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Published by CQ Press, an Imprint of SAGE Publications, Inc.

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Mosquito-Borne Disease

Can the U.S. prevent a Zika outbreak?

loodthirsty and ubiquitous, the mosquito is a carrier of death and disease. The roster of mosquitoborne illnesses is long: yellow fever, West Nile virus, chikungunya, dengue and the deadliest of all, malaria, which kills more than 400,000 people a year and sickens at least 200 million. The latest scourge is Zika, a fast-moving virus that can cause severe birth defects, including devastating brain damage in newborns. As mosquitoes spread Zika throughout the Americas, many travelers and athletes plan to avoid next month's Olympics in Brazil, the disease's epicenter. With the mosquito season now underway in the United States, health officials warn that Zika could become endemic in this country, particularly along the Gulf Coast. The outbreak has drawn renewed attention to the weakness of U.S. public health efforts and criticism of Congress' failure to approve funding to combat Zika. Experts say Zika offers the latest evidence that the mosquito threat will grow as Earth's climate warms and the insect's habitat expands.



A mother in Recife, Brazil, holds her baby, who was born with microcephaly, a birth defect that can be caused by Zika-carrying mosquitoes. Health officials warn the virus could become endemic in parts of the United States. Congress this summer failed to approve funding to fight Zika.

CQ Researcher • July 22, 2016 • www.cqresearcher.com Volume 26, Number 26 • Pages 601-624



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Mosquito-Borne Disease

BY ALAN GREENBLATT

THE ISSUES

hey weigh a fraction of an ounce and live, at most, a month or two. But mosquitoes have been called the "most dangerous animal" on Earth, and the unfolding crisis over the Zika virus is only the latest example of why. ¹

Most mosquitoes are merely a nuisance. But bites from some species can have deadly consequences. Mosquitoes — or more accurately the viruses they carry — kill about 725,000 people a year, mostly in tropical and subtropical regions where the insects thrive. By contrast, sharks, perhaps the most feared animal on the planet, kill about 10. ²

Despite recent progress, malaria remains the deadliest mosquito-borne disease, killing more than 400,000 people each year and sickening

at least 200 million. ³ Yellow fever, once the most feared mosquito-borne illness in North America, has recently broken out in Africa, and China has seen its first cases. West Nile virus, chikungunya and dengue fever — mosquito-borne diseases that were not serious threats in the Americas until recently — are making significant inroads in the United States. (*See glossary*, p. 604.)

And now mosquitoes are spreading Zika, a virus that has emerged in at least 60 countries. Brazil, site of the 2016 Summer Olympics, is the epicenter of the disease in the Americas, recording close to 500,000 cases since the outbreak began in late 2014 — some 100,000 cases alone this year, including several thousand involving pregnant women whose babies were born with birth defects. ⁴



Aedes aegypti, known as the yellow fever mosquito, carries viruses that can cause a number of devastating illnesses, including dengue, chikungunya and Zika, a fast-moving virus now spreading throughout the Americas. Experts say Zika offers the latest evidence that the mosquito threat will grow as Earth's climate warms and the insect's habitat expands.

"Everything we look at with this virus seems to be a little scarier than we initially thought," said Anne Schuchat, principal deputy director of the Centers for Disease Control and Prevention (CDC). ⁵

Public health officials warn that the outbreaks of Zika and other viruses are signs that mosquitoes pose a greater threat to humans as the climate warms and the insects' habitat expands into more temperate climes. In fact, scientists fear more disease outbreaks of all types due to global commerce, human encroachment into animal habitats and climate change. "We're seeing a whole new set of viruses that either were very rare or were thought to be limited to one particular area," says Marten Edwards, an entomologist at Muhlenberg College in Pennsylvania. "We're all one airplane flight away" from getting infected, he says.

Until a year ago, Zika was little known and rarely diagnosed. Scientists first identified it in the Zika Forest of Uganda in 1947, but it was hardly studied because of its rarity - scientists knew of only 14 cases before 2007 and because it didn't appear to kill humans or farm animals. ⁶ Then, in 2007, a Zika outbreak hit 500 of the 7,000 residents on the Pacific Island of Yap, near the Philippines. As would occur elsewhere, Zika spread rapidly, then seemingly disappeared as the local populace built up immunity. No one in that epidemic died. ⁷

From Yap, Zika headed eastward to French Polynesia, near New Zealand, where a 2013 outbreak reached all 76 inhabited islands. Since then it has struck the Americas. In Brazil, which has been hardest hit, Zika has led to the births of about 5,000 micro-

cephalic babies in the past year. ⁸ Microcephaly, a condition in which a baby's head and brain are smaller than normal, can lead to developmental problems and vision and hearing loss. In severe cases, a shortened lifespan can result. ⁹

Researchers have linked Zika to other birth defects and more serious conditions, such as the neurological disease Guillain-Barré Syndrome, a rare, potentially fatal disorder in which the body's immune system attacks the nerves.

Scientists expect Zika eventually to reach every country in the Western Hemisphere except Canada, plus mainland Chile, according to the Pan American Health Organization, the Americas branch of the World Health Organization (WHO).

"Zika is very much on the move," writes Donald G. McNeil Jr., a *New York*

Selected Mosquito-borne Diseases

Chikungunya

Symptoms: Fever and joint pain and possibly muscle aches and headaches. **Where it occurs:** Africa, Asia and Europe. It first appeared in the Americas in Caribbean countries in 2013; the first locally acquired case in the continental United States was reported in Florida in 2014.

Species that spread it: Most often Aedes aegypti and Aedes albopictus.

Dengue

Symptoms: Fever and at least two of the following: severe headache, severe eye pain, joint pain, muscle and/or bone pain, rash, mild bleeding, low white-cell count. **Where it occurs:** Endemic in more than 100 countries, primarily in tropical urban areas; the Americas, Southeast Asia and Western Pacific most affected. Dengue is endemic in Puerto Rico; outbreaks have occurred in Hawaii and South Texas. **Species that spread it:** Mainly Aedes aegypti but also Aedes albopictus.

Malaria

Symptoms: Typically fever, headache, chills and vomiting. Left untreated, those infected may develop more severe complications and die.

Where it occurs: More than 100 countries and territories, including large areas of Africa and Asia. Most deaths occur among African children. About 1,500 cases are reported annually in the United States among immigrants and returning travelers. **Species that spread it:** Anopheles, particularly Anopheles gambiae.

West Nile Virus

Symptoms: Often, none. About one in five of those infected develop a fever accompanied by headache, body aches, joint pains, vomiting, diarrhea or rash; weakness and fatigue can last for months. About 10 percent of those who develop neurological symptoms such as seizures will die.

Where it occurs: Africa, Europe, Middle East, North America, West Asia, U.S. Species that spread it: Numerous, particularly Culex.

Yellow Fever

Symptoms: Initially, fever, chills, severe headache, back pain, body aches, nausea, vomiting, fatigue or weakness, but most people have mild or no symptoms. About 15 percent develop severe illness and up to half may die.

Where it occurs: Tropical areas of Africa and Central and South America. In a few cases, returning travelers from Africa carried it to China this year.

Species that spread it: Aedes and Haemogogus.

Zika

Symptoms: Fever, rash, joint pain, but most people have mild or no symptoms. In some cases, the virus can cause birth defects and neurological disorders. **Where it occurs:** Pacific islands, Africa, Latin America, the Caribbean. No locally acquired cases have yet occurred in the continental United States.

Species that spread it: Primarily Aedes aegypti.

Mosquito Species

Aedes aegypti: The yellow fever mosquito bites mainly humans.

Aedes albopictus: The Asian tiger mosquito is larger and blacker than Aedes aegypti and feeds on humans, pets and wild animals.

Anopheles: The common malaria mosquito; females taking blood meals to boost egg production pose biggest threat to humans.

Culex: Breeds prolifically; preys on birds and humans.

Sources: Centers for Disease Control and Prevention; World Health Organization

Times global health reporter, in his new book about the disease. "Transmission is increasing in Central America and the Caribbean and will keep doing so at least until the fall." ¹⁰

No one has yet contracted Zika from a mosquito bite within the continental United States. But about 1,305 people have become infected while traveling abroad, and in U.S. territories another 2,905 people have gotten Zika, according to the CDC. On July 19, the Florida health department announced it is investigating a possible first locally transmitted Zika case. ¹¹

In February, the WHO declared Zika a global health emergency. With Brazil set to host the Summer Olympics and Paralympics, there have been calls to postpone, move or cancel the Games, but health officials say the presence of tourists during Brazil's winter season, when mosquitoes are mostly dormant, will not increase the disease's spread. (*See sidebar, p. 612.*)

Scientists blame Zika's spread on the *Aedes aegypti* mosquito, the primary vector, or carrier, of the virus. The Asian tiger mosquito (*Aedes albopictus*), which causes chickungunya, has a wider range within the United States and might also carry Zika, but it is not known to be an effective carrier.

Zika is especially troublesome, scientists say, because it is the first mosquito-borne virus that can be spread via sex and is known to spread between pregnant women and their fetuses. On July 15, the CDC reported the first known case of a woman infecting her male partner through sex. The agency said women should use protection if their partners have traveled to Zika-infested regions, regardless of whether their partners are male or female. ¹²

In most cases, Zika appears to be harmless. Four out of five people infected with the virus aren't even aware of it because they have no symptoms. Others may experience mild problems, such as fever, rash or headache. Once exposed to Zika, humans are believed to be

immune to the virus. However, an infected person can spread it through sexual contact or by being bitten by a mosquito that then goes on to bite others.

What's more, because Zika has emerged so rapidly — and the virus is mutating as it travels — scientists still are determining its full effects.

In areas where Zika is present, the question of whether to advise women to delay pregnancy is controversial within public health circles. Many doctors have told patients they should wait, but the CDC and the WHO have not taken a formal position, although they have urged pregnant women or the partners of women trying to get pregnant not to travel to areas with high prevalence for Zika. Officials in some Latin American countries have warned women that they should postpone pregnancy. ¹³

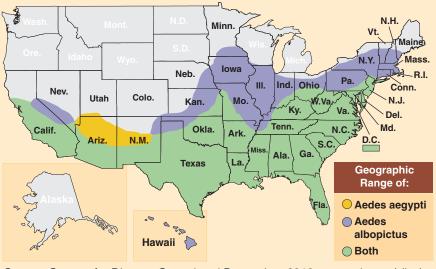
In February, President Obama asked Congress to approve nearly \$2 billion to fight the virus, but disagreements over how to pay for the funding have so far stymied congressional action. Republicans fear giving the administration a "blank check" and the flexibility to move money around without accountability, while Democrats have objected to provisions attached to the GOP's Zika bill. In July, Senate Democrats blocked a \$1.1 billion GOP package because it would have cut health care funding, barred money for Planned Parenthood's birth control efforts, changed non-health-related environmental regulations and altered a rule allowing Confederate flag displays at veterans' cemeteries. 14

Public health agencies have shifted funds from other programs to ramp up anti-Zika efforts, but many officials fear they will not have enough money to combat the virus vigorously. "Right now, in the continental U.S., we are not prepared to handle Zika if we start seeing transmission," says Peter Hotez, dean of the National School of Tropical Medicine at Baylor College of Medicine in Houston.

Disease-Carrying Mosquitoes Range Across U.S.

The Aedes aegypti mosquito, the primary carrier of Zika, dengue, chikungunya and other viruses, typically is found during the warmer months in 28 mostly Southern states, stretching from California to Florida, and as far north as the southern tip of New York. The Asian tiger mosquito (Aedes albopictus), which ranges as far north as southern Maine and across the Midwest, may also carry Zika, but that connection is uncertain, scientists say.

Range of Disease-Carrying Mosquitoes in U.S., 2016



Source: Centers for Disease Control and Prevention, 2016, www.cdc.gov/zika/vector/range.html

Areas of the Gulf Coast, from Florida to Texas, are fertile breeding grounds for *Aedes aegypti* mosquitoes. Urban areas with high concentration of poverty may be especially vulnerable, Hotez says. Poor people tend to be exposed to mosquito-borne illnesses more frequently because they may live in areas with inadequate sanitation, mosquito abatement programs and access to health care. In addition, many do not have air conditioning or screens, so they leave doors and windows open, letting in more mosquitoes.

"Some of the poorest counties in Texas, for example, . . . are probably at the highest risk for the Zika circulation and have the least resources to do anything about it," said Scott C. Weaver, director of the Institute for

Human Infections and Immunity at the University of Texas Medical Branch in Galveston. ¹⁵

And the disease may spread elsewhere. "No one who has studied *Aedes aegypti* is really surprised at all that it would spread a disease rapidly as a vector," says Edwards, the Muhlenberg entomologist. The mosquito is "a problem that's been there all along, waiting for a virus to spread."

Because of the way Aedes aegypti has evolved, it is particularly hard to kill off. Spraying campaigns don't work well because the mosquito can lay its eggs in tiny bodies of water, including indoors. Female mosquitoes suck blood to nourish their eggs. "It can lay eggs in a bottle cap with a couple of drops of water, or the cellophane wrapper of a cigarette pack," says Daniel Epstein,



A technician prepares blood for feeding genetically modified mosquitoes at a laboratory operated by the British biotechnology firm Oxitec in Campinas, Brazil, on Feb. 11. Oxitec recently received tentative approval for the trial release in the Florida Keys of genetically altered mosquitoes, whose offspring would not survive.

a communications officer with the Pan American Health Organization.

Scientists are experimenting with genetic engineering techniques to kill off mosquitoes, but the approach is controversial because of fears it could affect the larger ecosystem. The urgency of the Zika crisis, however, is lending momentum to their efforts.

As people wait to see whether Zika will become prevalent in the United States and other countries, here are some of the questions scientists, public health officials, lawmakers and the public are debating:

Is the U.S. public health system prepared for Zika?

Many doctors and health officials worry that Zika could overwhelm the public health system.

"We are underfunded, under-resourced and outgunned by the mosquito," says LaMar Hasbrouck, executive director of the National Association of County and City Health Officials.

A recent study by the Trust for America's Health, a nonprofit advocacy group, found that public health spending remains below the levels before

the 2007-09 recession. The nation ramped up public health spending in response to the terrorist attacks of 2001, partly in fear that terrorists might attack the United States with chemical or biological weapons. But funding for the CDC, as well as the federal program that provides grants to states and localities for response to public health emergencies, is down from its peak levels more than a decade ago. Many states have cut their own funding in recent years as well. ¹⁶

Money aside, other experts say, the public health system has a number of attributes. The United States has advanced health care facilities and personnel ready to treat Zika, and health officials say they have been preparing for months to contain the virus should it appear locally, including readying plans to isolate patients. The CDC is already monitoring hundreds of patients with Zika.

Local education campaigns and other efforts have helped prevent dengue and other viruses from spreading in recent years, experts say. "We have been very successful so far in controlling epidemics," says José Szapocznik, who chairs the Public Health Services Department at the University of Miami.

"If you were to ask any state health official, they would probably say at this point in time they're generally pleased with the progress they're making to respond to and contain Zika, should it become a locally acquired and transmitted disease," says James Blumenstock, chief program officer for public health at the Association of State and Territorial Health Officials.

But because the U.S. public health system is decentralized and fragmented, Blumenstock and other health officials say Zika could pose a serious test in terms of response. "If we really need to ramp up and respond to larger numbers," Blumenstock says, "we could be reaching a tipping point on resources where there's a limit to how much the nation's public health system can offer protection."

The United States has no single public health system. States and localities carry out much of the work of educating the public and combating epidemics. The picture varies so much from state to state — and within states — that a coherent or consistent response to health threats isn't always possible, according to Celine Gounder, an infectious disease specialist and former New York City assistant health commissioner.

The number of personnel at state health departments ranges from several hundred to just a few. And at the county level, the amount of resources and personnel devoted to public health depends on how much politicians are willing to spend on what sometimes seem like distant threats. ¹⁷

But those in public health circles like to say that a town doesn't wait until a fire breaks out to build a fire-house, and the town doesn't shut down the firehouse if no fires occur. But many health officials feel that's exactly what happens in public health. The urgency of a new threat can bring additional money, but it's purely reactive. Communities do not prepare in advance,

and after a threat ebbs, funding and attention do so as well.

Public health professionals decry this pattern of lurching from crisis to crisis. "We can't just keep running from one fire to the next, whether the current most pressing threat is Zika, Ebola, Legionnaire's disease or lead in the water supply," Gounder writes. "Yet historically, there's been little long-term political will to sustain public health funding." ¹⁸

Blumenstock and other public health officials worry that, with Zika, the nation isn't even lurching effectively, because Congress has failed so far to respond. Congressional inaction has forced the Obama administration to shift money meant to deal with the Ebola virus, for which Congress appropriated more than \$5 billion in emergency funds in 2014, to the Zika threat. ¹⁹

They say that even if state and local health departments effectively respond to Zika, they'll have done so by raiding funds meant to address other problems. Then they may be stretched too thin to effectively deal with severe problems such as a measles outbreak, a severe flu season or a bad hurricane season, Blumenstock and Gouder say.

"Preparedness money has been cut, so the core capacity of the public health system has diminished to the lowest I've seen in many, many years," says Bryan Callahan, a senior program officer at the Bill & Melinda Gates Foundation, which is the largest nongovernmental funder of anti-malaria efforts. "The public health folks always do what they can with what they have, but they're teetering dangerously close to being unable to deal with this crisis in any meaningful way."

"I'm confident that certain public health agencies are able to respond to Zika, but this is not uniform," says Amesh Adalja, an expert on infectious disease at the Center for Health Security at the University of Pittsburgh Medical Center (UPMC). "It's basically a lottery [as to] whether you have a county health department that has the capacity to respond to infectious diseases."

Should mosquitoes be eradicated?

A couple of years ago, billionaire philanthropist Bill Gates called mosquitoes the "most dangerous animal on earth," noting that "when it comes to killing humans, no other animal even comes close." ²⁰

But officials disagree over whether governments should attempt to eradicate the mosquitoes that carry deadly viruses. According to the American Mosquito Control Association, which represents mosquito control agencies, 174 different mosquito species are prevalent in the United States. Most are harmless, and no one suggests trying to wipe them all out. But some scientists consider *Aedes aegypti*, the primary carrier for Zika, dengue and yellow fever, a tempting target for eradication.

"Eradicating *Aedes aegypti* would be a good thing," says Crystal Boddie, a senior associate at the UPMC Center for Health Security and a former program manager with the federal Department of Homeland Security. "It carries all these diseases and poses a big risk to our public health."

Mosquito larvae are a food source for fish, and bats and birds eat adult mosquitoes. Mosquitoes can also act as pollinators for plants. Boddie says because *Aedes aegypti* is not native to the Western Hemisphere, wiping out the species shouldn't cause huge disruptions in the food chain. But other experts warn that targeting a species for elimination, particularly through heavy use of pesticides, can have unintended consequences on the ecosystem.

"You cannot reverse this epidemic through pesticides alone," says Szapocznik. "There's just so much we can fumigate. All those pesticides have adverse consequences for other animals and humans."

Killing mosquitoes with pesticides could damage animal habitats, particularly if poisonous chemicals are used in mass quantities. International efforts to wipe out mosquitoes to prevent malaria in the 1950s and '60s led to

environmental poisoning stemming from widespread use of the chemical DDT, which eventually was banned in the United States. ²¹

Mosquito control experts have long tried to use natural predators against the insects. For example, they have distributed fish that eat mosquito larvae and encouraged residents to build houses for bats, which can eat 1,000 mosquitoes per hour. ²²

Although insecticides remain a primary tool, scientists today are looking at newer methods. The Gates Foundation is sponsoring studies in Brazil and Colombia to release mosquitoes infected with Wolbachia, a bacteria that severely limits mosquitoes' ability to transmit viruses. Once a mosquito has the bacteria, it will be passed on to its offspring. Earlier studies were promising, says Callahan, the foundation official. "Wolbachia works not only in dengue but a whole host of viruses, including Zika, chikungunya, West Nile and yellow fever," he says.

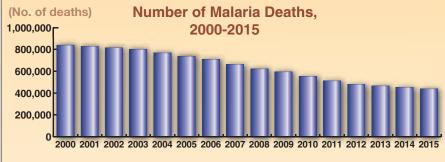
Scientists also are experimenting with genetic modifications to limit mosquito populations. In March, the Food and Drug Administration (FDA) gave tentative approval to Oxitec, a British biotechnology company, to run a trial study in the Florida Keys. Oxitec wants to release genetically modified *Aedes aegypti* males, whose offspring would not survive.

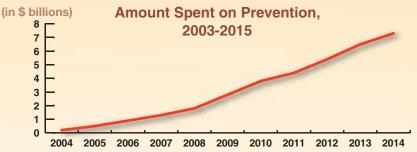
Local residents and critics of releasing genetically modified mosquitoes into the wild have expressed concerns about potential dangers, including toxic or allergic effects on humans and other wildlife, that they claim Oxitec has not addressed. "The company has been criticised by independent scientists for the poor quality of its risk assessments for the Cayman Islands and Malaysia [experiments] and lack of transparency and public consultation," according to GeneWatch UK, a nonprofit public interest group. ²³

Oxitec insists its technology is safe and says it is the result of extensive research. 24

Malaria Deaths Fall as Spending Increases

The number of malaria deaths worldwide fell by nearly half between 2000 and 2015, from more than 839,000 to fewer than 438,000, with most of the 2015 deaths occurring in Africa and Southeast Asia. Spending by the Global Fund to Fight AIDS, Tuberculosis and Malaria to reduce malaria deaths rose from \$200 million in 2004 to more than \$7 billion in 2015.





Sources: "World Malaria Report 2015," World Health Organization, http://tinyurl.com/zd2jvvy; "Results Report 2015," Global Fund to Fight AIDS, Tuberculosis and Malaria, p. 17, http://tinyurl.com/q3odyhl

Scientists also are exploring "gene drive" systems that can cause mutations, such as resistance to malaria, to be inherited by mosquito offspring. ²⁵ But this technique also has drawn claims that it upsets ecosystems or alters the spread of disease in potentially harmful ways. "We don't know whether the elimination of malaria specifically won't somehow have genetic effects that cause a super-virulent pathogen to be released or to bring in much greater catastrophic consequences," New York University bioethicist Brendan Parent said. ²⁶

Combating Aedes aegypti mosquitoes requires a special effort, say mosquito-control experts, with house-to-house inspections and efforts to persuade people to clean up all containers that can allow

the species to breed — which means attempting to get rid of objects as small as bottle caps.

But that's a daunting task, and even public health officials who believe mosquito eradication might be worthwhile doubt localities possess the resources for such an effort.

It is possible to eradicate particular species of mosquitoes from large areas. By 1970, 18 Latin American nations had eliminated *Aedes aegypti* within their borders. But countries have to get their neighbors to do the same or the mosquitoes will return over time. The United States ignored requests from other countries to participate in the eradication effort until 1965 and dropped its own effort just

four years later as interest in the project waned. ²⁷

Because yellow fever and dengue had largely disappeared from the United States, few public officials worried about *Aedes aegypti*. As a result, the Gulf Coast gave the mosquito a base from which to replenish and spread. "The U.S. kind of gave up its effort and stopped funding," says Epstein of the Pan American Health Organization. "*Aedes aegypti* came roaring back and reinfested the rest of the hemisphere."

Hotez, the tropical disease dean at Baylor, believes Zika's emergence may revive the question of *Aedes aegypti* eradication in the United States. With enough resources, he says, the species can be eradicated.

And that may be something people want because of the harm *Aedes aegypti* is causing humans.

"Zika has engendered a renewed interest in mosquitoes as being a vector and not just a nuisance," says Joe Conlon, technical adviser to the American Mosquito Control Association. "People who were against pesticides, now they just want them dead and don't care how you do it."

Should pregnant women with Zika have access to abortion where it is restricted or outlawed?

Because of the severity of microcephaly and other birth defects linked to Zika, many women's rights and health care advocates argue that pregnant women should have access to abortion. But many countries most severely affected by Zika do not allow abortions: El Salvador and Nicaragua outlaw abortion entirely, while Brazil and Venezuela prohibit abortion except when necessary to save the pregnant woman's life.

In February, the U.N. High Commissioner for Human Rights said that to respond effectively to the Zika threat, nations must repeal "laws and policies that restrict access to sexual and reproductive health" services. ²⁸

Anis, a Brazilian bioethics group, has petitioned that country's Supreme Court

to allow women infected with Zika to have abortions. In El Salvador, the health minister has argued that his nation must revise its abortion laws because of the risk of severe birth defects, but his efforts have been unsuccessful.

"It has made the issue more salient and has highlighted the cruelty behind some of these restrictive abortion laws," said Francoise Girard, president of the International Women's Health Coalition, a New York-based nonprofit that promotes reproductive rights. "There is an incredible amount of anxiety, fear and stress among women that are pregnant." ²⁹

Women's rights groups and public health advocates note that within the United States, states have passed more than 200 laws restricting abortion over the past five years. Many of these laws have passed in Southern states where Zika is expected to be most prevalent. ³⁰

After Texas enacted a law in 2013 that forced abortion providers to meet higher safety standards, half of the abortion clinics in the state closed. ³¹ The Supreme Court, in a 5-3 vote in late June, overturned that law, saying the restrictions were merely cover for making abortions harder to obtain. ³²

In addition, about a dozen states — most recently South Carolina in May — have banned most abortions after 20 weeks of pregnancy. Microcephaly is not detected through normal pregnancy screenings such as ultrasounds, and it can't be diagnosed even through more sophisticated tests such as CT scans and MRIs until at least 19 weeks into a pregnancy.

"The microcephalic development is not visible early on," says Szapocznik, the Miami public health professor.

But abortion opponents say Zika's spread is no reason to promote greater access to the procedure. They argue that abortion supporters have used other medical conditions in the past as reasons to increase access to abortion.

Not all pregnant women infected with Zika have children with birth defects. Abortion opponents stress that Zika's effects are still unknown, so gov-



A health worker prepares to inject the world's first dengue vaccine at a public school in Marikina City, Philippines, on April 4. Dengue is found in more than 100 countries, primarily in tropical urban areas. The virus is endemic in Puerto Rico; outbreaks have occurred in Hawaii and South Texas.

ernments should not rush to increase abortion rights.

"The kneejerk reaction of, 'We need more abortion,' to a relatively unknown occurrence is alarming," says Mike Gonidakis, president of Ohio Right to Life, which opposes abortion. "Of course, no one wants their unborn child to have Zika, but babies that are born with Zika, that's not a death sentence. What is a death sentence is abortion."

At a February hearing on Zika, Rep. Christopher Smith, R-N.J., a leading congressional opponent of abortion, recounted the story of a Brazilian woman born with microcephaly whose doctors predicted she would not walk or talk but who has been able to work as a journalist. "[W]e must work harder to prevent maternal infections and de-

vise compassionate ways to ensure that any child born with disabilities from this or any other infection is welcomed, loved and gets the care he or she needs," Smith said. ³³

In recent decades, many families have made it a point to try to adopt children with special needs or other disabilities, notes John Stonestreet, president of the Colson Center for Christian Worldview, a religious organization in Lansdowne, Va. "We've seen societies that consider individuals with disabilities to be less valuable than other members of society," Stonestreet says. "We've rightly condemned that as being heartless, inhumane and wrong."

Health officials hope that the Zika threat will stem the push against contraceptives in some states. In February,

Pope Francis drew headlines when he suggested that contraceptives, which violate Catholic doctrine, might be permissible as part of the effort to combat Zika. But he underscored that abortion is "an absolute evil" and would not be justifiable in the Zika fight. ³⁴

And the current version of the congressional funding bill for Zika died in the Senate in July after Democrats complained it blocked money to pay for contraceptives or condoms and didn't provide money for family-planning groups such as Planned Parenthood. Republicans and Democrats have since traded charges over which side is being more irresponsible. ³⁵

The political maneuvering has exasperated some health officials. "Public health has always been a partnership between the federal, state and local levels," says Georges Benjamin, executive director of the American Public Health Association, a trade group for professionals in the field. "Congress has failed to do its job, frankly."

Cindy Pellegrini, a lobbyist for the March of Dimes, which advocates for maternal and fetal health, said the GOP's bill was "doomed from the start" because it was loaded with provisions that Democrats opposed. ³⁶

BACKGROUND

Breaking Yellow Fever

A lthough malaria has been the major killer among mosquito-borne illnesses worldwide, yellow fever has done more to shape history in the Americas.

Yellow fever first broke out in the Americas in 1648, in Barbados, Havana and Yucatán, Mexico. By the 1690s, it was present in North America, notably in the port cities of Charleston, New York and Philadelphia. ³⁷ Although it didn't kill as many people and wasn't

as contagious as cholera or smallpox, it created more panic, journalist Molly Caldwell Crosby writes in her history of the disease, *The American Plague*. "Yellow fever became the most dreaded disease in North America for two hundred years," she said. ³⁸

In 1793, some 5,500 people died during an outbreak in Philadelphia, which was then the U.S. capital. ³⁹ Over a 35-year span during the 1800s, New Orleans suffered a dozen outbreaks, each causing more than 1,000 deaths. ⁴⁰

Yellow fever also helped reshape the continent. The French dictator Napoleon, who dreamed of building an empire in the Americas, saw thousands of his troops die from yellow fever in Haiti during a failed attempt to end a slave rebellion. Discouraged by the setback and other problems, he sold millions of acres to the United States in 1803 in what became known as the Louisiana Purchase.

Yellow fever was associated with the slave trade. Steam power and other navigational improvements cut the time crossing the Atlantic Ocean from 30 days to seven during the 19th century, meaning people infected with yellow fever could travel before its symptoms showed. ⁴¹ Although the disease could affect anyone, its spread contributed to prejudice against blacks and immigrants, as well as to the view that the American South was a distinct region within the country.

"Carolina is in the spring a paradise, in the summer a hell, and in the autumn a hospital," a German commentator wrote during the colonial period, an observation that still applied in the 19th century. ⁴²

A warm, wet winter in 1878 helped create perfect conditions for the *Aedes aegypti* mosquito. That year, a yellow fever epidemic spread from Brazil and killed 20,000 in the Mississippi Valley. The population of Memphis, Tenn., in July 1878 was 47,000. By September, only 19,000 people remained in the city, and 17,000 of them had yellow fever. ⁴³

In the late 19th century, scattered

physicians — the Scottish doctor Patrick Manson, working in China, and Alphonse Laveran, a French army physician stationed in Algeria - made the first connections between insects and disease. Their findings, and those of other pioneering scientists, were generally greeted with ridicule. The Washington Post wrote in 1890, "Of all the silly and nonsensical rigmarole of yellow fever that has yet found its way into print . . . the silliest beyond compare is to be found in the arguments and theories generated by the mosquito hypothesis." 44 Laveran was ultimately awarded a Nobel Prize for his work in 1907.

When French teams failed to complete the Panama Canal after one-third of the workers died from yellow fever or malaria, the U.S. Army prepared to take over. It created a Yellow Fever Commission in 1900, headed by Maj. Walter Reed, after whom the Army later named its flagship medical center.

To test the hypothesis that mosquitoes were responsible for spreading the disease, Reed paid human volunteers \$100 to be exposed to yellow fever, with another \$100 paid as a bonus if they contracted the disease. As Crosby noted, before World War I, soldiers were more likely to die from diseases than from bullets, "so volunteering for human experiments" that might determine the cause of disease "might not seem as much of a psychological departure as it would today." ⁴⁵

Reed proved the link between mosquitoes and disease. Using a process of elimination, he exposed his subjects to every manner of filth, thus showing that germs, infected clothing or air did not spread yellow fever. After a subject named John Moran, who was housed among mosquitoes in one of Reed's buildings, came down with a high fever, Reed smiled and said, "Moran, this is one of the happiest days of my life." ⁴⁶

William Gorgas, the Army's chief sanitary engineer, introduced draconian anti-mosquito measures in Havana,

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Chronology

1940s-1970s

Efforts to wipe out mosquitoes result in environmental damage.

1947

Zika virus first identified in Uganda's Zika Forest.

1951

American researcher Max Theiler wins Nobel Prize in medicine for his role in developing yellow fever vaccine.

1951

Malaria temporarily eradicated in the United States.

1954

Zika first identified in a human in Nigeria.

1955

The World Health Organization (WHO) initiates Global Malaria Eradication plan.

1962

Eighteen Latin American countries succeed in eradicating *Aedes aegypti* mosquitoes. . . American biologist Rachel Carson's influential book *Silent Spring* tells how the pesticide DDT wreaked environmental havoc.

1963

Dengue fever outbreak in Puerto Rico marks the disease's first appearance in the Western Hemisphere in 20 years.

1969

WHO largely abandons its mosquito eradication campaign, recommending that countries adopt control strategies.

1972

U.S. bans use of DDT.

1990s-2000s

Malaria and other mosquitoborne illnesses re-emerge as major concerns.

1995

Europe records 90,000 cases of malaria.

1999

Outbreak of West Nile virus in New York state represents the disease's first appearance in the Western Hemisphere.

2001

Maui sees its first case of dengue in more than 50 years.

2002

A malaria case in Virginia is the first in the U.S. in several years. . . . Global Fund to Fight AIDS, Tuberculosis and Malaria, a public-private partnership, is established and becomes the main conduit for Western aid.

2005

President George W. Bush announces the U.S. will spend \$1.2 billion over five years to fight malaria.

2007

In the first major outbreak of Zika, dozens of residents are infected on Yap, a Pacific island. Scientists detect separate Asian and African strains of the virus.

2008

Aid from governments and foundations devoted to fighting malaria increases to more than \$1 billion, up from \$100 million in 1998.

2010-Present

Zika and other mosquito-borne diseases become prevalent in the Americas.

2010

Campaigns succeed in halving malaria cases in 10 African countries over the past decade.

2012

West Nile virus kills 89 people in the Dallas-Fort Worth area, part of a record U.S. death toll of 286.

2013

Zika outbreak reaches all 67 inhabited islands of French Polynesia. . . . First known Zika case appears in the U.S.; the disease is diagnosed in a New York man who had been in French Polynesia.

2014

Chikungunya spreads in Florida, Puerto Rico and U.S. Virgin Islands.

2015

Brazil records 1.6 million cases of dengue, nearly triple the number in 2014. . . . As Zika spreads rapidly in Brazil, more than 3,000 babies are born with microcephaly. . . . The first locally transmitted U.S. case of Zika is reported in Puerto Rico.

2016

WHO declares Zika a global health emergency (Feb. 1). . . President Obama requests \$1.9 billion in emergency supplemental funding for Zika (Feb. 22). . . . Centers for Disease Control and Prevention says Zika virus in pregnant women can cause microcephaly in fetuses (April 13). . . . Vaccine shortages force WHO to approve yellow fever vaccinations of one-fifth strength (June 17). . . . Inovio Pharmaceuticals announces first trial of a Zika vaccine (June 20). . . Senate Democrats block passage of a \$1.1 billion funding package to combat Zika out of concern about its restrictions on birth control (July). . . .

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Experts Differ on Zika Threat at Summer Olympics

Some athletes are staying away from the Games in Brazil.

BC will be sending hundreds of people to Brazil to help with coverage of the Summer Olympics, but the "Today" show's Savannah Guthrie won't be one of them. Guthrie was set to co-host the broadcast of the Games' opening ceremonies on Aug. 5, but she is pregnant and on the advice of her physician will not be attending.

Both the Olympics and the Paralympics, which starts Sept. 7, are being held in Rio de Janeiro. The World Health Organization (WHO) has said the Olympics will not substantially worsen the spread of Zika. But with Brazil at the center of the disease's outbreak, many have questioned whether the Games should have been postponed, canceled or moved.

"[W]hile Brazil's Zika inevitably will spread globally — given enough time, viruses always do — it helps nobody to speed that up," Canadian immunologist Amir Attaran wrote in a widely cited article in the *Harvard Public Health Review*. "In particular, it cannot possibly help when an estimated 500,000 foreign tourists flock into Rio for the Games, potentially becoming infected, and returning to their [homes]." ¹

Several top golfers and American cyclist Tejay van Garderen are among the athletes skipping the Games due to health concerns. Britain's Greg Rutherford will be going to Rio in hopes of earning another gold medal in the long jump, but his partner won't be coming along, and they have frozen his sperm as a precaution. ² Hope Solo, the goalkeeper on the American women's soccer team, says she will participate but only "grudgingly."

"I'm not sure I'm even going to be leaving the hotel room, outside of practice," Solo told CNBC in May. "I strongly believe that no athlete should be put into this position — to decide between your Olympic dreams and your own health." 3

The National Institutes of Health announced on July 5 that it will fund a study to monitor the health of U.S. athletes and coaches for up to two years after the Games. ⁴ But while it may make intuitive sense that it's a bad idea to hold a global gathering at the center of an epidemic — 160,000 Brazilians have been infected with Zika this year — the WHO and other health officials insist the risk of infection is minimal.

For one thing, the Games are taking place during winter in the Southern Hemisphere, when mosquitoes are least active. Already, the number of new cases has dropped from more than 3,000 per week earlier in the year to about 30 per week in June. ⁵ "There's little mosquito-borne disease at that time," says Daniel Epstein, a communications officer with the Pan American Health Organization, a regional office of WHO.

Epstein adds that Brazilian officials will make every effort to ensure that Olympic venues are well sprayed. And, he says, substantial travel between Brazil and the rest of the world already occurs. "The number of people who are going to the Olympics and coming back are less than 1 percent of the people who are traveling back and forth to Zika-infested countries," Epstein says.

One epidemiological model projects that, at most, 16 foreign tourists will contract Zika at the Olympics. ⁶ At a news

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which the Army still occupied following the Spanish-American War. His targets were puddles and broken flower pots and drained or oiled pools of standing water. Cases dropped from 1,400 in 1900 to zero in 1902. ⁴⁷ Residents were fined if mosquito larvae were found on their property — a policy still in place in Havana today. ⁴⁸

Gorgas soon exported his sanitation methods to Panama, but many, including Secretary of War (and future President) William Howard Taft, remained skeptical about mosquitoes being the root cause of disease. Taft lobbied to remove Gorgas from his post. A doctor friend convinced President Theodore Roosevelt that fighting mosquitoes was the best way to combat yellow fever.

"You must choose between the old method and the new," the doctor, Alexander Lambert, told the president. "You must choose between failure with mosquitoes or success without them." ⁴⁹

After being stymied at first, Gorgas was given a staff of 4,100 workers and the entire U.S. supply of sulphur, kerosene and pyrethrum to use as insecticides. ⁵⁰ They worked — at least where Gorgas deployed them. Where an earlier French dig had failed, largely due to death and disease, the Americans succeeded, with only 350 deaths among the white American canal workers, the focus of Gorgas' sanitation efforts.

In 1937, microbiologist Max Theiler and other scientists funded by the Rockefeller Institute developed a cheap and effective vaccine for yellow fever. By 1942, 7 million doses were given to American and British soldiers fighting in Africa. Not one case of yellow fever occurred among them. ⁵¹

Attacking Malaria

Malaria remained a major problem. "People forget today, but even as recently as World War II, every country in the world had endemic malaria transmission within its borders, even inside the Arctic Circle," said Richard Feachem, the first executive director of the Global Fund to Fight AIDS, Tuberculosis and Malaria. ⁵²

For more than a century, humans had taken quinine, an extract of cinchona bark, to help prevent parasites that conference in June, Brazilian health minister Ricardo Barros said the chances of catching the Zika virus at the Games is "almost zero." ⁷

"There isn't a public health or Zika rationale to move the Olympics or delay the Olympics," says Thomas V. Inglesby, director of the Center for Health Security at the University of Pittsburgh Medical Center.

Foreign travel always has risks. Whether it is worth taking a chance on attending this particular Olympics, Inglesby says, is a personal choice.

A fair number of people are choosing not to go, whether due to Zika, Brazil's ongoing corruption and political turmoil or other reasons. Sixty-three percent of travel agents surveyed in June said they were seeing less interest in trips to Rio than there had been for recent Games in London and Beijing. ⁸

As a result, travelers who do head to this year's Games will get a better deal, said Julia Carter, sales director for Brazil Nuts, a South American tour operator based in Naples, Fla. "There are certainly more deals than there were six months ago," she said. ⁹

— Alan Greenblatt



Standing water in a slum near the site of the Summer Olympics in Rio de Janeiro is a potential breeding ground for Zika-carrying mosquitoes.

³ Matthew J. Belvedere, "Soccer star Hope Solo decides to go to the Rio Olympics despite Zika concerns," CNBC, May 10, 2016, http://tinyurl.com/hnvkbl8.
⁴ Bill Berkrot, "U.S. to fund Zika virus study of U.S. Olympic team," Reuters, July 5, 2016, http://tinyurl.com/j9095rm.

⁵ Dom Phillips, "Brazil says there is 'almost zero' risk of Zika during Olympics. Really?" *The Washington Post*, July 6, 2016, http://tinyurl.com/jlcfhla.

⁶ Marcello Nascimento Burattini *et al.*, "Potential exposure to Zika virus for foreign tourists during the 2016 Carnival and Olympic Games in Rio de Janeiro, Brazil," *Epidemiology & Infection*, July 2016, http://tinyurl.com/j59r7xg.
⁷ Shasta Darlington, "Risk of catching Zika during Olympics is 'almost zero,'

A Shasta Darlington, "Risk of catching Zika during Olympics is 'almost zero,' Brazilian official says," CNN, June 11, 2016, http://tinyurl.com/z720156.

cause malaria from growing in the gut. By the 1940s, researchers had developed the first synthetic anti-malarial treatments, chloroquine and amodiaquine. The U.S. Army was heavily involved in anti-malaria research during World War II because of the number of soldiers who contracted the disease while fighting in the Pacific jungles.

By 1944, the Army had begun using dichlorodiphenyltrichloroethane, or DDT, as an insecticide.

Some strains of malaria became resistant to chloroquine. Other treatments followed, but despite billions of dollars invested in research no vaccine has been developed.

Malaria was less of a problem in rich countries such as the United States and Britain than in Asia and, especially, Africa. For one thing, mosquitoes preferred to feed on herds of cattle instead of humans. In addition, as swampland was drained for pasture and increasing numbers of people moved from farms to cities, the disease declined. Malaria was eradicated in the United States by 1952, although cases have occurred sporadically among travelers. ⁵³

The Rockefeller Foundation had led the charge against mosquito-borne illnesses for decades, but after World War II primary responsibility for fighting malaria internationally switched to the World Health Organization, established in 1948.

Following the war, DDT was widely adopted for civilian use, replacing earlier pesticides, such as Paris green, a highly toxic compound powder that includes arsenic. DDT did not directly harm

human health but was fatal to mosquitoes, and the chemical became the foundation for an eradication campaign begun by the WHO in the 1950s.

In 1958, Congress allocated \$100 million for the anti-malarial program. By 1963, Congress had spent nearly \$500 million, with 93 countries around the world using U.S. dollars to finance spraying campaigns. ⁵⁴

Initial results were spectacular. In Sri Lanka, the number of malaria cases plummeted from 3 million in 1946 to just 18 in 1963. India, which saw 75 million infections and 800,000 deaths in 1947, had fewer than 100 malaria deaths in 1965. All told, 18 countries that were home to nearly one-third of the world's population were declared malaria-free. ⁵⁵

¹ Amir Attaran, "Off the Podium: Why Public Health Concerns for Global Spread of Zika Virus Means That Rio de Janeiro's 2016 Olympic Games Must Not Proceed," *Harvard Public Health Review*, May 2016, http://tinyurl.com/hsmlay?

² Susie Verilli, "Why I'm Not Flying Down to Rio," Standard Issue, June 7, 2016, http://tinyurl.com/zomln43.

⁸ Nell McShane Wulfhart, "Zika Fears and Political Chaos Keeping Rio Olympics Affordable," *The New York Times*, June 13, 2016, http://tinyurl.com/h8g9zdz.
⁹ *Ibid.*

Major Success: Malaria Deaths on the Decline

But limited donor interest, poverty inhibit further progress.

P ublic health experts call the fight against malaria, an ancient and deadly parasitic disease that attacks the liver and is spread by mosquitoes, one of the great global health success stories of the century. Deaths and transmissions have fallen sharply in recent years, an incredible achievement, experts say, given a lack of international attention to the disease a couple of decades ago.

But malaria remains a stubborn foe because both the malaria parasite and the mosquitoes that carry it have repeatedly developed resistance to pesticides and drugs used to fight the disease. Public health officials say more eradication tools — and money — are needed if progress is to continue.

Since 2000, annual malaria cases worldwide have dropped from an estimated 262 million globally in 2000 to 214 million in 2015, while malaria deaths have declined by nearly half, from about 839,000 to 438,000, with most of the deaths occurring in Africa and Southeast Asia, according to the World Health Organization. ¹ (*See graphic, p. 608.*) And over the next couple of years, the number of countries considered malaria-free, meaning the disease is not transmitted locally, could grow considerably. South Africa, Botswana, Nepal and Ecuador are among the countries on track to join that list.

"In 1900, just about every country in the world had endemic malaria," says Bryan Callahan, a senior program officer with the Bill & Melinda Gates Foundation, the largest nongovernmental funder of anti-malaria efforts. "Now, half the member states of the United Nations don't have it. That's a huge public health achievement."

Nevertheless, malaria remains a scourge, killing a child in Africa every two minutes. ² Earlier efforts to beat back malaria fell short, largely because anti-malaria efforts became a victim of their own success. Once eradicated from an area, malaria can return within a single transmission season, so the disease

requires constant vigilance. Thus, perversely, the more success achieved, the less likely donors were to remain interested in combating the disease, says Scott Filler, senior malaria coordinator for the Global Fund to Fight AIDS, Tuberculosis and Malaria, a public-private organization that is the primary international conduit for anti-malaria efforts.

"Malaria falls off people's list of priorities when fewer kids are dying," Filler says. "As we get more successful, unfortunately, people punish success by forgetting how bad it was."

Although efforts to find a vaccine have been underway for decades, none exists yet. And the malaria-carrying mosquitoes — about 40 species of *Anopheles* — and the malaria-causing parasite have proven adaptable to insecticides and drugs. Chloroquine was once the most common anti-malaria drug, but drugresistant strains of the disease have developed in many countries. Today's drug of choice is ACT (artemisinin-based combination therapies), but resistant parasites have developed in several Southeast Asian countries. ³

"We're reaching an inflection point where our tools won't be effective if we don't bring in new tools," Filler says.

Currently, insecticide-treated bed nets, which protect individuals — especially children — from being bitten while they sleep, are an important weapon against the disease. But some mosquitoes in Africa are developing resistance.

Filler says a new combination of insecticides will be used to treat bed nets in the next year or two, but he warns this will drive up costs. Progress against malaria will require continued financial investment, especially since most health gains have occurred in places where malaria is less severe. Plus, it remains a major killer in several West and Central African countries, many of them impoverished.

"The sudden lifting of the malarial burden brought about by liberal use of DDT in the years immediately after World War II was one of the most dramatic and abrupt health changes ever experienced by humankind," wrote historian William H. McNeill. ⁵⁶

But victory was short-lived. DDT destroyed a wide spectrum of insects and also poisoned animals. Nature writer Rachel Carson's landmark 1962 book, *Silent Spring*, warned that DDT and other pesticides had endangered ecosystems and threatened extinction of the bald eagle. Carson's book and her Capitol Hill testimony helped persuade Congress to cut off funding for

the mosquito eradication campaign in 1963. ⁵⁷ Abroad, DDT spraying had become controversial among the public; many people didn't want their properties treated because DDT can kill farmyard animals and pets, so some bribed sprayers to bypass them. ⁵⁸ By 1972, the United States had banned the use of DDT. ⁵⁹

However, by the time DDT was banned, the surviving mosquitoes had developed resistance to the chemical. As a result, the legacy of the DDT campaign — which never got underway in Africa for political reasons having to do with colonialism and the Cold War — was DDT-resistant mosquitoes. By 1969,

Sri Lanka was back up to 500,000 malaria cases, while India saw 1 million. ⁶⁰

Despite these setbacks, the campaign did eradicate malaria in many places and helped build a public health infrastructure that contributed to the fight against other diseases, such as smallpox. 61

Western Outbreaks

By the late 1990s, other mosquito borne-illnesses began to crop up in the Americas. The hemisphere's first case of West Nile encephalitis, which had been identified in Uganda in 1937,

In the past, malaria has been beaten back, only to reemerge as a major threat. A global eradication effort in the 1950s and '60s was eventually abandoned, in large part due to environmental problems with DDT, the primary chemical used for spraying, plus the mosquitoes developed resistance to the chemical. In addition, donors lost interest when deaths declined, and fighting malaria was not coordinated on an international basis. ⁴

Then, in 1999, the United Nations made fighting malaria a priority as part of its Millennium Development Goals. ⁵ A highly influential 2001 paper argued that treating malaria was not only a health issue but a prerequisite for ending poverty in many nations, largely because of the millions of people in the developing world who are debilitated by the disease each year. ⁶

Around the turn of the 21st century, the Gates Foundation and the Global Fund were established. The fund's efforts received major help from rich nations, including the United States. In addition, President George W. Bush began a billion-dollar initiative in 2005, with the goal of reducing malaria-related mortality by 50 percent in 15 countries in sub-Saharan Africa. ⁷ The Obama administration has continued to support the initiative.

"We know exactly what it takes to prevent and treat the disease," Bush said at a White House summit on malaria in 2006. "The only question is whether we have the will to act." 8

Serious obstacles, such as fraud and corruption, hamper the distribution of bed nets and other aid in some countries, experts say. 9

"Where malaria is worst is where health systems are weakest," says Filler. "The fight against malaria is a long, hard fight."

— Alan Greenblatt



A child with malaria lies on a bed at a hospital in the Nyarugusu refugee camp in northwest Tanzania on June 11. The disease kills a child in Africa every two minutes.

¹ "Results Report," The Global Fund to Fight AIDS, Tuberculosis and Malaria, Sept. 18, 2015, http://tinyurl.com/nmeg2yr; "World Malaria Report 2015," World Health Organization, p. 9, http://tinyurl.com/zd2jvvy.

² Jon Greenberg, "Malaria's toll: Close to one African child killed every 2 minutes," *Politifact*, April 25, 2016, http://tinyurl.com/hou62ew.

³ "Q&A on artemisinin resistance," World Health Organization, February 2015, tinyurl.com/mbaup5l.

⁴ Sonia Shah, *The Fever* (2010), p. 215.

⁵ For background, see Danielle Kurtzleben, "Millennium Development Goals," CQ Global Researcher, Sept. 4, 2012, pp. 401-424.

⁶ John Luke Gallup and Jeffrey D. Sachs, "The Economic Burden of Malaria," *American Journal of Tropical Medicine and Hygiene*, January 2001, www.ncbi.nlm.nih.gov/books/NBK2624/

⁷ For more information, see "Background," President's Malaria Initiative, https://www.pmi.gov/about.

 8 Alex Perry, Lifeblood: How to Change the World One Dead Mosquito at a Time (2011), p. 92.

⁹ *Ibid.*, p. 190.

occurred in New York City in 1999. The CDC originally misidentified it as St. Louis encephalitis, which was first identified in 1933 in that city and occurred primarily in the Mississippi Valley and Gulf Coast.

Tracey McNamara, a veterinarian and pathologist at the Bronx Zoo, determined that the same virus was responsible for bird deaths, and researchers subsequently identified it as West Nile. ⁶² By 2002, West Nile had spread to Louisiana and other Southern states and was responsible for 4,161 cases and 284 deaths in the United States. ⁶³ About 2,000 cases are diagnosed in the United States each year, typically

resulting in some 50 deaths, although there were 119 in 2015. 64

Mosquitoes of the genus Culex spread West Nile; these carriers like to breed in stagnant and dirty (or organic rich) water. By contrast, the *Aedes aegypti* mosquito prefers clean water, laying eggs in manufactured containers such as barrels, tires or bottles. *Aedes aegypti* mosquitoes, in fact, typically don't breed in bodies of water with natural bottoms of sand or mud. ⁶⁵

"Aedes aegypti evolved on the borders of what became the Sahara Desert," says Edwards, the entomologist at Muhlenberg College. "It became adapted to live in our stored water. If it didn't have humans providing water for it, it would not have been able to survive."

Non-experts once knew *Aedes aegypti* as the yellow fever mosquito, but in recent years it has been spreading other diseases, including dengue, chikungunya and Zika. Dengue, which was barely considered a problem in the Western Hemisphere during the 1950s, has become an increasing concern in the Americas, with the number of cases growing thirtyfold from the 1960s to the 2010s, according to the WHO. In 2010, the Americas had 1.7 million cases. ⁶⁶ Last year, Brazil alone saw 1.6 million dengue cases, nearly triple the country's rate in 2014. ⁶⁷

MOSQUITO-BORNE DISEASE

"Dengue doesn't have a high mortality rate but causes huge health costs," says Callahan of the Gates Foundation. "People often wind up having extreme gunya in Florida and Texas and Hawaii, now we can't ignore a problem that makes visible the mistakes we make in vector control."



Garbage in the streets of Luanda, capital of Angola on the West African coast, can catch rainwater and become mosquito-breeding grounds. Along with Congo, Angola is suffering an outbreak of yellow fever, which is carried by the Aedes aegypti mosquito.

symptoms of bone ache, backache, high fever. People feel that their muscles are contracting so severely it will break their back." In fact, dengue is sometimes called "break-bone fever" because of the severe pain it causes in the joints and muscles.

Since 2001, dengue outbreaks have occurred in Hawaii, Texas and Florida. Public health officials have warned that the spread of dengue — and more recently, chikungunya — shows that the United States needs to step up its mosquito and surveillance efforts.

Since 2014, chikungunya, which rarely infected U.S. travelers even a decade ago, has been transmitted locally in the Caribbean and Florida. ⁶⁸ Last year, ⁴⁴ states recorded cases of chikungunya. ⁶⁹

"There was a perception that mosquito-borne diseases were not a problem, because we'd overcome yellow fever and malaria," says Thomas V. Inglesby, director of the Center for Health Security. "With cases of chikun-

CURRENT SITUATION

Zika's Challenges

In Congress, the debate continues over how to provide funding to fight Zika. President Obama asked the House and Senate in February for \$1.9 billion to prevent the spread of Zika in the United States. The money would be used to bolster efforts among federal agencies and offer grants to states for treatment, disease prevention and vac-

Congress was slow to respond to the president's request. Republicans, who control both chambers, said they were concerned that the administration's plan was not well thought out and lacked specifics.

cine research, Obama said. 70

"It doesn't take a lot of thought to realize that this is a request for a blank check," Senate Majority Whip John Cornyn of Texas said in April. "What they want to do is play a shell game with this money. They want to get the money and if they don't need it to deal with Zika, they can transfer it for other purposes, again without any transparency, without any real political accountability." ⁷¹

Indeed, the Obama administration did shift funds previously appropriated to fight Ebola to get its Zika response up and running. On the local level, the change meant health departments had to do shifting of their own: A survey in April found that two-thirds of local health departments cut their preparedness budgets, while more than 40 percent reduced their medical staffing and supply budgets. ⁷²

On May 17, the Senate passed a bipartisan compromise to provide \$1.1 billion for mosquito control, public education and vaccine development. The next day, the House passed a bill to provide \$622 million for the Zika fight, limiting spending to the current fiscal year and shifting leftover Ebola funding to Zika to offset the cost.

A deal was then worked out in June between the House and Senate, with input primarily from Republicans. It would provide \$1.1 billion, equaling the Senate version, but \$750 million of the funding would have to come from cuts in other programs. In addition, the bill included provisions that Democrats opposed, such as a stipulation that no funding in this legislation go to Planned Parenthood or other family-planning groups. Another would allow the display of Confederate flags in veterans' cemeteries. ⁷³

The House passed the bill on June 23 along party lines. But the White House issued a veto threat. "This plan from congressional Republicans is four months late and nearly a billion dollars short of what our public health experts

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At Issue:

Should genetically modified mosquitoes be used to fight disease?



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WRITTEN FOR CQ RESEARCHER, JULY 2016

he Zika virus, like the dengue, chikungunya and yellow fever viruses, is transmitted by mosquitoes, most commonly *Aedes aegypti*. Vaccines can protect people but take time to develop. Until a Zika vaccine is available, attention remains on reducing the mosquito population. Insecticides are used widely but work inefficiently, indiscriminately and only temporarily.

Hence attention has turned to biological approaches, which deserve serious consideration. The first, simplest and most extensively tested of these is the release of male mosquitoes endowed with a lethal gene. The laboratory-reared mosquitoes, developed by the British biological engineering firm Oxitec, are sex-sorted, and the males are released to find and mate with females. The lethal gene becomes active and the offspring die, rapidly reducing mosquito numbers. People are not affected because male mosquitoes don't bite them.

The Oxitec mosquito has been tested in the Cayman Islands, Malaysia and Brazil since 2009 and has reduced mosquito populations by as much as 99 percent. However, because these insects are genetically modified, they are heavily regulated, and the approval process can take years. In the United States, the Food and Drug Administration is regulating the Oxitec mosquito as a "new animal drug," an odd use of regulations designed to ensure that a new drug is safe and effective.

A second biological approach is based on the observation that infection of mosquitoes with certain Wolbachia bacteria interferes with their fertility and their ability to transmit viral diseases. If an uninfected male mates with a Wolbachia-infected female, most of the eggs won't hatch and the infected mosquitoes will take over the population. Wolbachia infection also reduces the mosquitoes' ability to transmit dengue and Zika. While preliminary evidence shows that transmission is blocked at least transiently, some scientists are concerned about the long-term effects of replacing uninfected mosquitoes with Wolbachia-infected ones.

A recently developed gene-editing system that goes by the unwieldy acronym of CRISPR/Cas9 has considerable potential. For examples, the CRISPR/Cas9 system can be designed in a test tube to promote the rapid spread of a fertility-reducing gene in the mosquito population. Male mosquitoes genetically modified with such a gene construct would be released to mate with wild females, as described for the Oxitec mosquito. By reducing fertility, this approach might result in the complete elimination of the targeted species of this invasive pest.



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WRITTEN FOR CQ RESEARCHER, JULY 2016

any countries are able to control mosquito transmitted disease without wiping out all mosquitoes. Before attempting to control mosquito populations via genetic engineering, we should consider the risks and alternatives.

Mosquitoes provide a food for animals and help pollinate plants. Genetically engineering mosquitoes to die off could threaten species that rely on them, including already at-risk amphibians, bats and birds. Likewise, eliminating one mosquito species may open more space for another that carries the same diseases.

The lack of independent research on the impact of genetically engineered mosquitoes constitutes a troubling factor in the drive to release billions of these insects. Few studies, if any, have been done to understand the unintended evolutionary effects of introducing new genes into a species. While the public duty to control viral diseases such as Zika and dengue is paramount, Oxitec, the company manufacturing the genetically engineered mosquitoes, has not demonstrated that its release of the mosquitoes in Brazil, the Cayman Islands and Malaysia has reduced disease, or that these mosquitoes will not have unintended effects on humans or animals. In addition to potential threats to ecosystems and a lack of evidence about the efficacy of using genetics to minimize diseases' spread, there is little information about what ingesting these insects could do to people.

Furthermore, genetically engineered mosquitoes are an expensive biotech "fix" to a problem of diseases related to poverty. Areas with the highest rates of mosquito-borne illness are those with inadequate housing and lack of resources for insecticides. But genetically engineered insects are costly and, like the pesticides they are intended to replace, must be used over and over again — even as communities still have to pay for pesticides on the non-genetically engineered species.

The risks of releasing genetically engineered mosquitoes are clear, but the benefits are not. We need independent, transparent ecological risk and safety assessments and a regulatory system equipped to deal with the novel risks from these experimental mosquitoes before they are released into our environment. The release of genetically engineered mosquitoes must be compared to other methods used to reduce mosquito populations, such as infecting mosquitoes with Wolbachia bacteria, as well as vaccines. When vaccines keep people from getting disease, mosquitoes can't pass it on.

When a thorough assessment is done, genetically engineered mosquitoes will likely be shown to be an unproven and expensive gamble in the effort to reduce diseases such as Zika and dengue.

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have said is necessary to do everything possible to fight the Zika virus and steals funding from other health priorities," White House press secretary Josh Earnest said in a June 23 statement. ⁷⁴

On June 28, Senate Democrats blocked the bill's passage, criticizing

their efforts in time to prevent Zika outbreaks. At this point, Congress won't appropriate funds until September at the earliert. Even then, the money has to reach state and local officials, who must hire personnel to carry out public education campaigns and surveillance, prevention and treatment efforts.



Fumigation targets Aedes aegypti mosquitoes in Jakarta, capital of Indonesia, on Feb. 6. Environmentalists say using pesticides to kill virus-carrying mosquitoes can damage animal habitats. Instead, some experts advocate using natural predators against the insects, such as fish that eat mosquito larvae, and bats, which gorge on mosquitoes.

Republicans for the unrelated provisions. ⁷⁵ Democrats have tried, unsuccessfully, to get Senate Republicans to reconsider their stance but Senate Majority Leader Mitch McConnell, R-Ky., said on July 12 that he will not bring a new bill to the floor. ⁷⁶ Instead, on July 14, he brought up the same package Democrats had rejected, leading to the same result.

Local Response

With Congress deadlocked, local and state health officials worry that they may be unable to ramp up

"It's sobering to think that going into this mosquito season, half of the counties in the United States didn't have a mosquito-control effort in place, including counties in Texas," says Inglesby of the Center for Health Security. "In some places, it's clearly one person who is driving around with a fogger on the truck, who switches to snow plowing in the wintertime."

Experts say public health departments cannot easily hire a number of new people and expect them to be up to the task, which in the case of Zika may require delicate interviews with possible victims about their sexual history. Many of those interviews will

likely have to be conducted with people with limited English skills.

Health departments at the local level are hoping to increase their laboratory capacity as well, so they can quickly monitor and detect outbreaks. That, in turn, will allow a state to rapidly and aggressively direct resources toward an affected area.

Response to an outbreak will also allow mosquito abatement efforts to go into overdrive. In 2009, in response to only three dengue cases in Key West, the Florida Keys Mosquito Control District brought out its helicopters to spray. It also sent teams door to door to encourage residents to chlorinate their pools and use larvicides where rainwater collected. ⁷⁷

But few jurisdictions have that kind of mosquito control infrastructure in place.

What's more, blanket spraying won't be much of a help against *Aedes aegypti* mosquitoes, which often hide in small containers, including in people's homes. The species has "become ubiquitous and hard to get rid of," says the Pan American Health Organization's Epstein.

Getting rid of *Aedes aegypti* may be particularly difficult in high-poverty areas where governments have fewer resources than in richer areas. They may also have poorer garbage collection, with more refuse piling up and becoming rain catchers and mosquito-breeding grounds.

"Our whole infrastructure for controlling mosquitoes has been depleted over the years," says Hotez of Baylor. "Right now, we're not in a position to control *Aedes aegypti*, which is the only way you can prevent Zika, because we're not going to have a vaccine in time."

At least 18 public and private labs are working on a Zika vaccine. ⁷⁸ In June, Inovio Pharmaceuticals, a company based in Plymouth Meeting, Pa., announced that it will start the first initial, small-scale trial of a Zika vaccine. ⁷⁹ But no vaccine is expected to reach the market before 2018, at the earliest. ⁸⁰

Vaccines that are promising in the

lab must first undergo clinical tests, in which human volunteers receive the vaccine. In the case of Zika, the disease's spread might complicate efforts because scientists may find it harder to determine whether patients developed immunity due to the vaccine or natural exposure to the disease. For these reasons, vaccine development is focusing on pregnant women and women of child-bearing age, said Anthony Fauci, director of the National Institute of Allergy and Infectious Disease. ⁸¹

The hit-and-miss nature of mosquito control in the United States also has Hotez and some other public health experts concerned about the resurgence of yellow fever and the possibility of its reappearance in this country.

Angola and Congo in western Africa, with more than 900 confirmed cases, currently have yellow fever outbreaks. Although a vaccine is available, health care workers and doctors may run short of doses if yellow fever continues spreading. With stockpiles depleted, the WHO in June approved "fractional dosing," or vaccinations of just one-fifth the normally prescribed strength, a dosage it says can work in patients for 12 months or longer. ⁸²

"We are vulnerable to yellow fever," Hotez says, noting that globalization means the disease can travel with humans and then be spread by local *Aedes aegypti* mosquitoes. ⁸³ "Yellow fever could return to the U.S., in the same areas where we're worried about Zika."

OUTLOOK

Emergency Fund Needed?

Many public health experts agree that Zika is going to be a scourge in the Americas for the foreseeable future, and a vaccine likely won't be ready for years.

And Zika is not the only challenge scientists face. They have been working on a vaccine for dengue for more than a decade, and millions of dollars have been spent over the years in search of a successful vaccine against malaria.

Public health officials also fear the emergence of a new, unknown virus. Given the combination of climate change, globalization and human encroachment into animal habitats, fresh epidemics are taken almost as a given. "The world's getting smaller, so we're more likely to have sporadic outbreaks of diseases no one's ever heard of," says Conlon, the American Mosquito Control Association adviser.

The litany of outbreaks in recent years, including Ebola, the H1N1 flu virus, and severe acute respiratory syndrome, or SARS, should have acted as wakeup calls to policymakers — but that hasn't been the case, says Benjamin of the American Public Health Association, pointing to the slow response to Zika. ⁸⁴ "I was a perpetual optimist, but Congress has shown me that even in a major crisis they're unable to respond in a timely way," he says. "We're not even lurching effectively from crisis to crisis, and that's got to change."

Given how Congress has responded — or failed to respond — to public health crises, many public health professionals would prefer a standing reserve fund that could be tapped when an emergency arises, such as those available for responding to natural disasters.

"The nation's public health system is no different from any other system that's critical to national security," says Blumenstock of the Association of State and Territorial Health Officers.

The idea has some appeal even to members of Congress, who don't particularly like the pressure or the criticism they come under when having to craft an emergency supplemental spending bill from scratch. Rep. Rosa DeLauro, a Connecticut Democrat, has introduced a bill that would authorize \$5 billion

for a public health emergency fund. And Sen. Bill Cassidy, a Louisiana Republican, introduced similar legislation on July 15.

But it may be a stretch to expect Congress to set aside \$5 billion to cope with future emergencies, when members were reluctant to provide less than \$2 billion for Zika, a threat already at hand. Some members, such as Senate Majority Whip Cornyn, say Congress must ensure the executive branch spends the funding wisely; others are hesitant to set aside money on something that may not happen.

Nevertheless, Conlon says the nation cannot afford to wait. "I know this is a hard sell when there's not an immediate threat," he says, "but if you think of 'immediate' as two to three years, rather than two to three weeks, then there is an immediate threat."

The Center for Health Security's Inglesby says the problems Zika is creating, following a series of other public health crises, might generate "enough momentum now, so we could at least have a new system put in place in a year or two, related to a disaster relief fund."

Like other health experts, Inglesby underscores the importance of having a more robust public health system in place, one that not only can respond quickly to outbreaks but continually monitors threats and educate the public about them, especially by retaining experienced lab personnel and maintaining surveillance systems.

Public officials have long had a mind-set that mosquito-borne illnesses and other "tropical" diseases are more of a problem in Africa and Asia than in the United States and Europe. But Zika and the recurrence of diseases, including yellow fever and dengue, should give the lie to that notion, says Hotez of Baylor.

Hotez suggests that poverty is a prime indicator when trying to predict the course of an infectious disease. Rather than thinking in terms of separate outcomes for developed and developing

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countries, he says, "we find that most of the world's neglected and emerging infections are happening among the poor in developed countries."

Thus, policymakers in the United States and other rich nations cannot assume that infectious diseases are someone else's problem, or that they can easily be contained before becoming endemic at home.

"No one is forecasting that these types of threats or emergencies are going to go away," Blumenstock says. "They're going to become faster and more furious."

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About the Author



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FOR MORE INFORMATION

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Centers for Disease Control and Prevention, 1600 Clifton Rd., Atlanta, GA 30329; 800-232-4636; www.cdc.gov. Federal agency that researches and provides information on infectious diseases and other threats to public health and safety.

Global Fund to Fight AIDS, Tuberculosis and Malaria, Chemin de Blandonnet 8, 1214 Vernier, Geneva, Switzerland; +41-58-791-1700; www.theglobalfund.org/en/. Coordinates global aid from governments, nonprofits and the private sector; acts as the main international coordinator of the fight against malaria.

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Orders for abortion pills rose in seven Latin American countries after officials warned of Zika outbreaks in those countries, according to a women's organization providing the pills.

Stobbe, Mike, "When Zika hits, a push for birth control and abortion?" The Associated Press, May 11, 2016, http://tinyurl.com/z4sk8jz.

Some health experts say the Zika situation recalls the rubella epidemic of the 1960s, in which thousands of pregnant women chose to have abortions rather than risk bearing children with birth defects.

Dengue and Chikungunya

"CDC Confirms Case of Chikungunya in Brownsville," KRGV.com, May 31, 2016, http://tinyurl.com/hwrejcq.

The Centers for Disease Control and Prevention confirmed the United States' first locally acquired case of the mosquito-borne virus chikungunya since 2014 in Brownsville, Texas, near the U.S.-Mexico border.

LaFrance, Adrienne, "A Surprising Link Between Zika and Dengue," *The Atlantic*, June 23, 2016, http://tinyurl.com/j8vmy2g.

New research finds that some antibodies in dengue fever can either help neutralize Zika — or worsen it.

Lathrop, Janet, "Improving Prediction of Dengue Fever Epidemics," *News & Media Relations*, University of Massachusetts, June 16, 2016, http://tinyurl.com/zq25lwb.

A U.S.-based research team collaborated with public health officials in Thailand on identifying better ways to provide real-time information on dengue fever outbreaks.

Public Health Preparations

Beck, Julie, "Zika Is the 'Most Difficult' Emergency Health Response Ever, CDC Official Says," *The Atlantic*, June 24, 2016, http://tinyurl.com/zvx3fxg.

The CDC's principal deputy director says Zika is more complex than other diseases, making it extremely challenging for his agency to combat.

Cohn, Meredith, "Conspiracy theories muddy Zika public health message," *The Baltimore Sun*, May 31, 2016, http://tinyurl.com/zhlvs4s.

Researchers worry that misinformation about Zika — such as it being the product of genetically engineered mosquitoes — could undermine efforts to control its spread.

Luthra, Shefali, "The States That Can't Stop Zika," *Kaiser Health News, The Daily Beast*, June 10, 2016, http://tinyurl.com/hgaym3e.

Florida and Texas have undertaken Zika prevention efforts focused on targeted spraying and mosquito surveillance, but health experts say funding cuts to women's health care programs in those states makes them especially vulnerable to the disease.

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Blamont, Matthias, and Ben Hirschler, "France's Sanofi partners U.S. Army to speed up Zika vaccine," Reuters, July 6, 2016, http://tinyurl.com/zpw9mer.

The French drugmaker Sanofi reached agreement with the U.S. Army on a research and development deal to speed up development of a vaccine against the Zika virus.

Doucleff, Michaeleen, "How An Electric Shock Could One Day Protect You From Zika," NPR, June 28, 2016, http://tinyurl.com/hyr3rv9.

A company developing a Zika vaccine is testing a system that administers a harmless low-voltage electrical shock to help place the vaccine in a person's cells.

Thompson, Dennis, "Success in Mice Shows Zika Vaccine 'Feasible,' "Philly.com, June 28, 2016, http://tinyurl.com/h537tmx.

A co-leader of an Army biomedical research team involved in the search for a vaccine against Zika says studies in mice show that two possible vaccines could be effective.

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