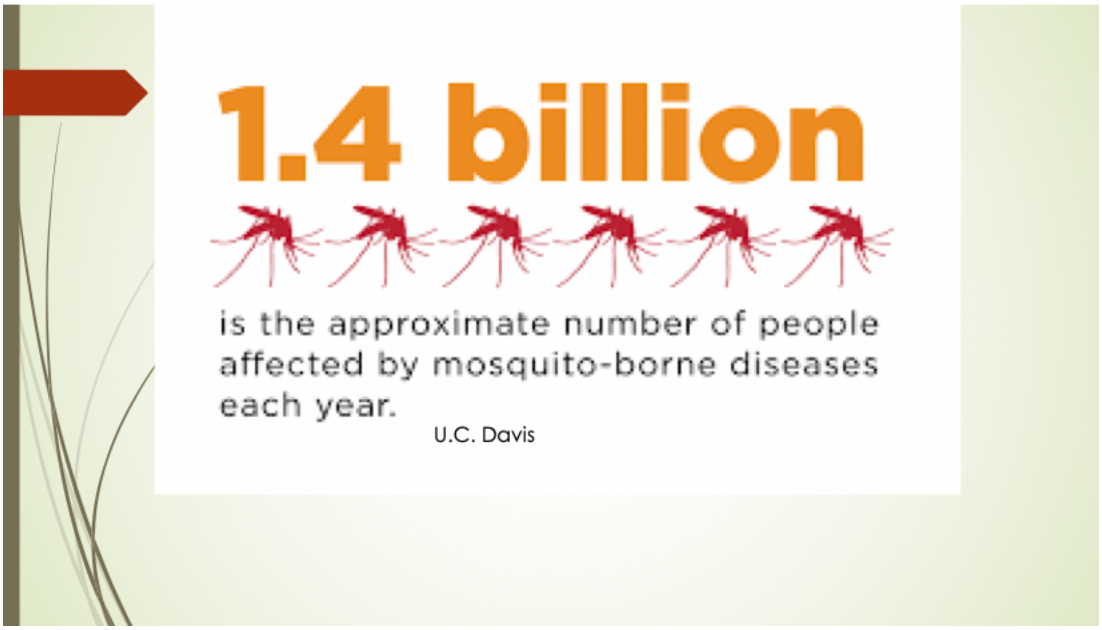
To emphasize the importance of mosquito borne diseases, foundations such as the Bill and Linda Gates foundation have committed over $2.9 billion to fight malaria with new vaccine research, prevention, and education. In addition, they have committed another $2 billion for Aids, Malaria, and HIV.

Anthropologists, historians, and scientists from many disciplines have concluded that the mosquito and her diseases have accompanied people around the world for thousands of years and, in recorded history, have been far more lethal than any manufactured weapons or inventions.

I found that there is support for the claim that the mosquito is "the deadliest animal on earth".

(https://nypost.com/2019/08/03/forget-sharks-mosquitoes-are-the-deadliest-maneaters-on-earth/

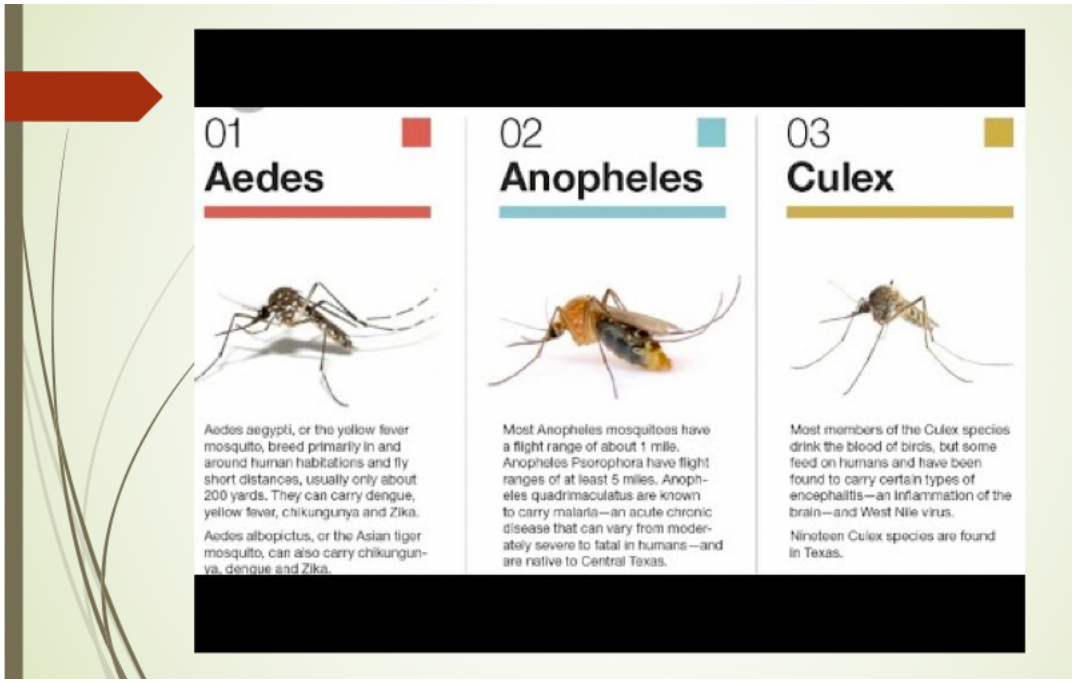
The purpose of this paper is to provide a new appreciation of the mosquito as a well-designed host of pathogens which have affected at least 3000 years of human history and promise to continue to cause large scale human suffering in the future.



There is still an active fight to beat these diseases, and I hope this information can help us become part of the fight against the human suffering the mosquitos carry.

The cast of characters

My story has several villains and dozens of supporting actors. Let me start by listing the main cast of characters who have been responsible for helping to determine the fate of history through death, suffering, economic waste, and, to say the least extreme annoyance.



While there are about 3,500 species of the family Culicidae from the order of Diptera (Mosquitoes), my main villains are the three species that carry and deliver diseases to humans. These villains are all female, because only the females carry and deliver disease. The males are basically good for one thing—mating.

(The word "mosquito" (formed by mosca and diminutive -ito)
[2] is Spanish for "little fly".[3] Mosquitoes have a slender segmented body, one pair of wings, three pairs of long hair-like legs, feathery antennae, and elongated mouthparts.)

Culex is a genus of mosquitoes which includes our common annoying house mosquito. However, there are also several species of Culex which serve as vectors of one or more important **diseases** of birds, humans, and other animals. The **diseases** they vector include arbovirus infections such as West Nile virus, Japanese encephalitis, or St. Louis encephalitis, but also filariasis and avian malaria.

Anopheles mosquitoes is the only species known to carry the malaria parasite. Of the 460 species, over 100 can transmit human malaria, only 30–40 commonly transmit parasites of the genus Plasmodium, which cause malaria in humans in endemic areas.

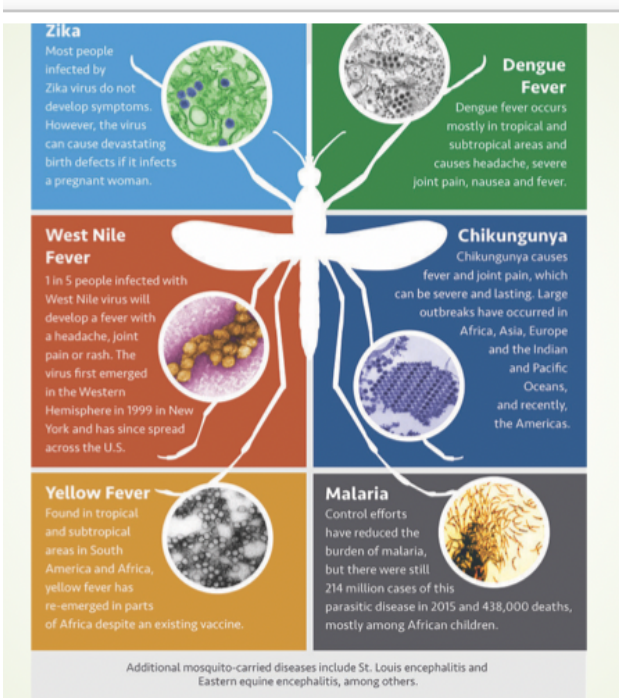
(Four different species of protozoa cause malaria: *Plasmodium falciparum*, *Plasmodium malariae*, *Plasmodium* ovale and *Plasmodium* vivax[3] (see *Plasmodium*).)

Aedes mosquitoes, of which the voracious Asian tiger is a member, carry yellow fever, dengue, and encephalitis. Bridge vector species of these mosquitoes carrying EEE may include *Coquillettidia pertubans, Aedes sollicitans,* and *Ochlerotatus canadensis*.

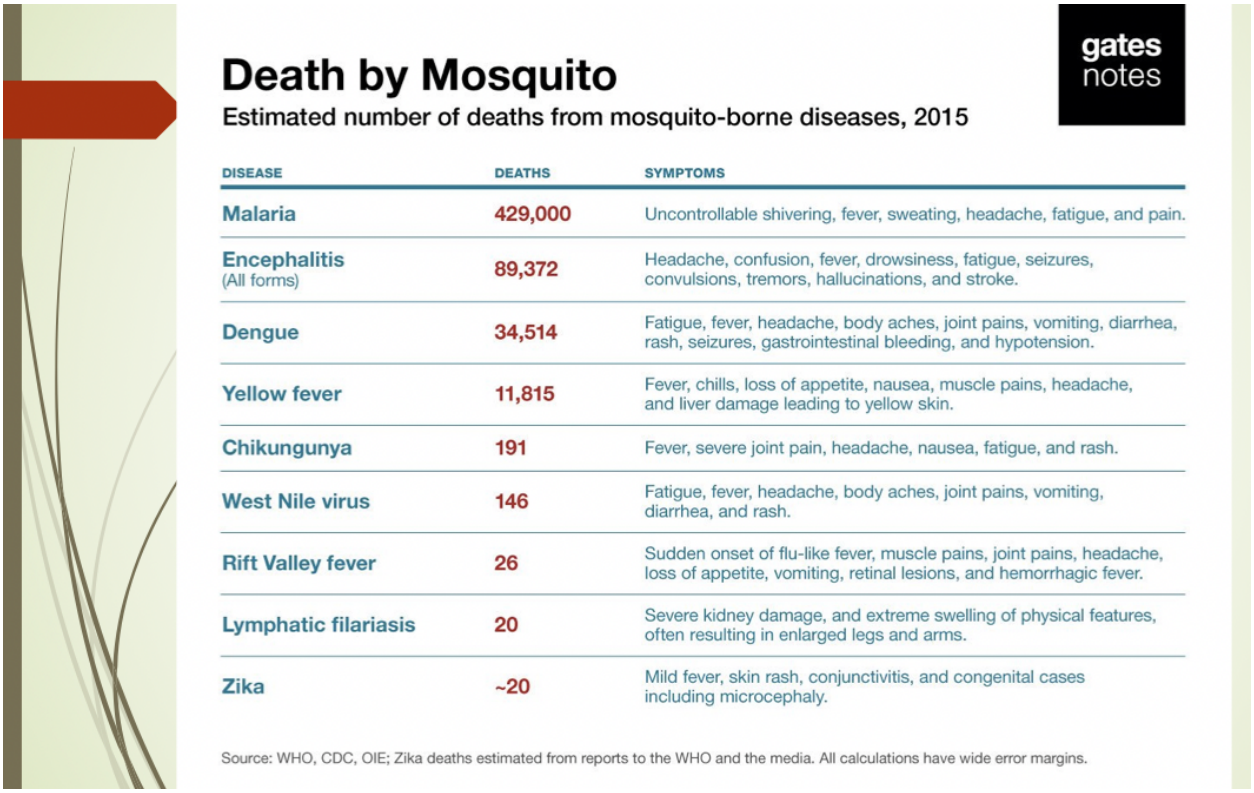
Asian Tiger Mosquito was imported in 1985 in some old tires that were shipped to the U.S. for recycling. *albopictus* has been demonstrated [1]. These include Eastern equine encephalitis virus [92,93], La Crosse virus [94,95], Venezuelan equine encephalitis virus [96,97], West Nile virus [72,98,99] and Japanese encephalitis virus [1]. Usutu virus has been isolated from *A*

The diseases

Our main characters do not act alone- they are vectors, or carriers, of a large supporting cast, of protozoa, viruses, or parasites.



malaria, dengue, West Nile virus, chikungunya, yellow fever,[1] filariasis, tularemia, dirofilariasis, Japanese encephalitis, Saint Louis encephalitis, Western equine encephalitis, Eastern equine encephalitis,[2] Venezuelan equine encephalitis, Ross River fever, Barmah Forest fever, La Crosse encephalitis, and Zika fever,[2] as well as newly detected Keystone virus and Rift Valley fever.



Death by Mosquito

Estimated number of deaths from mosquito-borne diseases, 2015

gates notes

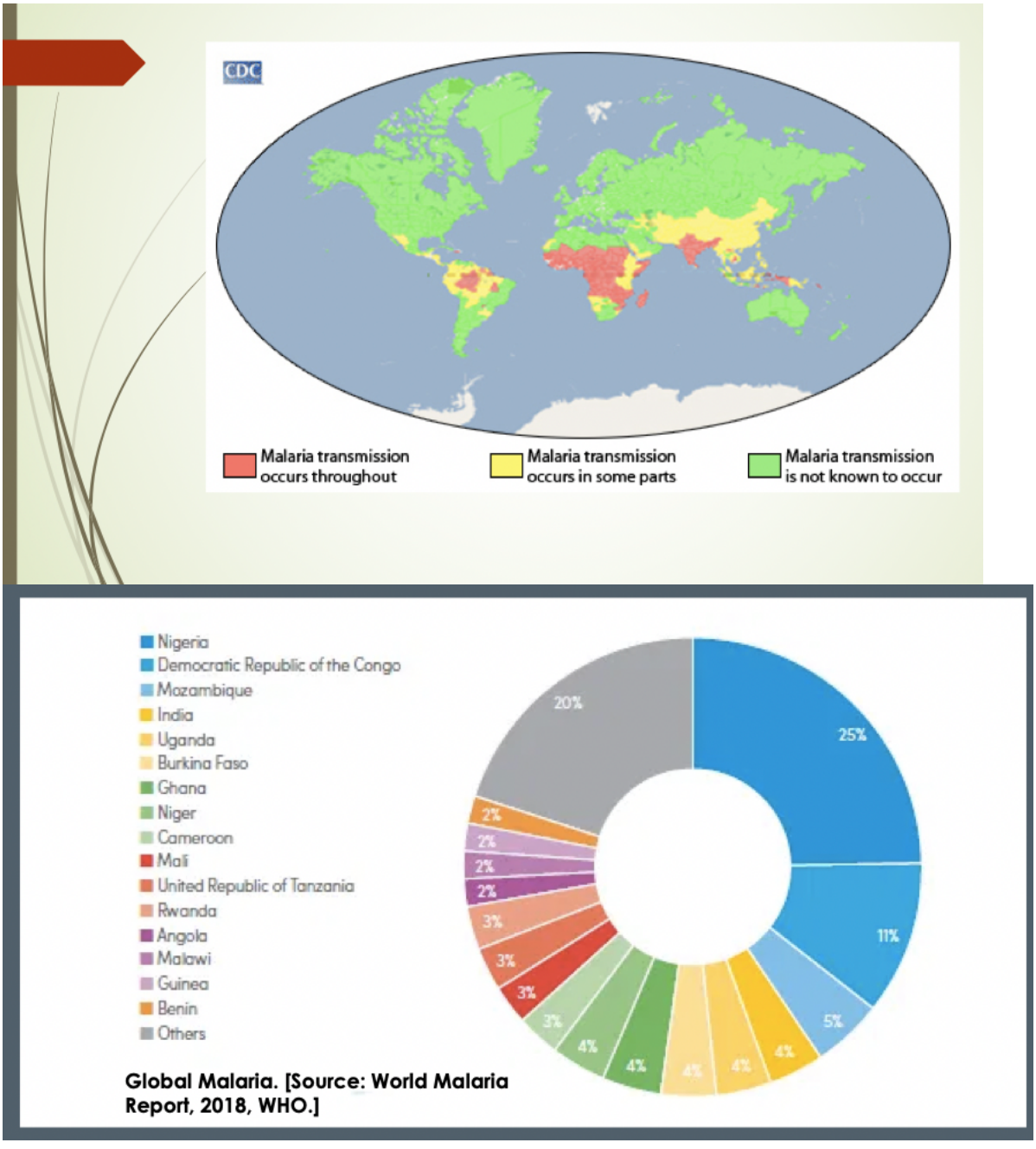
DISEASE	DEATHS	SYMPTOMS
Malaria	429,000	Uncontrollable shivering, fever, sweating, headache, fatigue, and pain.
Encephalitis (All forms)	89,372	Headache, confusion, fever, drowsiness, fatigue, seizures, convulsions, tremors, hallucinations, and stroke.
Dengue	34,514	Fatigue, fever, headache, body aches, joint pains, vomiting, diarrhea, rash, seizures, gastrointestinal bleeding, and hypotension.
Yellow fever	11,815	Fever, chills, loss of appetite, nausea, muscle pains, headache, and liver damage leading to yellow skin.
Chikungunya	191	Fever, severe joint pain, headache, nausea, fatigue, and rash.
West Nile virus	146	Fatigue, fever, headache, body aches, joint pains, vomiting, diarrhea, and rash.
Rift Valley fever	26	Sudden onset of flu-like fever, muscle pains, joint pains, headache, loss of appetite, vomiting, retinal lesions, and hemorrhagic fever.
Lymphatic filariasis	20	Severe kidney damage, and extreme swelling of physical features, often resulting in enlarged legs and arms.
Zika	~20	Mild fever, skin rash, conjunctivitis, and congenital cases including microcephaly.

Source: WHO, CDC, OIE; Zika deaths estimated from reports to the WHO and the media. All calculations have wide error margins.

Worldwide, malaria carried by the mosquito, is a leading cause of premature mortality, particularly in children under the age of five, with an estimated 207 million cases and more than half a million deaths in 2012, according to the World Malaria Report 2013 published by WHO. The death toll increased to one million as of 2018 according to the American Mosquito Control Association.[4]

Malaria is endemic in 91 countries, with about 40% of the world's population at risk. By undermining the health and working capacity of hundreds of millions, it is closely linked to poverty and stunts social and economic development.

But nowhere—past or present—has the mosquito exacted a greater toll than on Africa.



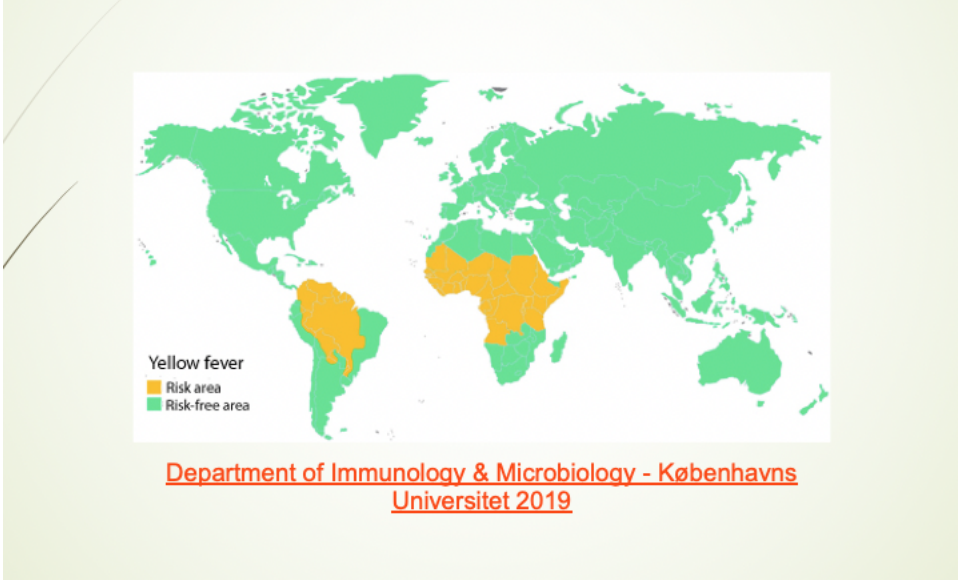
Global Malaria. [Source: World Malaria Report, 2018, WHO.]

At least 32 African countries are now considered at risk of yellow fever, with a total population of 610 million people at risk. In recent years, by virtue of climate, ecology, and poverty, sub-Saharan Africa has been home to 80 to 90 percent of the world's malaria cases and deaths,

although some predict that resurgent malaria in southern Asia is already altering that proportion. A powerful defensive pathogen, it was a leading obstacle to Africa's colonization. Portuguese traders who entered the African coastal plain in the late 1400s and early 1500s were the first foreigners to confront the killing fever. For the next 3 centuries, whenever European powers tried to establish outposts on the continent, they were repelled time and again by malaria, yellow fever, and other tropical scourges. By the 18th century, the dark specter of disease earned West and central Africa the famous epitaph, “the White Man's Grave.”

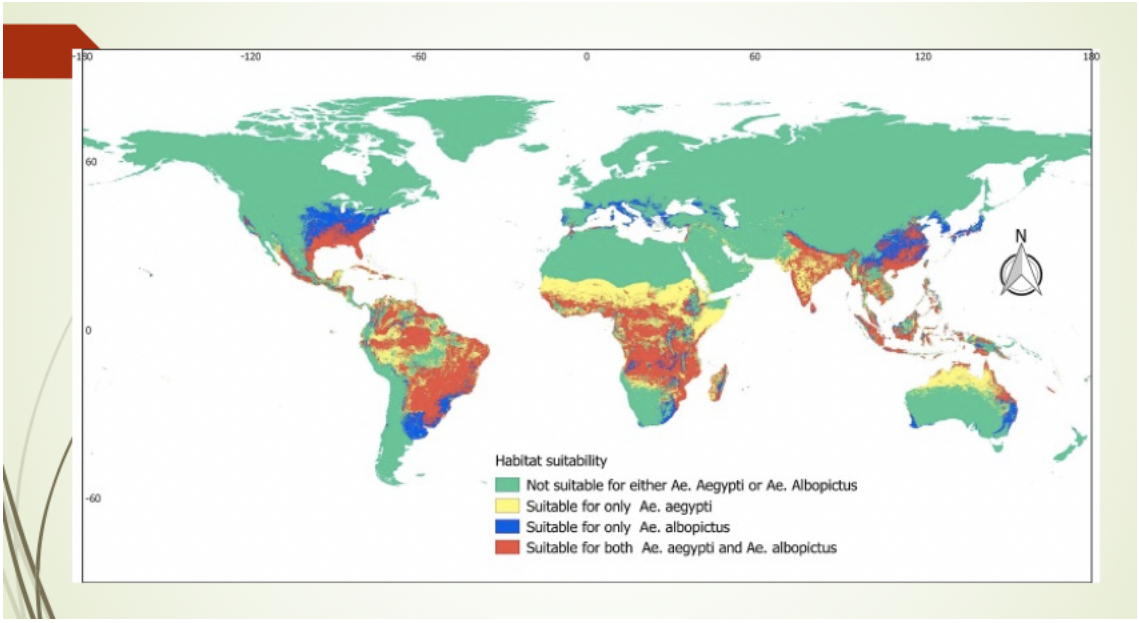
Part of the problem today is that there is no tried and true vaccine for any of the mosquito borne diseases other than Yellow fever. (There is current test of a new Dengue and Malaria vaccine) Although a successful vaccine was discovered for Yellow Fever in 1937, between 30,000 and 50,000 people still die annually from the disease. again—95% occurring in Africa.

Yellow Fever



In addition to Africa, Yellow fever is also endemic in 10 South and Central American countries and on several Caribbean islands. Bolivia, Brazil, Colombia, Ecuador, Peru, and Venezuela are considered at

greatest risk. Although the disease usually causes only sporadic cases and small outbreaks, nearly all major urban centers in the American tropics have been re-infested with *Aedes aegypti*. Due to the loss of organized mosquito control programs and subsequent re-infestation of the primary vectors(Carriers), Latin America is now at potentially devastating risk of urban epidemics more than at any time in the past 50 years. Lymphatic filariasis (elephantiasis) infects about 120 million people in tropical areas of Africa, India, South-East Asia, the Pacific Islands and South and Central America.



2018

Cost of Mosquito Borne Illness

Fortune Magazine, April 18

Since malaria is so devastating, it not surprisingly, has a big economic impact, too. Globally, it costs about **$12 billion a year** in direct costs (such as medical treatment, illness and fatalities). In countries where the disease is common, it can reduce a country's **Gross Domestic Product (GDP) by up to 1.3%**. Okorosobo et al. (2013)[22] estimate that the malaria "penalty" to GDP ranges from 0.41% of GDP in Ghana to 8.9% of GDP in Chad, all of which could be regained following elimination of malaria. Complete eradication of the disease would increase GDP in Uganda by 50 million USD.

Also in nations where malaria is common, the disease can represent as much as 40% of public health spending and can account for 60% of visits to health clinics — as well as 20-50% of hospital admissions. Unfortunately, many of the nations and individuals most affected by malaria also face economic barriers, making treatment and economic loss all the more unaffordable. Azemar and Desbordes (2009)23 find that in the median sub-Saharan African country, foreign direct investment could increase by as much as one-third as a result

of malaria and HIV eradication, slightly more than one-half of this is attributed to malaria.

According to the American Journal of Tropical medicine and Hygiene, Dengue fever costs $2.1 billion annually in the America's for direct and indirect costs. 50 million to 100 million are affected.
West Nile costs were estimated at $200 million for an outbreak in California 2002, and $2.98 million in California in 2005 alone

From 2011 to 2015 $330 million was spent on Yellow Fever vaccine.

The mosquito's profound effect on America

The conventional perception is that diseases caused by mosquito-transmitted pathogens are mostly associated with tropical areas (*1*). Indeed, such areas include the ranges of temperature and other climatic conditions that are ideal for the vectors of these pathogens. Moreover, because such diseases are clearly more prevalent in these areas, we might easily assume that the association between the tropics and mosquito-transmitted pathogens indicates that temperate regions are at less risk for these diseases because of their cooler climates.

However, this expectation of safety should not be taken for granted. In fact, cases of disease caused by mosquito-transmitted pathogens such as West Nile virus (WNV) occur readily in North America (*2*), and several encephalitides occasionally occur in the United States (*3*). In addition, history reveals that yellow fever and malaria were once very common in the United States and resulted in millions of cases (*4*,*5*). More than 100,000 deaths occurred in the United States in the 18th and 19th centuries from yellow fever alone, https://www.cdc.gov/

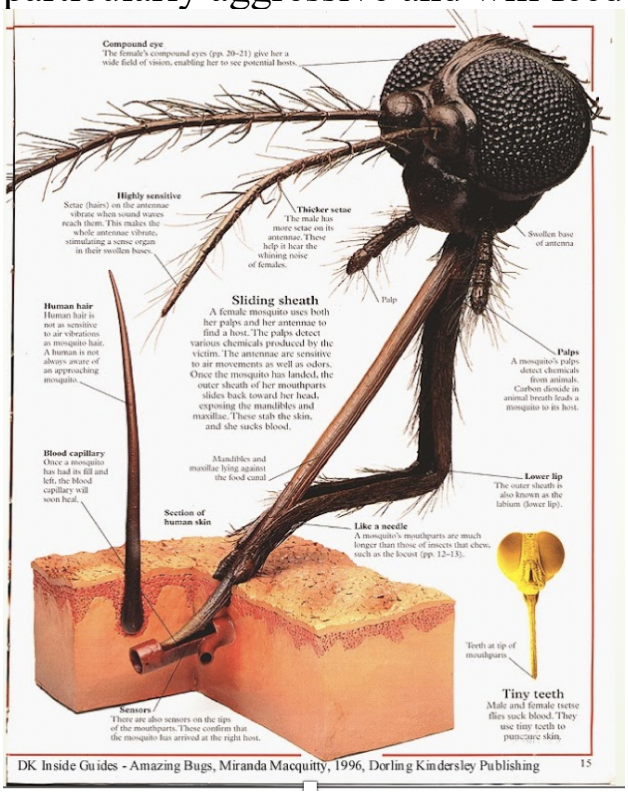
Mosquito disease transmission

How the mosquito feeds:

The thousands of mosquito species feed on the blood of various hosts—vertebrates, including mammals, birds, reptiles, amphibians, and some fish; along with some invertebrates, primarily other arthropods. The mosquito that generally bites you is the female because she needs the blood protein and iron to produce her eggs

The female chooses her targets through a combination of smell, heat and visual cues, and continue seeking bloodmeals until their abdomens are full. The females can live up to about a month and feed every two or three nights during that time.

The most common mosquito species feed at dawn and dusk, and for a few hours into dark. However, there are some species that are particularly aggressive and will feed at both times.



Mosquitoes locate bloodmeals first by using sensors on their antennae to detect trace amounts of carbon dioxide released in human breath. That CO2 rises in plumes that mosquitoes can sense from hundreds of feet away. Of course people working, exercising or acting in a large group release more CO2

A mosquito seeking prey follows the plume toward its source. Once it's close enough, it begins to pick up other chemical odors that signal the presence of people. Human skin produces more than 340 of these chemical signatures, including octenol, a substance also found in the exhalation of cows.

Certain people will smell better to the mosquito than others, and scientists are not exactly sure why. Larger people and pregnant women tend to attract mosquitoes, possibly because they release more CO2. Cholesterol and folic acid also act as attractants, as do perfumes, colognes, and lotions.

The mosquito also depends on its large compound eyes, designed for spotting motion, to help guide it in. Two simple eyes, called ocelli, are photosensitive, so the mosquito keys on lights and bright colors as well.

Finally, thermal sensors on the insect's antennae and around its mouth detect heat emanating from warm-blooded bodies, allowing it to land on exposed skin and find capillaries closest to the surface.

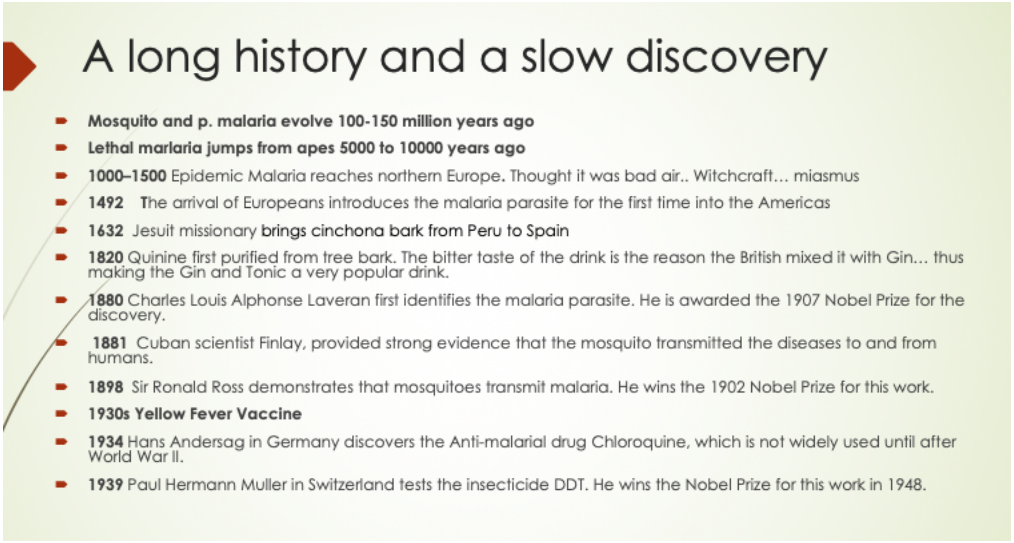
The mosquito has amazing equipment to perform her task. She is designed for a perfect and often undetectable stealth exchange.

The female mosquito inserts two serrated mandible cutting blades and saws into your skin, while two other retractors open a passage for the proboscis.

With this straw she sucks your blood, while a sixth needle pumps in saliva that contains the anticoagulant that prevents that blood from clotting. This shortens her feeding time, lessening the likelihood that the host swats the insect away. She has very sensitive nerves or sensors that tell her when she is full and at that point she can barely fly away. She processes the blood to extract the needed nutrients for her eggs and then deposits the remains through her anus. If you look closely you will see what appears to be blood after she bites you.
Unfortunately when she bites you, she also injects saliva and often some pathogens that she has picked up at her last feed.

Mosquitoes transmit disease in a variety of ways. In the case of malaria, parasites attach themselves to the gut of a female mosquito and enter a host as she feeds. In other cases, such as yellow fever and dengue, a virus enters the mosquito as it feeds on an infected human and is transmitted via the mosquito's saliva to a subsequent victim

History and Discovery



There are increasing supported theories that mosquito borne diseases had already started to kill off the dinosaurs before an asteroid or extreme climate helped to make them extinct.

There is new evidence that the mummy Lucy found high in the Andes was taken down by a fever and a malaria like mosquito carried illness. There are references to malaria like diseases that Influenced and effected warfare, geographic expansion, and cultural exchange, in ancient China, the Middle East, and especially Africa.

Malaria killed Alexander the Great, decimated the Roman army, and wiped out soldiers in the Crusades.

When talking about the mosquito and human history, it is critical to go back in time and imagine what people knew before the mid 19th century about the insect and the disease it carried.

People had many theories about the mysterious fevers and vomiting and death that seemed to occur certain times of the year and in certain locations. They often watched their children struggle and die at an early age with no explanation. From religious rites to witchcraft, people

struggled with what they could not explain. Was it the humours, was it a scourge from God? but what was it? Was it some toxic emanation or Miasmus as some believed?
(Plaques and poxes- The impact on human history on epidemic diseases. Bullet MD)

- **Mosquito and p. malaria evolve 100-150 million years ago**
- **Lethal marlaria jumps from apes 5000 to 10000 years ago**
- **1000–1500** Epidemic Malaria reaches northern Europe**.** Thought it was bad air.. Witchcraft… miasmus
- **1492** **T**he arrival of Europeans introduces the malaria parasite for the first time into the Americas
- **1632** Jesuit missionary brings cinchona bark from Peru to Spain
- **1820** Quinine first purified from tree bark. The bitter taste of the drink is the reason the British mixed it with Gin… thus making the Gin and Tonic a very popular drink.
- **1880** Charles Louis Alphonse Laveran first identifies the malaria parasite. He is awarded the 1907 Nobel Prize for the discovery.
- **1881** Cuban scientist Finlay, provided strong evidence that the mosquito transmitted the diseases to and from humans.
- **1898** Sir Ronald Ross demonstrates that mosquitoes transmit malaria. He wins the 1902 Nobel Prize for this work.
- **1930s Yellow Fever Vaccine**
- **1934** Hans Andersag in Germany discovers the Anti-malarial drug Chloroquine, which is not widely used until after World War II.
- **1939** Paul Hermann Muller in Switzerland tests the insecticide DDT. He wins the Nobel Prize for this work in 1948.

https://www.ucsf.edu/news/2011/08/103884/progress-fighting-malaria-timeline

The Mosquito and American History

Columbus and The Columbia Exchange
The Europeans introduce Malaria to the new world

In 1492 Columbus sailed the ocean……This is the history we all learned. Columbus, with his men and cargo aboard the Nina, Pinta, and Santa Maria are a story known to almost every one of us in this room. However, when Columbus landed on Hispaniola (now Haiti), he was

carrying passengers my history teachers never talked about. On Board his ships were at least three protozoa or parasites known as Plasmodium malariae, P. vivax and falciparum. (malaria carriers) Also onboard was old world Anopheles mosquitos who had plenty of time on the voyage to brew up a great army of infected men ready to disembark in the new world. Alfred Cosby in his seminal work " The Columbian Exchange: Biological and Cultural Consequences of 1492", states that global ecosystems were forever rearranged in the largest interchange in natural and human history. (mosquitoes 145). As a side note it is worth mentioning that on Christmas day 1492, Columbus's flagship Santa Maria was destroyed when it ran aground. This forced at least one ship load of crewmembers to remain on Hispaniola while the rest returned to regroup in Spain. When they returned 11 months later, they found the island in ruins. The sailors were all dead, and the native Taino people were in the midst of a malaria and influenza epidemic. Just twenty-two years after Columbus stepped onto Hispaniola, a census revealed that the local Taino population had dropped from between five and eight million people to just twenty-six thousand. Along with smallpox and influenza, mosquito-borne diseases led, by Winegard's estimate, to the deaths of ninety-five million indigenous inhabitants of the Americas, from a pre-contact population of about a hundred million.

Jared Diamond clarifies in his book Guns, Germs and Steel, how the new visitors (the Europeans and the mosquitos with their hitchhikers) forever altered the history of the world.

The Slave Trade

Cristus Atucks, November 2012

While the anopheles mosquito and malaria came to the Americas in 1492, Mosquitoes also played a role in steering slave ships from Africa across the Atlantic. Yellow fever in the Americas was a direct result of the slave trade.

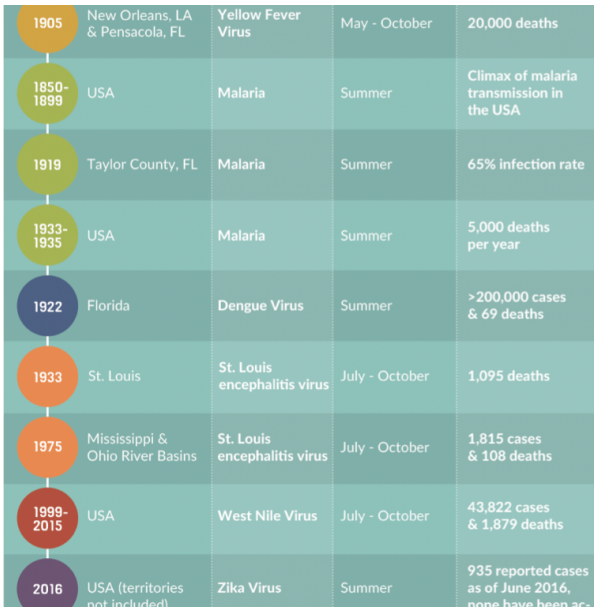
The Aeges Eqypti mosquito, the only carrier of the virus Yellow Fever, landed in Barbados in the fall of 1647, after England and Portugal signed a treaty in 1642, opening Portugal's slave dungeons on the African coast to London merchants. Yellow fever mostly hit the European servants, because many of the African slaves had already survived the virus on the other side of the ocean. As white servants

died by the thousands, the planters replaced them with black slaves. Plantation owners in the Americas believed that Africans withstood the onslaught of mosquito-borne disease better than indigenous slaves or European indentured servants.

African slaves initially were protected from malaria by age-old genetic defenses (sickle cell anemia, and G6PD deficiency) plus partial immunity gained through lifelong exposure. Their descendants, as well as Native Americans and settlers of European ancestry, were more vulnerable, however. Deforestation and "wet" agriculture such as rice farming facilitated breeding of *Anopheles* mosquitoes. Having successfully crossed the Atlantic, the virus and its *A. aegypti* carriers jumped from Barbados to the rest of the Caribbean by the mid-1650s. From there it took root in monkey populations throughout Brazil and Latin America. As slave ships entered other harbors yellow fever crippled Philadelphia, then the U.S. capital, in the 1790s. It also devastated European troops in the Caribbean and Gulf Coast regions, convincing Napoleon to sell Louisiana to Thomas Jefferson's administration in 1803. Later that century, a major outbreak crippled French effort to build the Panama Canal. (Once Dr. Walter Reed (1851-1902) confirmed that yellow fever was a mosquito-borne, viral disease, the U.S. was able to eradicate *A. aegypti* habitats—and complete the canal in 1914.) (Time magazine) History of Yellow Fever in the US, Bob Arnebeck.

American Epidemics of Mosquito Borne Illness

City/Region	Pathogen	Peak Transmission Period	Estimated Number of Cases
1668-1669 New York & Philadelphia	Yellow Fever Virus	Summer months	Unknown
1793 Philadelphia	Yellow Fever Virus	August - November	5,000 deaths
1795 New York City	Yellow Fever Virus	July - October	730 deaths
1798 Boston, New York, & Philadelphia	Yellow Fever Virus	Summer	>5,000 deaths
1800 Baltimore	Yellow Fever Virus	Summer	1,200 deaths
1833 & 1853 New Orleans	Yellow Fever Virus	Summer	>10,000 deaths
1855 Norfolk	Yellow Fever Virus	June - October	2,000 deaths
1878 Mississippi River Basin	Yellow Fever Virus	May - October	20,000 deaths
1888-1889 Jacksonville, FL	Yellow Fever Virus	Summer	4,700 cases & 450 deaths
1905 New Orleans, LA & Pensacola, FL	Yellow Fever Virus	May - October	20,000 deaths



1905	New Orleans, LA & Pensacola, FL	Yellow Fever Virus	May - October	20,000 deaths
1850-1899	USA	Malaria	Summer	Climax of malaria transmission in the USA
1919	Taylor County, FL	Malaria	Summer	65% infection rate
1933-1935	USA	Malaria	Summer	5,000 deaths per year
1922	Florida	Dengue Virus	Summer	>200,000 cases & 69 deaths
1933	St. Louis	St. Louis encephalitis virus	July - October	1,095 deaths
1975	Mississippi & Ohio River Basins	St. Louis encephalitis virus	July - October	1,815 cases & 108 deaths
1999-2015	USA	West Nile Virus	July - October	43,822 cases & 1,879 deaths
2016	USA (territories not included)	Zika Virus	Summer	935 reported cases as of June 2016, none have been ac-

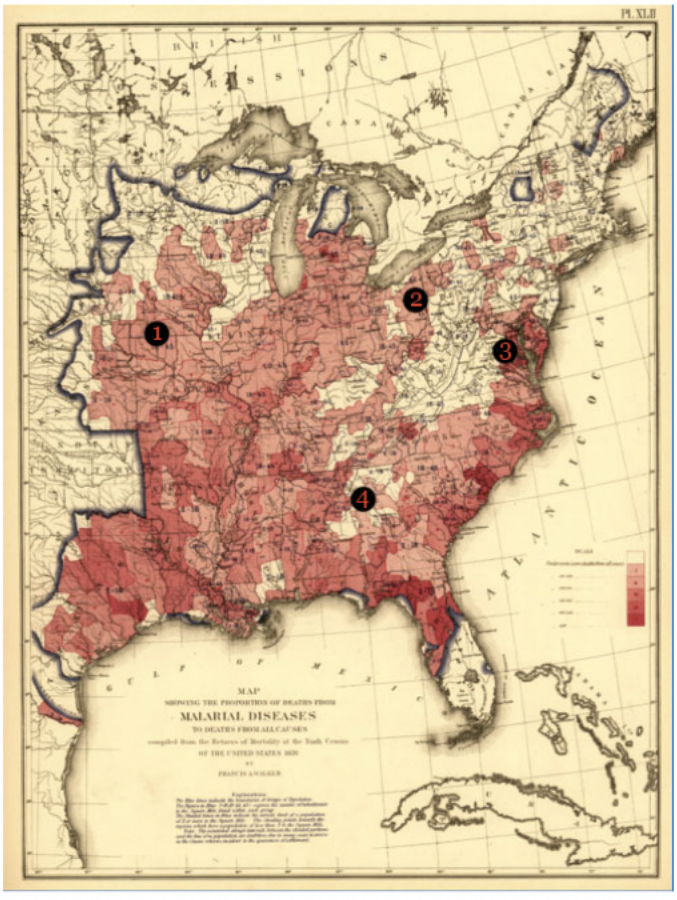
War of Independence

U.S. owes its independence in part to mosquitoes and malaria.

In 1780, the southern colonies, a region with widespread malaria, became a decisive theater in the American Revolution. British troops had almost no experience with malaria, and thus no resistance to it. American militiamen, and much of the Continental Army, had grown up in the South and faced malaria every summer of their lives. At times, half the British Army was too sick to move. No one knew that mosquitoes carried malaria, and the British did not have the means to combat it. (https://www.smithsonianmag.com/science-nature/how-lowly-mosquito-helped-america-win-independence-180959411/#IX4zpCHed7pjFrZB.99)

Civil War

Malaria
1870



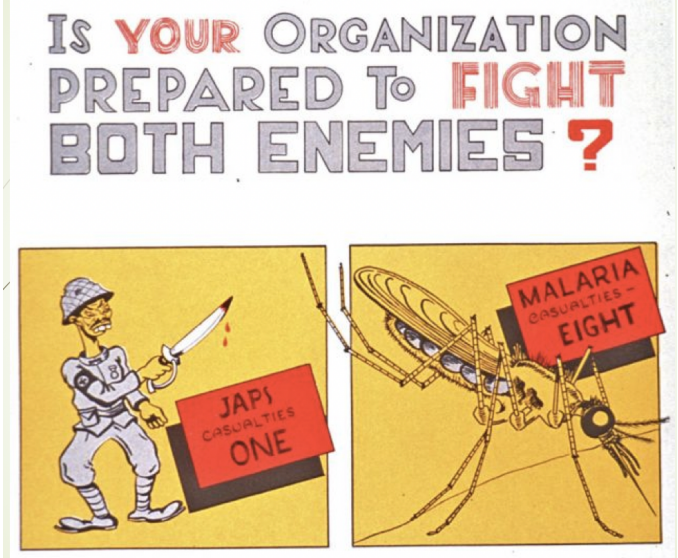
Malaria struck presidents from Washington to Lincoln, and in 1862, Washington, D.C., and its surroundings were so malarious that General McClellan's Army en route to Yorktown was stopped in its tracks. Of the 620,000 soldiers who perished during the American Civil War, the overwhelming majority died not from gunshot wounds or saber cuts, but from disease.

Until the Tennessee Valley Authority brought hydroelectric power and modernization to the rural South in the 1930s, malaria drained the physical and economic health of the entire region.

Michigan

Malaria also ravaged our own founders in Michigan and Holland,“Willis, F. Dunbar in "Michigan: A History of the Wolverine State," writes that the disease "was so prevalent that it was rather unusual to escape it." Ruth Hoppin, who grew up in a pioneer family in St. Joseph County near Three Rivers, recalled that "the pale, sallow, bloated faces of that period were the rule; there were no healthy faces except of persons just arrived." A. D. P. Van Buren, whose family came to Calhoun County near Battle Creek in 1836, noted that the first question asked of new settlers was whether or not they had contracted malaria yet, and "if answered in the negative, the reply would be, `Well, you will have it; everybody has it before they've been here long.'" (Michigan Settlers vs. Malaria, or How the Midwest Was Won: August 2, 2001)

.**WWII**

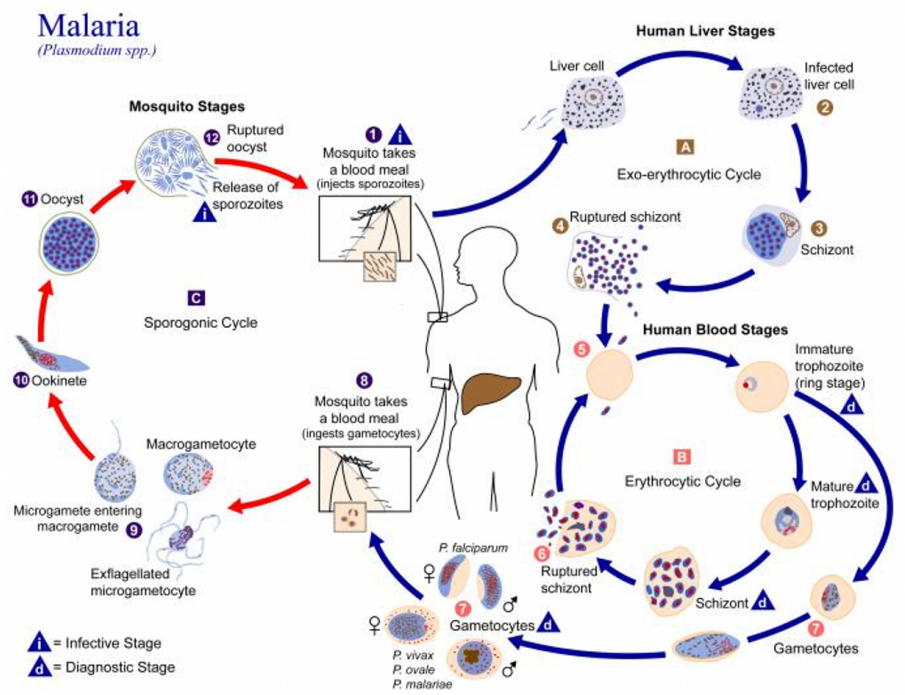


During WWII and the early days of the Pacific campaign, more soldiers fell to malaria than to enemy forces.
Americans gained an advantage over the Japanese because of malaria, according to Gordon Patterson, author of "The Mosquito Wars," and a history professor at the Florida Institute of Technology.

The U.S. had moved 10,000 troops into active malaria zones in the South Pacific, but because the Americans had far greater resources to fight malaria relative to the Japanese, they were able to stay a much healthier fighting force, he said
In fact, said Patterson, malaria was such a concern for America during World War II, the military created extended malaria programs to monitor and prevent the disease. One of the staging stations for these programs was in Atlanta. It eventually changed its name and became known as the Centers for Disease Control and Prevention.

Malaria – an amazing "shapeshifter"

I want to take focus on the malaria parasite "plasmodium" just to illustrate the incredible adaptation and interconnection between the parasite, the mosquito and the human hosts.



As we saw earlier, Malaria was not known to be carried by mosquitos until the mid 1800s largely due to the shapeshifting life cycle of the parasite itself.

PLASMODIUM is the most deadly of the human malaria parasites. The particular virulence of this species derives from its ability to subvert the physiology of its host during the blood stages of its development. The parasite grows and divides within erythrocytes, feeding on the hemoglobin, and remodeling its host cells so they adhere to blood vessel

walls. (0Eric Hanssen, ... Leann Tilley, in Methods in Cell Biology, 2010

To understand how, it helps to know a bit about how your immune system works.

"I've never seen the funny shape on the outside of this thing. I'm going to attack it."

Your system is very good at detecting unusual objects in your body. It looks at the proteins on the surface of an invader and says, "I've never seen the funny shape on the outside of this thing. I'm going to attack it." After the invader is defeated, your body remembers what it looked like and will go after it if it ever shows up again.

Unfortunately, malaria is a lot more complex than viruses or bacteria. For one thing, it is caused by parasites. Parasites don't look as weird to your body as viruses or bacteria do. In fact, they more closely resemble your own cells, so your immune system has a harder time fighting them off.

Another problem is that the malaria parasite goes through three different stages in your body. It looks radically different in each stage, and as the infection goes on, you have all three going on at once.

Stage 1 begins when an infected mosquito bites you and injects a little saliva under your skin. This dose of saliva might contain only 100 parasites (called sporozoites in this stage). They are small and don't cause any inflammation in your body, so your immune system doesn't bother to look for them. You're not feeling any symptoms yet.

Within an hour or two, the sporozoites make their way to your liver for stage 2. Coming out of your liver, they take a new form (called merozoites) and start invading your red blood cells. This invasion

causes the symptoms—fever, chills, and so on—that make malaria such a miserable and deadly disease.

Now your body knows it's sick and your immune system kicks in. But this is where the parasite's shapeshifting comes into play.

The measles vaccine helps your immune system learn to identify the virus by looking for certain proteins on its surface? That works because those proteins look the same on each clone of the measles virus in your body. With malaria, each one can present up to 60 different proteins—and thanks to a mechanism that tells the parasite to alter its surface periodically, they shuffle these proteins around in different combinations every few days.

"It's as if there's a door on the surface of the parasite, but it keeps changing the locks."

As a result, by the time your immune system has figured out how to attack one shape, the parasite has transformed, and your body's defenses are useless. Your immune system adjusts, but not before the parasite has shifted again. It's as if there's a door on the surface of the parasite, but it keeps changing the locks, so your body never has the right key.

Finally, in stage 3, a few of the merozoites develop into male and female cells. These hang out in your bloodstream, waiting for the next mosquito to come bite you. Once they're in the mosquito's stomach, they form new sporozoites, which make their way to the bug's saliva glands and get injected into the next human, where the cycle starts all over again.

So that is the life cycle of malaria.

Yellow Fever

Yellow fever can produce fever-induced delirium, liver damage bleeding from the mouth, nose and eyes, and coma. Internal corrosion induces

vomit of blood, the color of coffee grounds, giving rise to the Spanish name for yellow fever, vómito negro (black vomit), which for about 25% of the cases is followed by death.

Yellow fever is spread through three transmission cycles; urban, sylvatic, and intermediate. The disease is mainly transmitted to humans through the bite of an infected mosquito, *Aedes aegypti*, and these mosquitoes acquire the virus by feeding on other infected humans. This is known as the urban cycle. The sylvatic, or jungle, cycle involves transmission of the virus through non-human primates in the wild. Humans can then become infected by these mosquitoes when visiting or working in the jungle.

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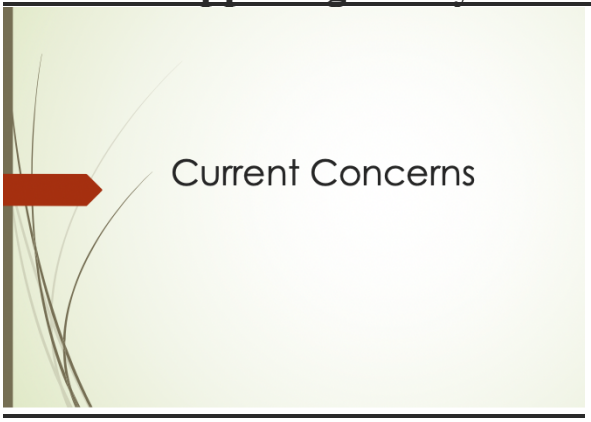
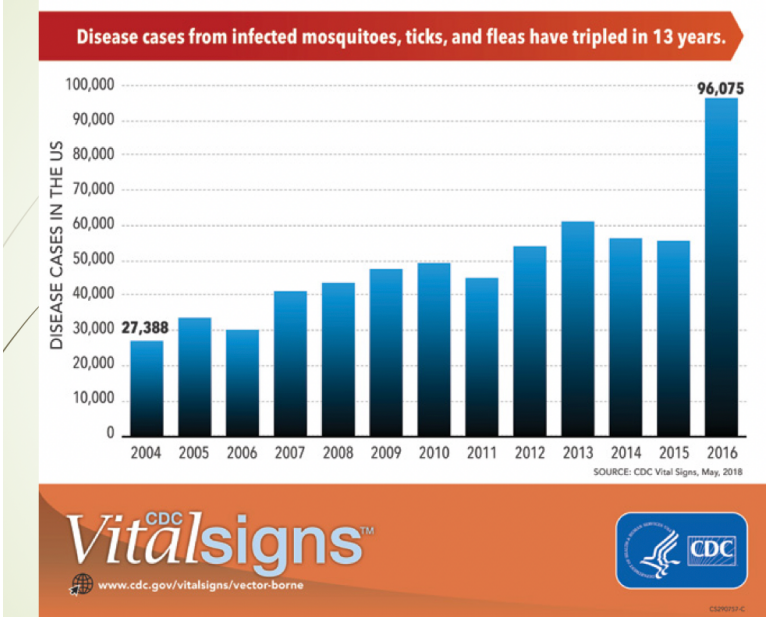
What is happening Today? And what about the future?



Karen Masterson appraises the disease vector's role in scientific and military history.

Even with various ways to repel mosquitoes today (including DDT, which earned notoriety for its harmful effects on the environment), we still battle. We spend an average $11 billion a year trying to protect ourselves from them — mostly for naught. And they continue to slaughter us.

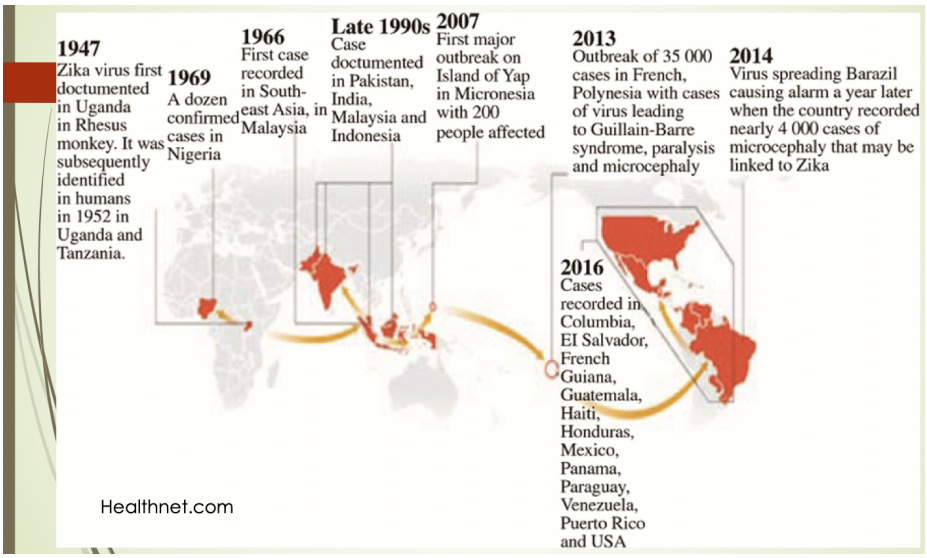


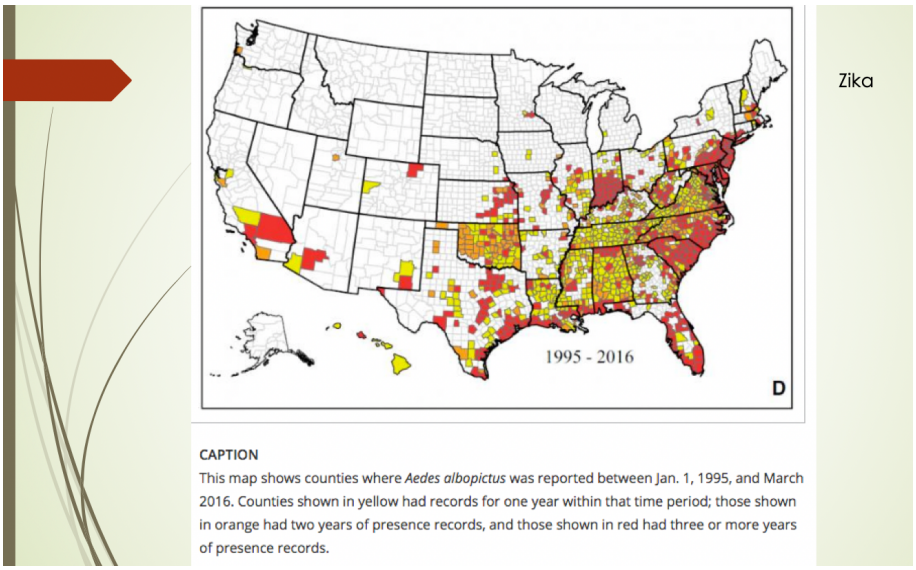
Aedes Albopictus

Potential Outbreaks in the United States, Asian Tiger Mosquitoes

One research group is tracking what could become a vector for outbreaks in the United States—the Asian tiger mosquito. An invasive species introduced to the United States in the 1980s, the Asian tiger mosquitoes lay their eggs in manmade containers, tires or shipping bins, all over the world. The embryos can stay dormant for six months or more, until the conditions are right for hatching.

The scariest thing about the species is that they're excellent vectors of disease.

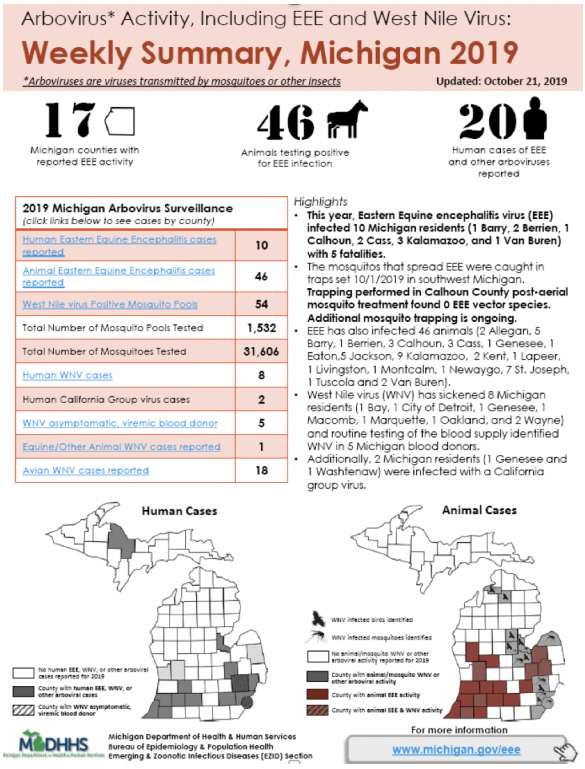


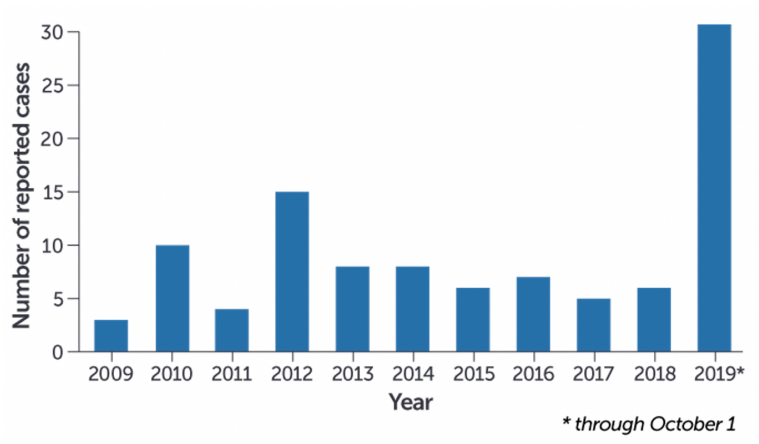


Zika

"In other parts of the world, they're very important in the transmission of dengue, yellow fever, and Zika," Harrington says. "In New York state, they've been found infected with West Nile virus, and they're very important in heartworm transmission in dogs. In the laboratory, at least, they're known to transmit 20 or more different viruses that affect human and animal health. It's actually the best overall mosquito vector of viruses."

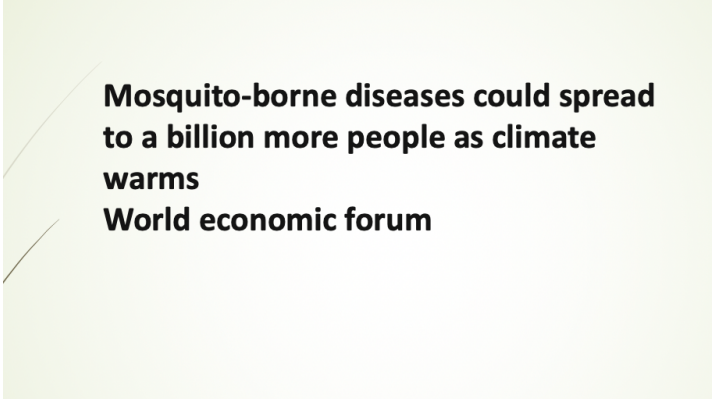
The species has already spread throughout the southeastern United States and is moving north.





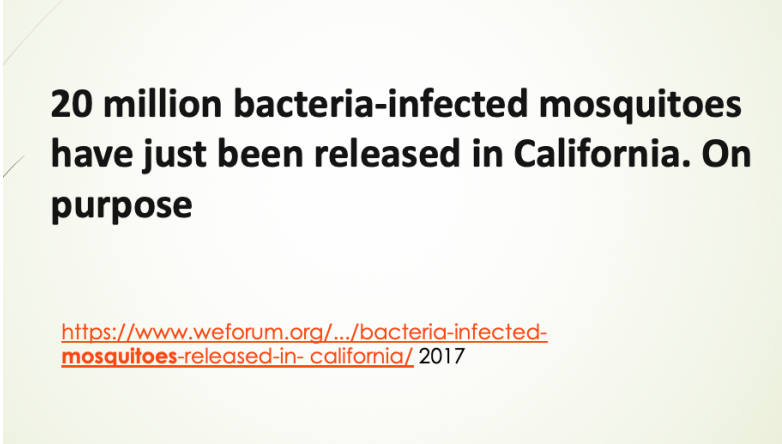
EEE

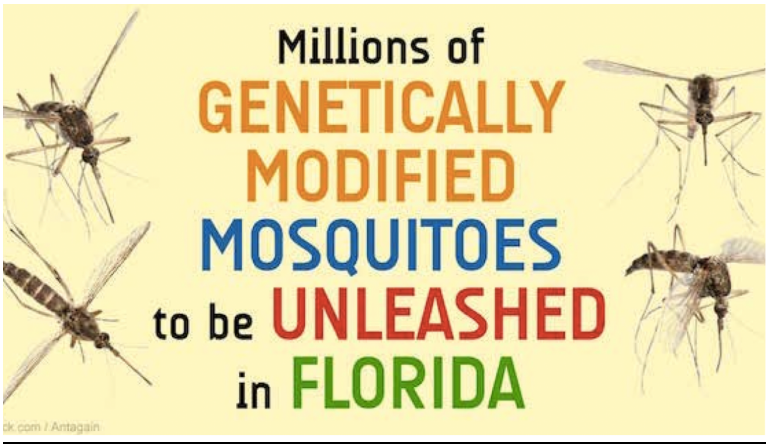
Though we discovered a successful vaccine for yellow fever in the 1930s, today more than 30,000 people die of the disease a year. The Zika virus, which if contracted during pregnancy can cause serious birth defects like microcephaly, was declared a global emergency by the Centers for Disease Control and Prevention when it hit the Americas in 2016.



What will we do to manage the scourge of Mosquito Borne diseases?

The future of mosquito-borne diseases will depend on the improvements and implementation of chemotherapy and vaccination, as well as on biological and integrated control measures. Bacillus thuringiensis H-14, B. sphaericus, Lagenidium giganteum and other fungi are promising biological mosquito control agents. Other control measures include parasitoids, nematodes, larvivorous fish, Toxorhynchites mosquitoes, insect viruses, growth hormones, sex attractants, natural products, sanitation, and water management. Vector control should be combined with training of personnel and carried out on an international scale. The use of simple approaches like the use of insecticide treated bed nets, and social programs of education in rural Africa have had some effect.





What about the effect our mosquito management has on the environment and health?

BILL AND MELINDA GATES

According to the 2018 World Malaria Report, there were more than 200 million malaria cases in 2017. An estimated 435,000 people died from malaria in 2017, mostly children under age 5, and more than 90 percent of them in Africa.

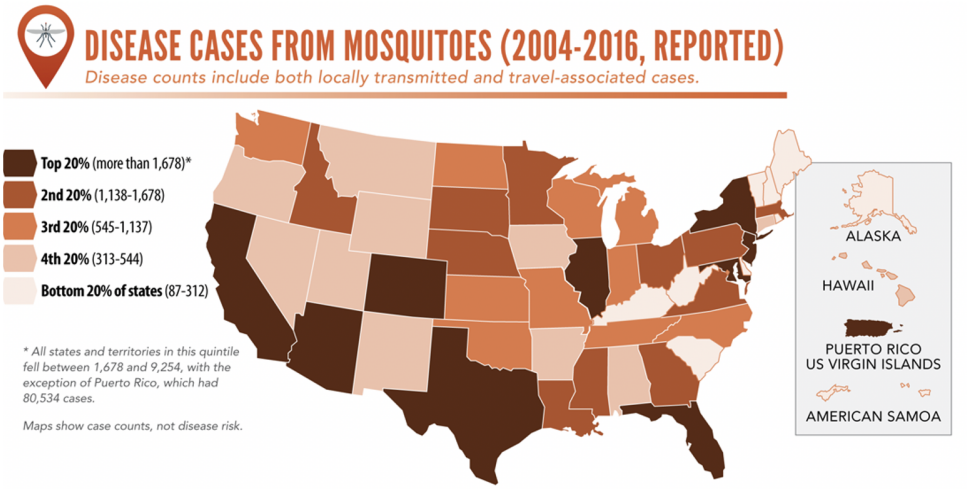
Since the early 2000s, major investments in diagnosis, treatment, and prevention helped reduce malaria cases by more than 40 percent and reduce deaths by more than 60 percent worldwide.

Despite significant historic progress, we've now plateaued. Headwinds such as insecticide and drug resistance and stagnant funding put future progress in question without concerted action by donors and affected countries.

The only sustainable approach to addressing malaria is eradication of the parasite. Eradication is biologically and technically feasible, with commitment and collaboration from global partners and affected countries, and ongoing investment in transformative new tools and strategies.

End of Paper

ADDENDUM



Dengue

Dengue is the world's most important mosquito-borne virus disease, with 2500 million people worldwide at risk of infection and 20 million cases a year in more than 100 countries. In 1995, the worst dengue epidemic in Latin America and the Caribbean for 15 years struck at least 14 countries, causing more than 200 000 cases of dengue fever and almost 6000 cases of the more serious dengue haemorrhagic fever. The World Health Organization posted an update on the virus globally, citing research[1] that estimates the real number of

West Nile

West Nile virus (WNV) is a **mosquito**-borne arbovirus that was discovered in 1927 in the West Nile sub-region of Uganda. The first serious outbreaks of WNV occurred in the mid-1990s in Algeria and Romania. The virus was introduced in the United States in 1999, with the first case being identified in New York City. That year, 62 human cases, 25 horse cases, and countless bird diagnoses were reported in New York State. The CDC has since received more than 40,000 reports of people affected with WNV in the lower 48 states, making it the most common virus transmitted by mosquitoes to humans in the U.S. Because only a portion of all cases are reported, the CDC believes the actual

number of illnesses may be as high as 700,000. West Nile virus, which in severe cases can cause encephalitis, entered the U.S. along the east coast in 1999 and has had serious ongoing implications for the rest of North America as it has spread across the country. 47 out of 50 states and the District of Columbia reported West Nile virus infections in people, birds, or mosquitoes in 2017. 2003 was the largest WNV outbreak in the U.S. with 9,862 cases reported and 264 deaths. 2012 was the deadliest year for WNV in the U.S., with 286 deaths reported to the CDC. West Nile virus is a concern in North American bird populations and remains the #1 mosquito-borne disease threat to humans in the U.S., with over 46,000 cases reported between 1999-2016.

Chikungunya: A Human Virus

WNV, EEE, LAC, and a few other mosquito-borne encephalitis viruses have an animal reservoir and cannot be transmitted from human to mosquito. Chikungunya is a human virus. Mosquitoes become infected when they feed on a person already infected with the virus and then spread the virus by feeding on other humans. Because of this ability, the virus has the potential to spread quickly, especially in urban areas with larger populations. with local cases reported in the U.S. in Florida (2014) and Texas (2015).