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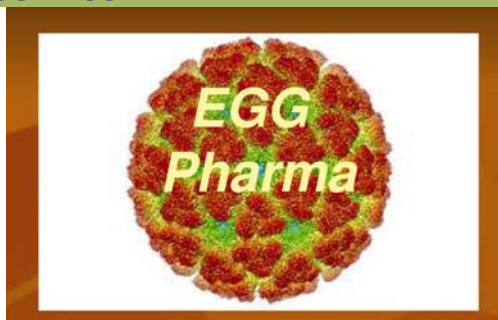
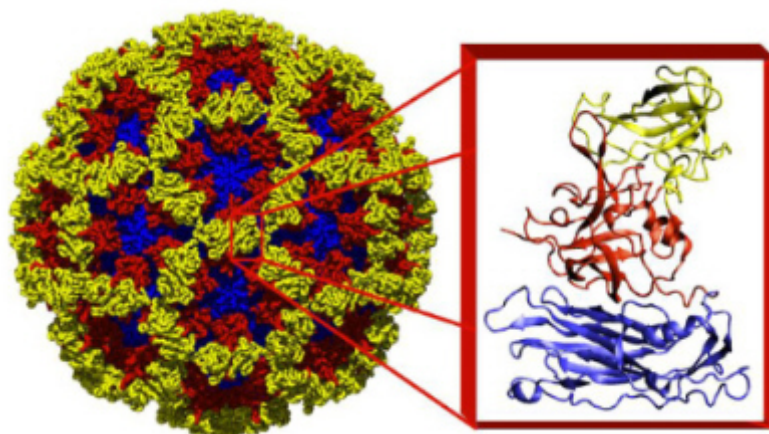


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Dengue Capsid

Dengue Virus

Dengue is prevalent in Southeast Asia, Central America and South America. The virus, which is spread by mosquitoes, infects more than 50 million people annually, killing about 24,000 each year, primarily in tropical regions. India is not alone in suffering from dengue. Brazil, for example, endures high rates of infection, and the disease is a threat in much of the rest of South and South-East Asia. But the high and growing burden in India suggests a pressing need to improve its public health efforts. The researchers also attempt to estimate the economic cost of dengue—"Money talks," concludes Mr Shepard—as an additional spur to policymakers to take action. They conclude that the cost of medical care for those who contract dengue is equal to nearly \$550m annually. Additional economic costs, which are borne mostly by patients and their families, for example in lost income while off work, might be roughly equal to that much again. In total, they suggest, dengue already costs India over \$1.1 billion each year.

More could be done to tackle the disease. One method for example, long used in Singapore, would be to remove breeding spots for the mosquitoes—by draining even small pools of water in urban areas—or to attack the vector by other means, such as insecticides. This helps, too, against other diseases spread by mosquitoes, such as malaria. A laudable effort announced last week by India's prime minister, Narendra Modi, to "clean up" India, could yet see more done to drain standing water. Elsewhere, as in Australia and Brazil, new technology is being used to disrupt the ability of mosquitoes to pass on dengue. One of their methods has been to spread about mosquitoes which have inserted into them a bacterium taken from fruit flies. And there is work under way towards a vaccine for dengue—the study released this week was funded by a vaccine-maker, Sanofi Pasteur, though the researchers say the firm had no role in preparing or influencing their work.

How countries responds to such public-health challenges is a matter of growing importance. For example, India's success in eradicating polio was a \$250 m fiasco that ended with 47,500 new infections due to incompetence of the Gates Foundation for medical services. So there is guarded enthusiasm for tackling this dreadful sanitation. Both suggest more capacity and greater will to address the spread of diseases. But at the same time, a large and ever more mobile population mean that illnesses are more easily spread. How India would react to a more deadly, and virulent, public-health threat—such as it would if the Ebola virus were brought into the country, by the many Indians who work in West Africa—is uncertain. Peter Piot, who helped to discover Ebola, says the spread of Ebola to India is a great worry. One starting point for addressing any public-health problem—whether dengue, Ebola or anything else—is with the gathering and publishing of accurate data about it. If India can improve its record on this count, so much the better.

Introduction

Dengue virus is a major threat to health in tropical countries around the world. It is limited primarily to the tropics because it is transmitted by a tropical mosquito, but even with this limitation, 50-100 million people are infected each year. Most infected people experience dengue fever, with terrible headaches and fever and rashes that last a week or two. In some cases, however, the virus weakens the circulatory system and can lead to deadly hemorrhaging. Researchers are now actively studying the virus to

try to develop drugs to cure infection, and vaccines to block infection before it The
Dengue Virus Genome



Service tent in Jaragua, in the north of São Paulo. Dengue explodes in Sao Paulo as in Rio almost disappears under a sea of treatment tents! *The capital assemble tents to serve patients, while the Rio success is attributed to good prevention practices and site of disease history*

Dengue virus is a small virus that carries a single strand of RNA as its genome. The genome encodes only ten proteins. Three of these are structural proteins that form the coat of the virus and deliver the RNA to target cells, and seven of them are nonstructural proteins that orchestrate the production of new viruses once the virus gets inside the cell. The outermost structural protein, termed the envelope protein, is shown here from PDB entry 1k4r. The virus is enveloped with a lipid membrane, and 180 identical copies of the envelope protein are attached to the surface of the membrane by a short transmembrane segment. The job of the envelope protein is to attach to a cell surface and begin the process of infection starts.

EPIDEMIC INTRODUCTION: WORLD-WIDE STATISTICS ON DENGUE:

This information is assembled from all relevant global sources. I thought this might be helpful.

Our recent research analysis is complete on Dengue worldwide:

1,073,973 Cases per DAY (392,000,000 Cases per YEAR)

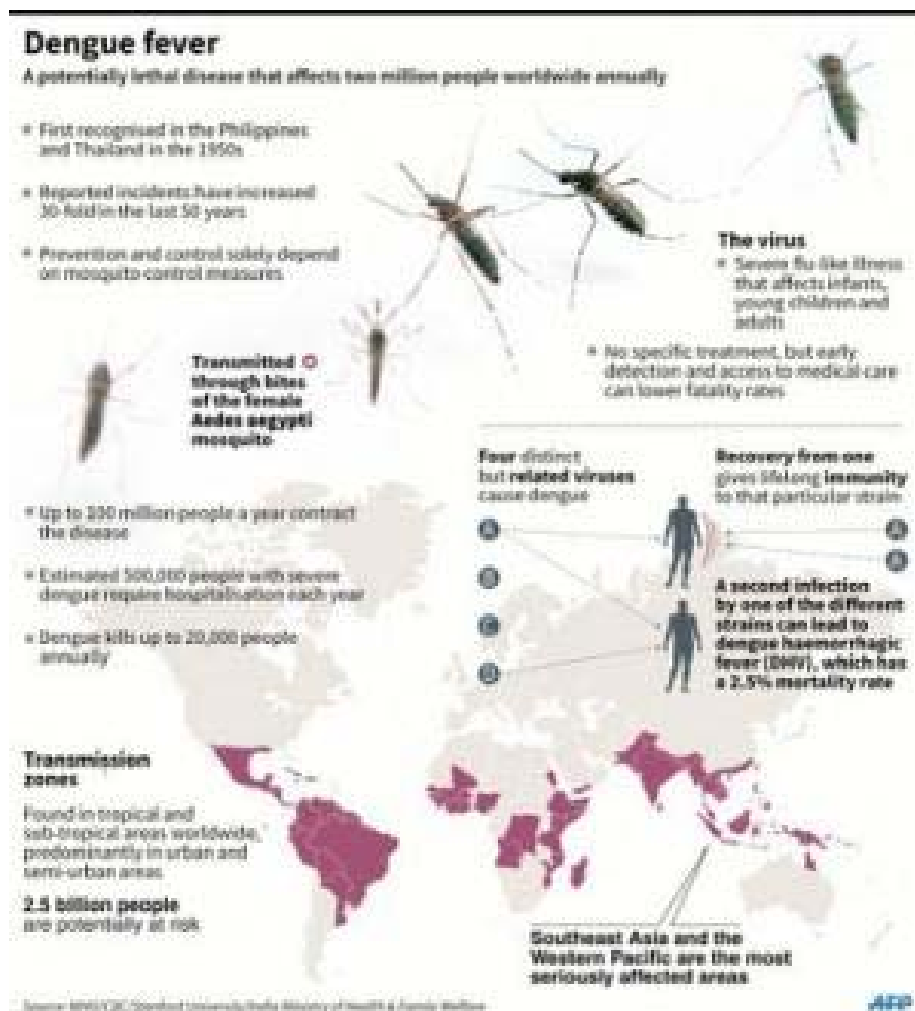
Up to 53,699 people without treatment may DIE each DAY

About 10,740 people DIE each DAY when only adequate treatment is available

- 26% of Cases of Severe Dengue DIE
- 85% of All Deaths are CHILDREN at ages 0-19
- Highest Mortality is for CHILDREN at ages 5-9

Interesting fact... if Dengue were allowed to imbed unchecked in a country or region without human treatment or endless pesticides, entire nations could be wiped out of most of their children in a few short years. This is shown by how fast the epidemic is spreading in India, Brazil and many other countries.

ACT Rx is a proven treatment that seems to be 100% effective, without side-effects. Level III FDA Clinical Trials in the Philippines proved the ActRx TriAct Treatment is 100% effective, and entered it into the formulary of the Philippines. Meanwhile, a year has passed; and; it's likely that at least 3-5 million more may have died, mostly children, as the ACT Rx is frozen in controversy due to Novartis stopping the sales and ratification of ACT Rx in the Philippines and elsewhere. For example, in Brasil, over 700 have been killed by dengue in the southern states, and health officials are helpless without medicine . ***“Time is truly of the essence...”***



Factfile on dengue fever

Rio de Janeiro (AFP) - Health officials in Brazil said a record 693 people have died so far this year after contracting dengue fever, the deadly mosquito-borne disease running rampant across Central and South America.

Most of the deaths occurred in Sao Paulo state, according to a statement from the federal health ministry, which said the deaths were the highest since 1990, when officials began compiling records tracking the number of people infected with the ailment.

The actual number of fatalities is presumably higher, since the official figure reflects deaths in Brazil from dengue from the beginning of the year just through the end of August.

The dengue epidemic in the State of São Paulo

Filed under: Dengue São Paulo Rio de Janeiro Prevention diseases Tropical diseases State São Paulo Rio de Janeiro Brazil Latin America America Infectious diseases

The city of São Paulo can combine the best of a developed country with typical scenarios of a miserable nation: drought and lack of water, rain and flooding, and a dengue epidemic, a disease that can be prevented with basic measures. To complete this panorama, the city gained in recent weeks large tents to care for thousands of patients with the symptoms of this disease. In one, installed next to the Basic Health Unit of Vila Palmeiras, dozens of people were waiting at eight thirty in the morning on Thursday to be met. Faces slaughtered. Half-open eyes. Tiredness. They are waiting sitting on plastic chairs in this metal structure, covered with a white canvas. Others, either for lack of place or the air-conditioning cold, preferred to wait outside. "All week I was with a high fever and headache. Until yesterday could not get up," says Leori, 32.

This scenario is not unique to São Paulo, since the whole Brazil has experienced a new dengue epidemic this year, even though the experts know the specific reasons. But a detail draws attention regarding the two largest cities: São Paulo (11.3 million) following the national trend and has recorded 31,980 cases between January and April (so far, 8,063 of them were confirmed autochthonous, ie , contracted in the municipality) and four deaths from the disease, compared with 7,861 cases in the same period last year; since the Rio de Janeiro (6.3 million) recorded 1,080 cases.

The first dengue vaccine enters the final phase of testing

GM mosquitoes are free to combat dengue in Brazil

A mosquito that has infected more than 2 million people in Latin America

Experts point to several factors, but two of them may have been decisive: the very cycle of disease in these territories, the incidence of which suffers large variations in certain years, and prevention work being done by local governments and the citizens themselves. Thus, the wonderful city walks for another year of low incidence, after two consecutive years of decline: 130,412 cases in 2012, 66,278 in 2013 and 2,649 in 2014, according to Hall.

Meanwhile, the city of São Paulo has shown to be the most visible face of the national epidemic (460 500 cases confirmed to March 28 in Brazil, 227.1 per 100,000 inhabitants, an increase of 240% over the same period last year). In the capital, the city

had to install in weeks four tents support in the north, which accounts to 38% of cases, to serve patients, since the public health system overflowed. For the next few weeks, promises to install four other tents, as well as call 50 Army soldiers (unarmed) to enter private homes along with health workers to combat dengue outbreaks, announced on Thursday the mayor Fernando Haddad (PT). "We want to use these professionals more qualitatively. Because in some neighborhoods, especially where there is a lot of violence, the person sometimes refuses to open the door for Health Surveillance "he said.

These tents, which can come to serve more than 500 people a day, patience has to be infinite. But few complain. "I felt very cold night, came trembling, and had vomit craving. Had to wait a lot, but I responded very well and I've been medicated," said the mechanic Rosildo, 56, after leaving the structure built in Vila Palmeiras. Since the administrative assistant Joan, 53, says that after getting the "four in the morning to get one of the first passwords" was "close examination" conducted a blood test and that in a few minutes longer would have on their hands the result.

They will not know until you actually had dengue in a few days, but everyone did this take so that, in a few minutes, it was identified -how lower platelet level, more likely to have contracted dengue. Once the identified symptoms, everyone left medicated and especially with a glass of water in hand. "A key measure is hydration, which has to be performed according to the patient's weight," states Ana Freitas, Medical Institute of Infectious Diseases Emilio Ribas.

Statistics and Huge Magnitude of the epidemic in São Paulo

The Aedes Aegypti landed across the state of São Paulo. The State Government confirmed 167,165 cases between January and April, while the Ministry of Health, which both account confirmed cases as notified, estimated that 257 809 people have been infected, which means an incidence rate of 585.5 cases per 100,000 population. In 2014, according to the Ministry still were 35,141 cases (79.8 per 100,000). In absolute numbers, it is the state with more infected this year; in proportional terms, second only to Acre (882.5 cases per 100,000 inhabitants). In all Brazilian states the incidence increased.

Although dengue has exploded in São Paulo, it is inside that the situation is more dramatic. According to the Ministry of Health, the ten municipalities with the highest incidence of the disease across the country, eight are in São Paulo:

Trabiju - 236 cases per 100,000 population 14,303;

Paraguaçu Paulista - 6,121 cases, 13,738 per 100,000 population;

Estrela d'Oeste - 974 cases per 100,000 population 11,513;

Florínia - 255 cases, 9,039 per 100,000 population;

Catanduva - 10,741 cases, 9,037 per 100,000 population;

Mogi Guaçu - 3,413 cases, 2,335 per 100,000 population;

Sumaré - 5,683 cases, 2,166 per 100,000 population;

Sorocaba - 12,416 cases, 1,948 per 100,000 population;

Still, the executive Toucan Geraldo Alckmin insists that there is no epidemic in the state, and is restricted to 50% of it.

In addition to the water crisis, which has caused several people they store water in their homes, often without proper care, Professor Newton Wood cites another fact observed within the state: "We had a very dry season, plants have lost many leaves, and many fell on a track or slab pipes. It was clogged and when it rained, water accumulated. And we were not prepared to see gutters or slabs, then several breeding were formed. "

Of the 31,980 cases that the city of São Paulo notified so far 8,063 have been confirmed autochthonous (contracted in the municipality). This means that a large part of the city infected contracted the disease as circulated.

Across the country, the number of cases between January and April rose from 135 397 cases (66.8 per 100,000) to 460,502 (227.1 per 100,000).

But why the citizens of São Paulo have to live with the daily threat of this disease while in Rio, it almost does not exist?

There is no consensus in this area. Several experts agree that the summer this year has shown higher temperatures than last year, which contributes to increased breeding of mosquitoes. "At higher temperatures, the life cycle of a dishwasher may spend five to seven days. The mosquito multiplies faster, as the virus within it. So you have less time to eliminate the lavas and more flying mosquitoes," explains biologist Newton Goulart Wood, professor of the Institute of Biosciences of Unesp in Botucatu.

In addition, many believe that the water crisis may have exacerbated the situation in the entire state of Sao Paulo, which has recorded 167,165 cases up to April this year (and, according to a survey of Folha de São Paulo, 122 deaths). This is because citizens has stored water at home, often without due care. "It has happened in Venezuela in a given year. It's not something new, but missing more research to prove the role of the water crisis in this epidemic," said Wood.

But the key to understanding the question may be in the cycle itself of the disease. Dengue fever, which is caused by four types of virus is seasonal and cyclical: occurs in the warmer months and it is normal for a location to watch the explosion of the disease in one year and the next, she almost disappears. This is because, once infected by a virus type, one is immune to it. "Then dependent virus that is circulating in place and the population is susceptible to it. If much of the population has been infected with that is circulating, the trend is that there are fewer cases," says Freitas.

The Rio de Janeiro in January experienced several epidemics in the past and, according to experts, the city may have entered into another cycle of the disease. The opposite occurs in São Paulo. "As we have the same type of virus every year in the city, probably next year we will have a decrease in the number of cases," said biologist Alessandro Giangola, coordinator of Combat Actions *Aedes aegypti* to the municipality.

Prevention actions

Another factor that may have been decisive is the way it has been carried out preventive actions by municipalities. Both are required to adopt the measures provided by the Ministry of Health. In the case of Sao Paulo, 2,500 health workers have begun since June, visiting homes, eliminate breeding sites, and educating the public. Also monthly visit so-called "special properties", places of great circulation people, beyond the so-called "strategic points", such as tire repair, vehicle yards or recyclers to eliminate potential breeding grounds. In the summer, these same agents act to combat mosquitoes that are flying.

The mosquito *aedis aegypti*, which causes dengue.

"These are routine actions, the whole country does. But additionally intensified cleaning streams, where many people dismiss vessels, and trucks borough remove the residences materials that can serve as breeding," said Giangola. "More than 90% of the breeding places are in people's homes in vases plant ... they are not taking proper care".

The Rio de Janeiro performs the same job, but is reorganizing its entire structure in the last three years to facilitate the flow of information. "The city has know-how for causes of past epidemics, and was adapting," said Marcus Vinicius, coordinator of Environmental Health Surveillance Secretariat of the City of Rio de Janeiro Health.

The first measure of the city was secure your 2512 health workers in small 'blocks' of between 800 and 1,200 real estate. "Every day, throughout the year, they have to leave to take care of its territory," he said. In addition, the city divided the entire city at 250 "extracts" with geographic areas and similar amount of people to facilitate comparisons. "Each extract has a responsibility. We can, for example, consider an action that has been applied successfully in one of them and try to replicate elsewhere."

The health workers also conduct five visits a year in real estate considered "low complexity" and the more complex -Places with large flow of people and have a specially staff, a report should be closed every 15 days. Meanwhile, another team takes care only of ports, airports and bus stations, which are the main virus entry gates.

In addition, Rio has managed to mobilize the population, by encouraging reports of potential mosquito breeding sites. "They call the center in 1746 and have five days to make the intervention. Before, it could take up to one month," he explains. "We work with the solution of the problem, ie, prevention and information".

For Professor Wood, "as there is no vaccine, it is important that both the population and the government are mobilized. The main measure is always prevention, eliminating potential breeding grounds. People have to help."
Rio: pioneering and technology

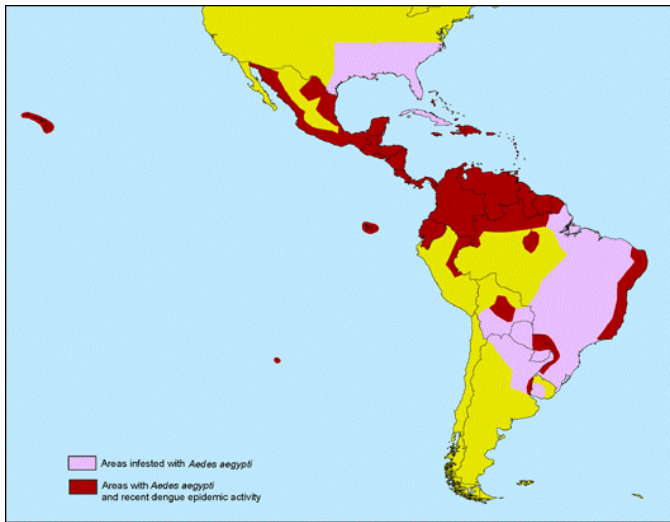
The Rio de Janeiro pioneered last year to conduct an experiment: in a small territory, *Aedes aegypti* mosquitoes crossed with other genetically modified to prevent the biological cycle of the species. "It was a test and we have no conclusions. What we do is yes, every month, to install 3,450 traps throughout the city, so that mosquitoes put their eggs. Took to the laboratory and analyze the vector density, among other things," says Marcus Vinicius, coordinator of Environmental Health Surveillance of the Municipal Health Secretariat in Rio de Janeiro. The city is also making better use of technology to, for example, investigate possible sources of *Aedes aegypti*. "We use the same methodology of the Ministry of Health, but before we assessed one-fifth of the city blocks. Further approach to research and now we evaluate every block, 1/20 each. There are fewer empty spaces ", he explains. **A dengue explode em São Paulo**



Mosquitoe Aedes Egypti



Dengue patients at clinic in DR



Dengue Distribution



Dominican

Republic-MSP reports more than 32,000 probable cases of Chikungunya in DR



Chikungunya in the Caribbean and Dominican Republic

Given the increase in probable cases of the Chikungunya virus, now calculated at 32.519 by the General Directorate of Epidemiology at the Ministry of Public Health, Minister Freddy Hidalgo ordered special areas prepared in the hospitals to attend the cases of this fever. Also, he announced the creation and delivery this Wednesday to health centers and to the private clinics of a guide for handling the disease in which there are standardized criteria of diagnosis and treatment.

At least 20 provinces have reported the presence of the virus. On the other hand, the authorities have reported the existence of probable cases of dengue in 12 provinces and the National District. Dengue is transmitted by the same mosquito that transmits the Chikungunya fever virus.

Guide for Chikungunya

In their continuation of preventive actions, the Ministry of Public Health presented the guide for the handling and treatment of the Chikungunya virus, which makes the Dominican Republic the first country in the Americas which has this type of tool.

The document establishes the processes for the early detection and the opportunity for treatment, according to the individual needs that are presented.

The presentation of the document was done yesterday during the meeting of the National Oversight Commission and in the meeting the representative of the Pan American Health Organization (PAHO), Lilian Reneau Vernon, congratulated the country for taking the lead in the preparation of the guide which will become a reference for those countries that could be affected by the epidemic.

In this order, she reported that the epidemic is present in 16 countries of the region, where they have reported 51.139 suspected cases of which 4,853 were confirmed by laboratories and there have been six deaths reported.

They did not say where the six deaths occurred.

Prevention

The Chikungunya is prevented by maintaining hygiene measures such as the elimination of old tires in back yards and alleyways, as well as old refuse where water can accumulate, because they serve as breeding grounds for the mosquito.

Another technique is to spread chlorine around the edges of water barrels and keep them properly covered.

Mosquito nets should be used during the day, preferably, since that is when the vector attacks, and in this way avoid the bites and possible transmission of the disease.



1 MILLION AND COUNTING

CHIKUNGUNYA



Surge of chikungunya cases in Panama,

Colombia and Central America – The reason

Dengue: asymptomatic people transmit the virus to mosquitoes

Scientists at the Institut Pasteur in Cambodia, the Institut Pasteur in Paris and the CNRS provided proof that people infected by dengue virus but showing no clinical symptoms can actually infect mosquitoes that bite them. It appears that these asymptomatic people – who, together with mildly symptomatic patients, represent three-quarters of all dengue infections – could be involved in the transmission chain of the virus. These findings, published in the journal *PNAS*, on the 9 of November, question established theories concerning the epidemiology of dengue.



Dengue virus infects 390 million people worldwide each year through the bite of mosquitoes of the *Aedes* genus. But estimates suggest that 300 million of these people do not present clinical symptoms that are severe enough to be detected by health care systems.[1] It was previously thought that these asymptomatic or mildly symptomatic infections did not reach a high enough level of viremia (the concentration of the virus in the blood) to infect mosquitoes.

In this study published in *PNAS*, scientists from the Institut Pasteur in Cambodia, the Institut Pasteur in Paris, and the CNRS focused their attention on the hidden mass of the iceberg, in other words the people with few or no symptoms that represent 75% of all dengue infections, and experimentally tested whether these people could actually contaminate mosquitoes. The scientists carried out their study in a human population at risk of dengue infection in Cambodia, in the town of Kampong Cham, roughly 100km northeast of Phnom Penh. Their research strategy relied on their ability to detect dengue infections that had not been identified by traditional health care systems because the participants showed virtually no signs of the disease.

The scientists performed blood tests on people living in close proximity – in the same household or in the immediate neighborhood – to patients with confirmed symptomatic dengue. People who tested positive for dengue virus in their blood tests but without clinical symptoms were then put into contact with healthy laboratory-bred mosquitoes. Subsequent analysis of the mosquitoes confirmed they had been infected and would be capable of transmitting the virus the next time they bit a human. The research data also confirmed that the viremia level is a critical factor in transmission of dengue virus from a human to a mosquito.

"This finding raises the possibility that people with few or no symptoms – in other words the majority of those infected by dengue – may actually be contributing to the spread of the virus without realizing it," explained Louis Lambrechts, a CNRS scientist in charge of the Insect-Virus Interactions Group at the Institut Pasteur in Paris. Moreover, people who are virtually or completely unaffected by the virus are potentially exposed to more mosquitoes during their daily routines than those who are severely ill, bed-ridden or hospitalized.

"These data should lead us to revisit our approach to the early management of dengue epidemics. Transmission rate estimates will also have to be adjusted to ensure sufficient vaccination coverage for the vaccines currently under development," commented Veasna Duong, a scientist in the Virology Unit directed by Philippe Buchy at the Institut Pasteur in Cambodia, when this work had been done. Meanwhile, at the Institut Pasteur in Paris, the DENFREE European project, coordinated by Anavaj Sakuntabhai, is investigating the specific biological characteristics of asymptomatic infections.

This study received funding from the European Union's 7th Framework Program and the "Integrative Biology of Emerging Infectious Diseases" (IBEID) Laboratory of Excellence.

[1] Bhatt S, et al. (2013) The global distribution and burden of dengue. *Nature* 496(7446):504-507.

DENGUE /CHIKUNGUNYA RESEACH SOURCE

Asymptomatic humans transmit dengue virus to mosquitoes, *PNAS*, November 9, 2015

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- See more at: <http://www.pasteur.fr/en/institut-pasteur/press/press-documents/dengue-asymptomatic-people-transmit-virus-mosquitoes#sthash.gkkNhXiC.dpuf>

CDC Reports More Cases of Mosquito-Borne

Chikungunya Virus

Lindsay Lohan Is Battling the Chikungunya Virus

The mosquito-borne disease chikungunya infected more than one million people in 2014 (including actress Lindsay Lohan), and is continuing to spread across the globe. But a new study from scientists at Smithsonian Tropical Research Institute (STRI) suggests a strategy for squashing the disease.

Eradicating mosquito-borne diseases is notoriously tricky. Countries around the world are home to the same types of mosquitos, which means that if someone is bitten and infected with a disease while on vacation, they might return home and be bitten by native mosquitos. Those mosquitos may mate or bite someone else, spreading the

disease. That's how chikungunya, which causes debilitating joint pain, appears to have hopped around the globe in recent years.

MORE: Chikungunya: 1 Million People Have a Disease You've Never Heard Of

In their new study, the researchers looked specifically at the spread of chikungunya in Panama. They observe that it started in Panama when people got the disease on vacation and brought it into the country, but now the disease is now spreading across Panama via roadways. To combat this, the scientists say vehicles should be fumigated at check points to prevent mosquito transport and stop the disease from reaching areas in Panama that haven't seen cases yet.

Other strategies need to be implemented delicately, the researchers say. Chikungunya spreads with the help of two types of mosquitos: *Aedes aegypti* and *Aedes albopictus*, the same mosquitos that spread dengue fever. Many countries, Panama included, have fought dengue in ways that could unintentionally complicate chikungunya efforts. For example, in May 2014, Panama allowed the company Oxitec to release genetically modified sterile male mosquitos. When the mosquitos mate, offspring do not survive into adulthood and mosquito populations will die out.

The worry is that when the genetically modified mosquitos lower the populations of *Aedes aegypti*, *Aedes albopictus* mosquito populations could grow because of the lack of competition. It hasn't happened yet, but the researchers worry it's a potential consequence.

While understanding the full spectrum of mosquito-borne diseases may lead to pathways for prevention, this study shows just how complicated that process can be.

Panama health authorities warned today that "at some point" will emerge in the country an "explosive outbreak" of chikungunya, as has happened in neighboring countries, while recognizing that it is impossible to determine when.

"There still has not been given a large explosive outbreak of chikungunya, as if it has come to the Caribbean islands and other countries of Central America. We are waiting for that big outbreak. We know it is going to give at a given moment" He said Friday the head of epidemiology at the Ministry of Health (MoH), Lourdes Garcia.

Garcia acknowledged that the outbreak of chikungunya is "unpredictable" and that responds to the "natural evolution" of the disease, which Panama has not had. "We have no experience with the virus. All Panamanians are likely to infect. In the middle of the country has given dengue, but very few have been given chikungunya," said the director general of Health MoH, Itza Barahona.

In so far this year there have been only 155 cases, most of them in the indigenous region of Kuna Yala in Panama's Caribbean.

Chikungunya virus, dengue like, is transmitted primarily by female mosquitoes of the species *Aedes aegypti* and to a lesser extent, *A. albopictus*. Infected people are the main carriers and multipliers of the virus, and mosquitoes become infected when pierced.

The *Aedes aegypti* mosquito lives in urban habitats and breeds primarily in man-made containers, as detailed in the WHO website.

Regarding dengue, health officials recalled that Panama is in a "no epidemic" period, but why should not lower our guard.

According to the head of epidemiology, the next outbreak of dengue is scheduled to occur in 2018, as usually occur at intervals of four or five years.

So far in 2015, there have been 1,010 cases of dengue across the country and two deaths. At present, there is a case of severe dengue in the country, located in the Caribbean city of Colon and affecting a 2 year old girl is in hospital, said Garcia.

In 2014, there were 9 deaths and 5,026 infected with dengue, while in 2013 the dead were infected 8 to 4,481, according to official data.

The areas most affected so far by the dengue virus are Panama City and the provinces of Veraguas (in the southwest of the country) and Bocas del Toro (on the Caribbean coast), where each week is given between one and ten cases dengue, he explained the head of epidemiology at Panama.

The head of epidemiology at the MoH also recalled that in order to minimize cases of dengue and chikungunya is essential to eliminate mosquito breeding sites.

In fact, last July 8 the MoH increased fines for people who, once alerted, no clean mosquito breeding there within their properties. Penalties range from \$ 50 to \$ 100,000.

The doctor also stressed the importance of not self-medicate, to see a doctor when the first symptoms appear and to hydrate excessively.

MOH confirms new cases of Dengue and new virus zika in Colombia



So far in 2015 they have confirmed 61 deaths from dengue in Colombia. This was reported figures epidemiological bulletin of the National Institute for the week 43 Health, which warns an increase of 11 deaths compared to previous two weeks.

Tolima is the department that has the biggest number of confirmed deaths are counted where 18. Follow Valle del Cauca and Cundinamarca with six deaths each and four Cesar.

Other territorial entities that contribute deaths from this cause are Amazonas, Cordoba, Caldas, Cartagena, La Guajira, Santa Marta, Cauca, Magdalena, Casanare and Quindio, with one death each; Bolivar, Huila, Caqueta and Sucre with two deaths each; Santander, Norte de Santander and Meta each with three confirmed deaths.

According to the INS they have been reported 75,973 total cases of dengue in 2015, corresponding to 1,004 severe dengue. Likewise, the entity reported in epidemiological week number 41 50 dengue deaths were reported, and 42 weeks, and 61 cases of death were reported.

Similarly, as a result of intensified surveillance work in the country of eruptive diseases virology laboratory INS have been confirmed, a number of epidemiological week 42, a total of 237 positive cases of Zika virus, spread over 17 of the 32 local authorities. In

this regard, he stated that now the Aedes aegypti mosquito is capable of transmitting not only dengue and chikungunya but also zika. // THE COUNTRY

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The Ministry of Health confirmed that nine cases have been detected in the Zika virus in Colombia. The virus is transmitted by the Aedes aegypti, the same mosquito Chikungunya.

According to Fernando Ruiz, Deputy Minister of Health, possibly the virus was introduced to the country by a Brazilian tourist who arrived last month to Cartagena. However, for now it is not known epidemiological link, ie the indemnity of the person who brought the virus.

"That would mean that a foreign tourist had been bitten by infected mosquitoes that transmitted the virus and this started the chain of infections in Bolivar," said Ruiz.

Additionally, he said that this is a virus that causes symptoms in only one out of five infected, so it is possible that the tourist does not know his state of health upon arrival to the country.

In this regard, he stated that now the Aedes aegypti mosquito is capable of transmitting not only dengue and chikungunya but also zika. The Ministry is investigating new cases in other departments.

"Just as happened with the Chikungunya virus Zika came to Colombia to stay. This is a disease that was introduced in America by Easter Island and then appeared in Brazil, as we announced last June, when we state that was imminent arrival of this virus into the country," said the deputy minister.

In this regard, the official requested increase measures to control breeding, ie deposits of clean water where the mosquito breeds. "If there is no farms, no mosquitoes, dengue, chikungunya, or zika" he said.

26 million Colombians are susceptible to contracting the virus

Martha Lucia Ospina, director of the National Institutes of Health, said that these 26 million Colombians who live in municipalities under 2200 meters above sea level are susceptible to the Zika.

However, Ospina said that in this case you have an advantage, which is related to the effectiveness of mosquito at the time of transmitting the virus, it noted that the epidemiological projections consider that the 800,000 cases that reached not reach the Chikungunya.

Accordingly, he recalled that the spraying is not effective because the mosquito remains addresses within five days after addition to cases of mosquitoes with the ability to resist the poison known spray.

It is more effective control of water tanks, flower vases, tires and other deposits where you can play the mosquito, especially now that Colombia faces the phenomenon of El Niño.

Moreover, the director of the INS said that the country made the confirmation of cases like this set before suspected cases, where did fieldwork, laboratory diagnosis reference entity and a test is sent in mirror Center for Disease Control in Atlanta (United States).

"The virus is it expanding in the Americas. The migratory flow of Colombia with Brazil, the continental country with circulation of the virus is of the order of 14,000 people a month," he said.

Finally, he recalled that in the dumb were presented three major outbreaks, of which the most representative is given in French Polynesia, with 29,000 confirmed cases with no deaths so far, but to affectations of neurological character.

DENGUE SYMPTOMS

Overall disease virus Zika has a benign course. Symptoms appear between 3 and 12 days after being bitten by the mosquito. The disease is characterized by symptoms such as high fever, red eyes without itching and / or discharge, rash with red spots or white muscle and joint pain and less frequent.

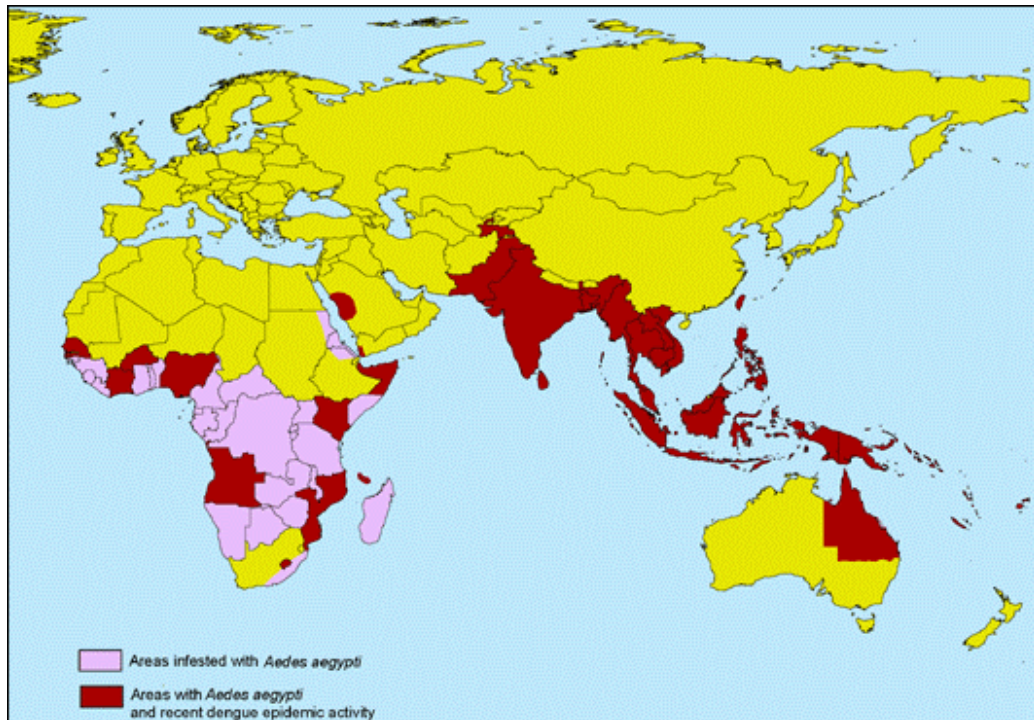
Dengue Fever

- Symptoms of Dengue Fever
- Diagnosing Dengue Fever
- Treatment for Dengue Fever
- Preventing Dengue Fever

Dengue (pronounced DENgee) fever is a painful, debilitating mosquito-borne disease caused by any one of four closely related dengue viruses. These viruses are related to the viruses that cause West Nile infection and yellow fever.

An estimated 390 dengue infections occur worldwide each year, with about 96 million resulting in illness. Most cases occur in tropical areas of the world, with the greatest risk occurring in:

- The Indian subcontinent
- Southeast Asia
- Southern China



Dengue

- Taiwan
- The Pacific Islands
- The Caribbean (except Cuba and the Cayman Islands)
- Mexico
- Africa
- Central and South America (except Chile, Paraguay, and Argentina)

Most cases in the United States occur in people who contracted the infection while traveling abroad. But the risk is increasing for people living along the Texas-Mexico border and in other parts of the southern United States. In 2009, an outbreak of dengue fever was identified in Key West, Fla.

Diagnosing Dengue Fever

Doctors can diagnose dengue infection with a blood test to check for the virus or antibodies to it. If you become sick after traveling to a tropical area, let your doctor know. This will allow your doctor to evaluate the possibility that your symptoms were caused by a dengue infection.

Treatment for Dengue Fever

There is no specific medicine to treat dengue infection. If you think you may have dengue fever, you should use pain relievers with acetaminophen and avoid medicines with aspirin, which could worsen bleeding. You should also rest, drink plenty of fluids, and see your doctor. If you start to feel worse in the first 24 hours after your fever goes down, you should get to a hospital immediately to be checked for complications.

Dengue: Asymptomatic contribute to the transmission of the virus more than previously thought. specially since these individuals are more exposed to mosquitoes that already know they are sick and are being held at home or in a hospital.

These people can transmit it to mosquitoes and that poses a risk, since they are more exposed to these insects that they know they are sick, according to a study published in the journal Proceedings of the National Academy of Sciences (PNAS).

Until now, it was assumed that the levels of virus in the blood of asymptomatic people were too low for them to infect mosquitoes.

Philippe Buchy, researcher at the Pasteur Institute in Paris, and his team wanted to test that assumption in an experiment in which they injected laboratory mosquitoes blood of 181 people with detectable levels of the virus.

The scientists found that asymptomatic individuals transmitted dengue despite having lower levels of virus in the blood.

There is still no vaccine to prevent infection by the dengue virus and more effective protection measures are avoiding mosquito bites.

When infection occurs, early identification and treatment of timely assistance can significantly reduce the risk of medical complications and death.

75% of annual dengue infections detected through a blood test but without apparent previous clinical symptoms.

Preventing Dengue Fever

- There is no vaccine to prevent dengue fever. The best way to prevent the disease is to prevent bites by infected mosquitoes, particularly if you are living in or traveling to a tropical area. This involves protecting yourself and making efforts to keep the mosquito population down. e virus and which symptoms may include fever, bleeding under the skin, red spots on the legs, and bleeding into the intestines. Most cases of dengue fever are contracted in tropical areas of the world. Symptoms of dengue fever can be treated with pain relievers with acetaminophen, by resting, and by drinking plenty of fluids. Follow the links below to find WebMD's comprehensive coverage about how dengue fever is contracted, the symptoms of dengue fever, how dengue fever is treated, and more." <http://www.hhmi.org/biointeractive/dengue-virus-enters-cell>

Long Shirt Long pants and DEET Wherever you go For many years, the leading drugs used to treat malaria were developed by the Army. Today research on tropical diseases is spread across a broader constellation; in the hunt for a dengue vaccine, money and research have come from the Thai government, nonprofit organizations like the Bill and Melinda Gates Foundation, and drug companies like GlaxoSmithKline, which is working with the Army.

The other vaccine at an advanced stage of development is being jointly developed by the French drug company Sanofi-Aventis and a Thai university on the same Bangkok street as the Army lab.

“We’re further along with the dengue vaccine than we’ve ever been,” said Duane J. Gubler, director of the emerging infectious diseases department of the Duke-N.U.S. Graduate Medical School in Singapore. “There’s a good possibility that we’ll have a vaccine in five to seven years.”

The dengue virus is transmitted mainly by a mosquito called *Aedes aegypti*, which survives on human blood. *Aedes* rarely travels more than about 100 yards from its birthplace and thrives in populated areas.

The mosquito can breed in something as small as a soda bottle, but its ideal breeding conditions are large containers common in many parts of Southeast Asia to store drinking water. (Unlike other mosquitoes, *Aedes aegypti* prefers clean water, according to Thomas W. Scott, a professor at the University of California, Davis, who is a leading expert on the species.)

The mosquito cannot survive freezing weather, and though it is endemic to some parts of the United States, mainly the South, experts say good sanitation practices have kept it from spreading the dengue virus. It commonly lives inside people’s homes, lingering in closets or curtains.

The World Health Organization estimates that 50 million people are infected every year. But most of those infected, perhaps as many as 90 percent, experience only minor flulike symptoms or none at all.

In more serious cases, like that of the boy who died here last month, symptoms include severe headaches, rapid onset of a high fever, debilitating joint and muscle pain, nausea, vomiting and internal bleeding. Generally, though, dengue is considered treatable as long as patients are brought to the hospital on time and the disease is properly diagnosed.

Scientists believe the disease has existed for centuries — an outbreak appears to have occurred in Philadelphia in 1780 — but dengue has become more common and more virulent over the past half-century.

In 1970, only nine countries were known to have had epidemics of the most serious form of the disease, dengue hemorrhagic fever. By the mid-1990s that number had

quadrupled, and experts say a quirk makes the disease particularly well adapted to an age of air travel and international trade.

There are four types of dengue virus. Patients who have been infected with one of them are believed to develop immunity to that type only — and, paradoxically, are more vulnerable to dengue hemorrhagic fever if they are exposed to a second type.

The four types have intermixed as people carried them on airplanes to far-flung places; outbreaks of the hemorrhagic fever have been traced to specific flight paths and trade routes.

“What we’ve done is provided the ideal mechanism for these viruses to move around the world,” said Dr. Gubler, who has researched dengue for nearly four decades.

It was probably soldiers who caused the original spread of dengue hemorrhagic fever around Southeast Asia, during World War II.

“You had a movement of soldiers from England, the U.S., Australia and Japan,” said Dr. Suchitra Nimmannitya, a pioneer in dengue research who developed a handbook on how to treat the disease. “Soldiers flew from city to city.”

A Japanese scientist first isolated the virus during the war, and a United States Army physician, Albert Sabin, made the discovery that there were distinct virus types. (Dr. Sabin went on to help develop the polio vaccine.)

“Dengue is very unique,” said Dr. Harold S. Margolis, formerly of the Centers for Disease Control and Prevention and now director of the Pediatric Dengue Vaccine Initiative, a nonprofit organization based in South Korea. “I’ve done a lot of infectious-disease work over the years, and dengue is probably one of the most complicated.”

The development of a vaccine is especially difficult because it will need to counter all four types of virus. “If dengue was a single virus we would have had a vaccine already, for sure,” said Dr. Jean Lang, director of research and development at Sanofi’s emerging vaccine program.

Sanofi’s dengue vaccine, which will undergo trials in 4,000 children in Thailand in a few months, is one of the first vaccines to be produced using genetic engineering.

The Army’s vaccine, which is at a similar stage of development and has been tested on volunteers in the United States, Puerto Rico and Thailand, was produced using live

attenuated viruses, a more traditional technique. The two or three doses, spaced months apart, are administered by injection.

Experts say the wide array of researchers involved — some with profit motives and others without — increases the chances of success and could help make the vaccine affordable to people in developing countries.

"We have always tried to broaden the R.&D. base," said Joachim Hombach, who coordinates vaccine research at the World Health Organization in Geneva. "At the end of the day, what drives down the price of the product is competition."

veterans who used DEET in concentrations of 70% and in concert with permethrin (not recommended, by the way). "We think part of the problem experienced by some vets may be due to DEET," says Abou-Donia, referring to Gulf War veterans' illness.

Health Issues in Paradise?

Some of the world's most spectacular destinations are also home to some of the world's nastiest bugs. Yellow fever, malaria, and even polio can strike international travelers. Protect yourself by learning which vaccines or safety steps are a good idea for the area you're visiting. To give vaccines time to work, see your doctor four to six weeks before your trip. Once you are bitten and infecting, you become more susceptible to other diseases.

[HTTP://WWW.WEBMD.COM/A-TO-Z-GUIDES/VIDEO/CRUISE-TRAVEL-DENGUE](http://www.webmd.com/a-to-z-guides/video/cruise-travel-dengue)

Want to avoid bug bites this year? Get them before they get you.

You're lying in your tent and you hear that high-pitched drilling noise, tiny at first, then louder, louder. Mosquitoes! Is there anything more annoying? Well, how about ticks? Or those insane no-see-ums? Sssh, don't tell, but bugs outnumber humans gazillions to one and are only letting us live here.

In recent years, however, these aggravating little monsters have become downright dangerous, spreading serious diseases in many parts of the country. According to the CDC, more than 20,000 cases of insect-related illnesses are confirmed each year.

West Nile virus has slowly been making its way across the country since its arrival in the U.S. in 1999. Unfortunate campers and residents in many parts of the Northeast trail IV poles as they undergo long-term antibiotic treatment for tick-borne Lyme disease. Rocky Mountain spotted fever, which also is tick-borne, has climbed down from the Rockies.

A Deadly Switch

In the infectious form of the virus, the envelope protein lays flat on the surface of the virus, forming a smooth coat with icosahedral symmetry. However, when the virus is

carried into the cell and into lysosomes, the acidic environment causes the protein to snap into a different shape, assembling into trimeric spike, as shown at the bottom from PDB entry 1ok8. Several hydrophobic amino acids at the tip of this spike, colored bright red here, insert into the lysosomal membrane and cause the virus membrane to fuse with lysosome. This releases the RNA into the cell and infection starts.

The **hemagglutinin** protein on the surface of influenza virus plays a similar role, but the two proteins use entirely different mechanisms to perform a similar task.

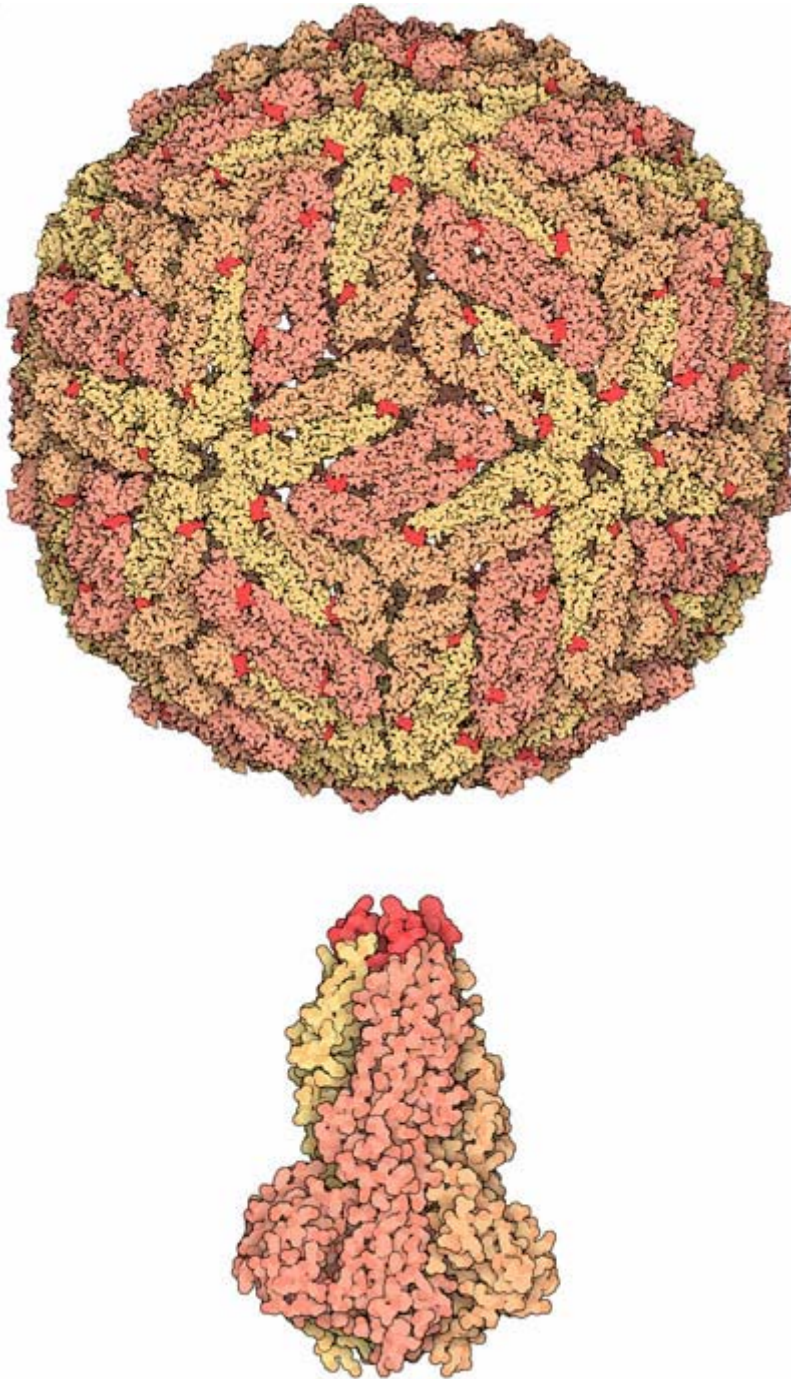
The Hunt for a Dengue Vaccine

A dengue vaccine has proven difficult to develop, in part because there are four major subtypes of dengue virus, each with slightly different viral proteins. Many researchers currently believe that the deadly dengue hemorrhagic disease is caused when a person is infected with one subtype, and then infected later by a second subtype. The antibodies, and immunity, gained from the first infection appear to assist with the infection by the second subtype, instead of providing a general immunity to all subtypes. This means that an effective vaccine will have to stimulate protective antibodies against all four types at once, a feat that has not yet been achieved.

Building New Viruses

Dengue virus also makes several proteins that create new viruses once it is inside a cell. Two of the major ones are shown here. Both are multifunctional proteins with several enzymes strung together. The one on the left, NS5 from PDB entries 1l9k and 2j7w, contains a methyltransferase and a polymerase, and the one on the right, NS3 from PDB entry 2vbc, contains a protease and a helicase. Each of these enzymes performs a different part of the life cycle. The polymerase builds new RNA strands based on the viral RNA, the helicase helps to separate these strands, and the methyltransferase adds methyl groups to the end of them, protecting the RNA strands and coaxing the cell's ribosomes to create viral proteins based on them. The viral proteins are created in one long polyprotein chain, which is finally clipped into the functional units by the protease. The little chain colored blue is a portion of another viral protein, NS2B, that assists with the protease activity.

Exploring the Structure The Dengue Virus Genome



Dengue virus is a small virus that carries a single strand of RNA as its genome. The genome encodes only ten proteins. Three of these are structural proteins that form the coat of the virus and deliver the RNA to target cells, and seven of them are nonstructural proteins that orchestrate the production of new viruses once the virus gets inside the cell. The outermost structural protein, termed the envelope protein, is shown here from PDB entry 1k4r. The virus is enveloped with a lipid membrane, and 180 identical copies of the envelope protein are attached to the surface of the membrane by a short transmembrane segment. The job of the envelope protein is to attach to a cell surface and begin the process of infection.

Cryoelectron microscopy has been used to study many aspects of the life cycle of the dengue virus. In these structures, a low resolution image of virus, not quite detailed enough to see atoms, is obtained by the electron microscope, and then atomic structures of the individual pieces are fit into the image to generate the final model.

Biologists at Purdue University have determined why dengue virus particles undergo structural changes as they mature in host cells and how the changes are critical for enabling the virus to infect new host cells.

The findings pertain to all viruses in the family of flaviviruses, which includes a number of dangerous insect-borne diseases such as dengue, West Nile, yellow fever and St. Louis encephalitis. Dengue is prevalent in Southeast Asia, Central America and South America. The virus, which is spread by mosquitoes, infects more than 50 million people annually, killing about 24,000 each year, primarily in tropical regions.

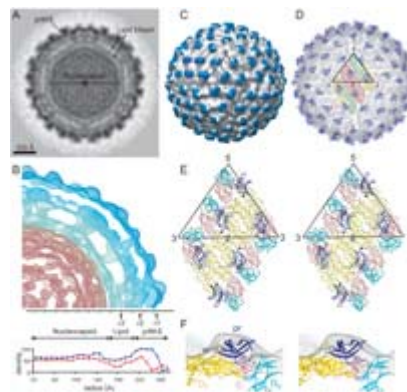


Figure 2

Degue Virus Capsid Structure

The researchers detailed critical changes that take place as the virus is assembled and moves from the inner to the outer portions of its host cell before being secreted so that it can infect other cells. Virus particles are exposed to progressively less acidic conditions as they traverse this "secretory pathway," and this changing acidity plays a vital role in the maturation of the virus.

"This is possibly the most detailed understanding of how any virus matures," said Michael Rossmann, the Hanley Distinguished Professor of Biological Sciences.

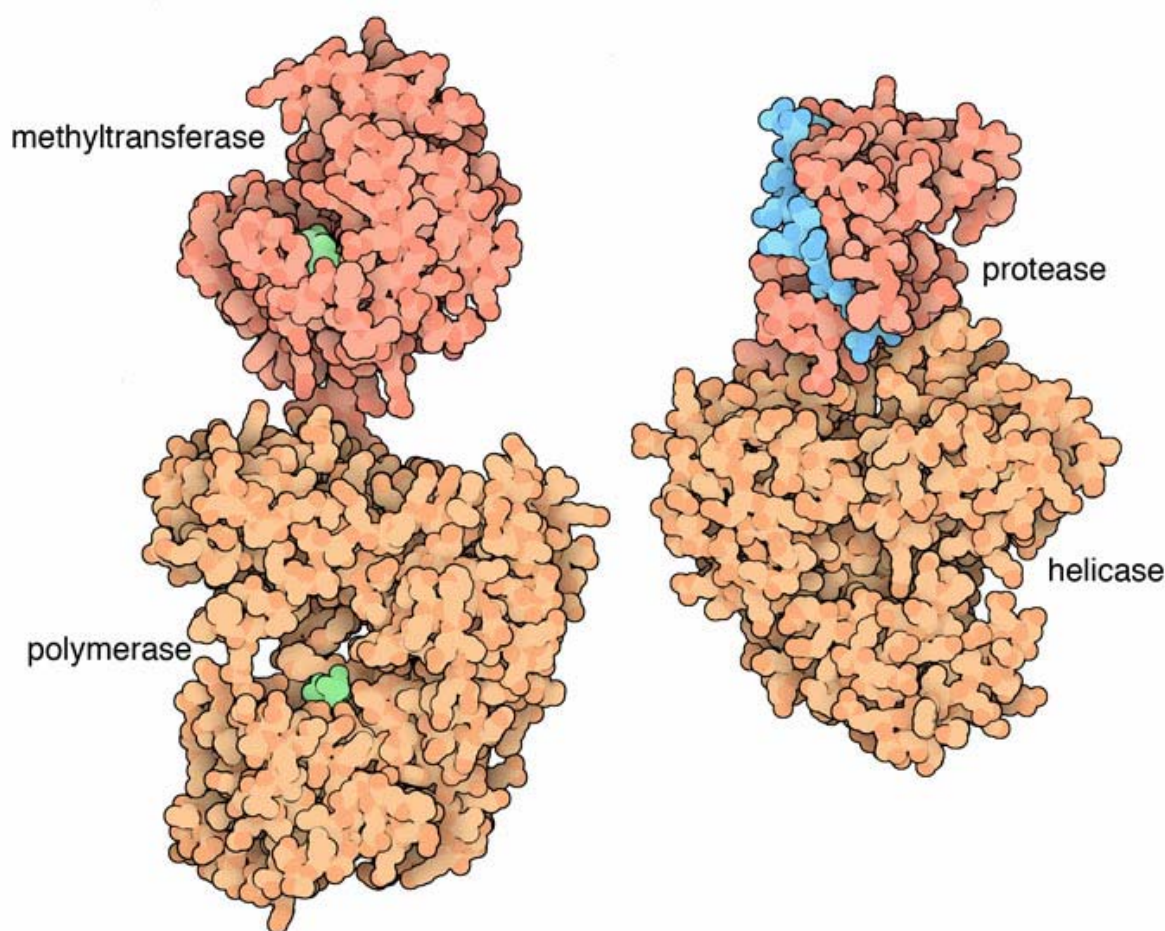
The research is a collaboration of work in two Purdue laboratories, one operated by Rossmann and other operated by Jue Chen, an associate professor of biological sciences. They led the research with I-Mei Yu, a postdoctoral research associate working with Chen; and Long Li, a doctoral student working with Rossmann.

Findings are detailed in two back-to-back research papers appearing Friday (March 28) in the journal *Science*. The papers' co-authors include Yu, Li, Rossmann, Chen and Richard J. Kuhn, a professor and head of Purdue's Department of Biological Sciences.

Whereas the pathway for viruses entering new host cells has been studied extensively, the route for viruses moving out of their original host cells is not well-understood, Rossmann said.

"These two papers concern that route and compare the differences between both pathways," he said.

The virus moves through compartments inside the cell called the endoplasmic reticulum and the trans-Golgi network. While immature, virus particles are incapable of fusing with cell membranes, preventing them from infecting their own host cells and



ensuring their maturation. Once mature, however, the virus is able to fuse to cell membranes, a trait that enables virus particles to infect new host cells, Chen said.

"There are many membranes in this trans-Golgi network, so the immature virus is always surrounded by membranes," Chen said. "In fact, the environment of the secretory pathway is very similar to what the virus encounters while it enters and infects a new host cell. So the question is, why doesn't the virus fuse to membranes on the way out?"

The researchers have examined the crucial role played by the changing acidity as the immature virus travels through the compartments.

"This change in acidity was already known, but its impact on the maturation process was not known until these new findings," Rossmann said.

As a virus particle matures along the pathway through the host cell, it changes the protein structure, or "conformation," in its outer shell.

Yu mimicked the trans-Golgi network environment in test tubes, enabling the researchers to study the virus's changing structure with increasing acidity.

The surface of each virus particle contains 180 copies of a component made of two linked proteins called precursor membrane protein and envelope protein.

The precursor membrane protein prevents the immature virus from fusing with membranes by covering an attachment site in the envelope protein. During maturation,

an enzyme called furin snips the connection between the two proteins, eventually exposing the envelope protein site and enabling the virus to fuse with membranes.

Yu learned, however, that the precursor membrane protein remains in place until the virus is ready to exit the original host cell. The researchers used a technique called cryoelectron microscopy to gain a more detailed view of the virus.

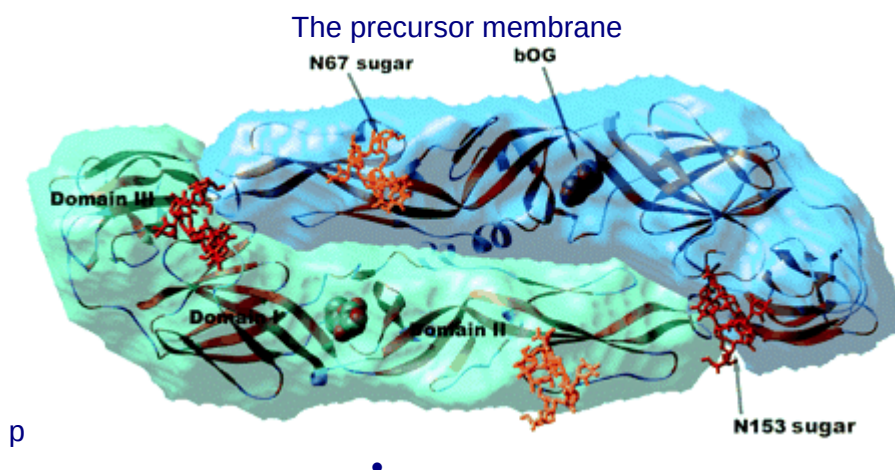
"So, the precursor membrane protein is retained on the virus surface even after the enzyme detaches the two proteins," Chen said. "This is a critical step because the virus is ready to mature but still is incapable of fusing with membranes until after it exits its own cell."

The researchers also determined that the environment must be acidic before the enzyme will snip the two proteins, and they examined the structure to learn specifically why the increased acidity is needed.

Li used fruit fly cells to produce large quantities of the linked proteins so that researchers could study them with a method called X-ray crystallography. Using crystallography, the researchers were able to visualize and study the combined structure of the precursor membrane and envelope proteins.

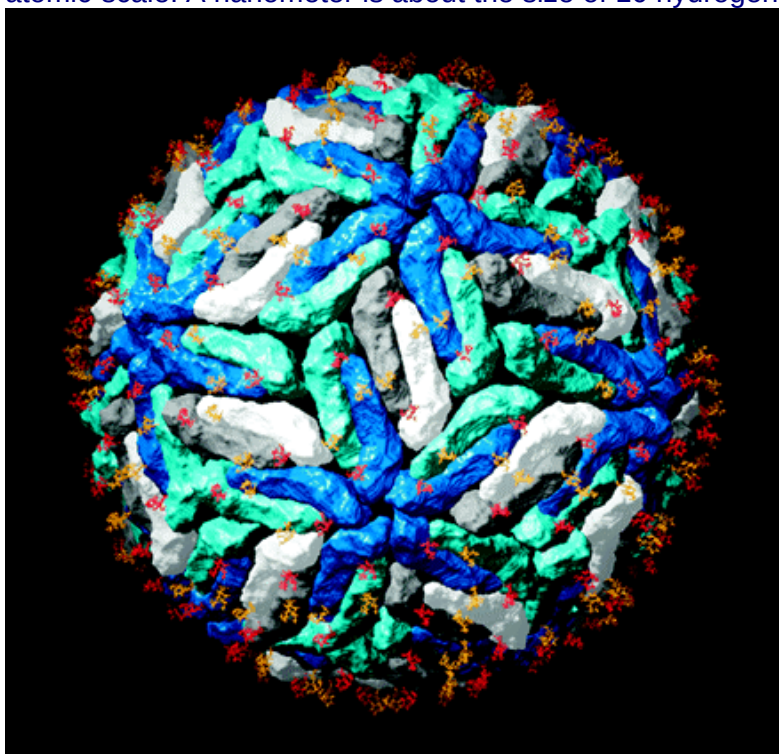
"Having a better understanding of this structure will enable us to learn why the immature form does not fuse with membranes," Rossmann said. "Ultimately, researchers might want to find ways to treat or prevent viral infections, but in order to do that we first have to learn how viruses work, how they mature and initiate infection."

To produce the complex of the two proteins, Li first had to replace the insoluble "transmembrane region" of the protein with a soluble segment, a step essential for using the fruit fly cells to manufacture the proteins. He also had to mutate the protein to remove sites where furin normally attaches, preventing the proteins from being snipped apart.



Semitransparent surface representation of the dengue virus E protein. The two subunits in the dimer are shown in different shades of blue. The backbone of the molecule is superposed in a yellow ribbon representation. The two glycosylation sites are indicated. To illustrate the location and size of the sugar moiety on a molecule produced in insect cells, the complete high-mannose glycans have been modeled, superposed to the core *N*-acetyl glucosamine residues that were visible in the crystal structure. The sugars linked to Asn-67 and -153 ...rotein is about as wide as 50

nanometers, or billionths of a meter, and the envelope protein is about 3 nanometers, or nearly atomic-scale. A nanometer is about the size of 10 hydrogen



atoms strung together.

Carbohydrate distribution on the viral surface. The dengue virus E protein was superposed on the Protein Data Bank ID code 1K4R coordinates, which correspond to the tick-borne encephalitis E protein ectodomain placed in the reconstruction of dengue virus obtained by cryoelectron microscopy (18). Each dengue E dimer is represented as in Fig. 1, with the dimers that lie at the icosahedral twofold axis in dark and light gray, and the dimers lying on local twofold axes in two shades of blue. The ...

ACT RX is a 2500 year old combination of Ayurvedic Cures: ANOTHER CHILD SAVED AND CURED FROM DENGUE FEVER

Twelve year old Mark Aaron Pinlac had been confined at Angeles Medical Center in Angeles City due to high fever, intense body pain, headaches and severe nose bleeding. He was diagnosed with Dengue hemorrhagic fever with his physician putting the boy on IV fluids and Paracetamol but the symptoms continued and his 62,000 platelet count continually dropped to a low of 38,000 and his nose continued to bleed.

Fearing for his life, since they had heard of the many deaths from Dengue, the Pinlacs chose to have the new ActRx TriAct® treatment administered to their



Mark Aaron Pinlac

son. Within an hour of spraying the first portion of the treatment, a sublingual spray, young Mark regained his appetite. Then that afternoon, he informed his parents that the body pain and headache had lessened and the nose bleed had stopped, never to return. Within 48 hours of the full treatment, which included the administering of Berberine and Artesunate tablets, all the Dengue symptoms were gone. Mark's platelet count normalized within 72 hours, with his parents amazed at his rapid recovery... only after the ActRx TriAct® treatment

There were no adverse side effects and Mark quickly returned to being an energetic young boy, with his family agreeing that they believed the natural and innovative ActRx TriAct® treatment had saved Mark's life.

NEW TREATMENT HELPS SAVE CHILD'S LIFE FROM DENGUE

The life of five year old Samantha Sofia Serrano has been saved from Dengue hemorrhagic fever, a serious disease that killed over 500 people last year in the Philippines alone, most of them children. The precocious young girl had been admitted to the hospital after two days of high fever. Diagnostic tests showed her platelets had already dropped to 60,000 and she was then admitted to the Garcia Medical Center where further tests diagnosed her with Dengue, where she was put on IV fluids and Paracetamol for the intense stomach pain and headaches. She then developed pneumonia, and started nose bleeding and evidenced blood in her stool. With her



Samantha Sofia Serrano

condition worsening in her third day in the hospital and platelet count reduced to 18,000, Samantha was getting weaker and weaker, her family decided to try the new treatment named ActRx TriAct® and the results were both dramatic and immediate. Within 15 minutes of administering the first portion of the treatment, a sublingual spray, Little Samantha asked for food. During the second day of treatment and the administering of Berberine and Artesunate tablets, her platelet levels increased and she became very active. There were no adverse side effects and no problems related to the treatment interfering with the antibiotics, which had been administered for pneumonia, and she was released from the hospital the following day healthy and happy. Her family stating that they believed that the groundbreaking ActRx TriAct® treatment had saved Samantha's life.

The ActRx TriAct® is a world-wide patented two-day regimen that consists of a single use of an Artemether Sublingual Spray in combination with doses of

Artesunate and Berberine tablets. This treatment was successfully tested with one hundred percent (100%) of enrolled Dengue patients from the San Lazaro Hospital for Infectious Diseases showing a drastic improvement within 24 to 48 hours. Moreover, there were no safety issues or adverse side effects.

The Philippine Council for Health Research and Development (PCHRD) of the Department of Science and Technology (DOST) assessed the results obtained in the field. Then, upon careful evaluation, Jaime C. Montoya, MD, MSc, CESO III finally concluded that "... a review of the (ActRx TriAct®) protocol shows that it is scientifically valid and sound, to be carried out in Hospitals".

"It has proven to be another excellent example of President Aquino's program of a Public/Private Partnership working for the good of the Filipino people," stated Former Senator, and now Climate Change Commissioner, Heherson "Sonny" Alvarez. "And after so much hard work, accomplished here in the Philippines, the companies providing this incredible cure will have an immense positive effect on the world."

SUMMARY

To accomplish the task of this undertaking, including getting FDA approval for ACT RX, Energime Green Group, Ltd (EGG, Bahamas), in partnership with the oldest pharmaceutical company of India-Lazerhead Healthcar, which holds licenses for both synthetic and holistic Ayurvedic drugs:(www.lazerhead.net); and under the direction of top Philippine Doctors –Dr Oneda and Dr Miranda- who were successful 100% of the time using ACT Rx to cure 300 Dengue Patients in FDA Level III trials, will start new \$10 million FDA trials in India and Sao Paulo Brasil in Dec 2015, under the supervision of EGG's Medical Director- Dr David Krasnow, a UCLA professor and eye doctor that has overseen 15 FDA trials in the USA; the original Flying Eye Doctor, Dr David is a world expert in diabetes (www.diabeteseyed.com) holds a Masters in Public health and Masters in Infomatics.

ACT RX SUMMARY OF TYPES OF VIRUSES IT CURES (All Flaviviruses & Malaria Virus):

1. The dengue virus is surrounded by 180 copies of the envelope protein. Many other viruses are surrounded by capsids composed of many identical proteins, and these often appear in multiples of 60, such as 180, 240 or 420 copies. What is significant about these numbers? Can you find examples of each in the PDB?
2. Dengue virus is a member of a family of flaviviruses that are spread by ticks and mosquitoes. Other examples include yellow fever virus and West Nile virus. Looking at the structures in the PDB, can you see similarities in the proteins made by these viruses?
3. Dengue virus replicates in the cytoplasm of infected cells, without entering the nucleus. **ACT Rx clears and cures all Flaviviruses:**

Flavivirus is a genus of viruses in the family Flaviviridae. This genus includes the West Nile virus, dengue virus, tick-borne encephalitis virus, yellow fever virus, and several other viruses which may cause encephalitis.

ACT RX CURES TICK and MOSQUITOE BORNE Species

Tick-borne viruses

- **Mammalian tick-borne virus group**
 - Absettarov virus
 - Alkhurma virus (ALKV)
 - Deer tick virus (DT)
 - Gadgets Gully virus (GGYV)
 - Kadam virus (KADV)
 - Karshi virus
 - Kyasanur Forest disease virus (KFDV)
 - Langat virus (LGTV)
 - Louping ill virus (LIV)
 - Mogiana tick virus (MGTV)
 - Ngoye virus (NGOV)
 - Omsk hemorrhagic fever virus (OHFV)
 - Powassan virus (POWV)
 - Royal Farm virus (RFV)
 - Sokuluk virus (SOKV)
 - Tick-borne encephalitis virus (TBEV)
 - Turkish sheep encephalitis virus (TSE)
- **Seabird tick-borne virus group**
 - Kama virus (KAMV)
 - Meaban virus (MEAV)
 - Saumarez Reef virus (SREV)
 - Tyuleniy virus (TYUV)

Mosquito-borne viruses

- **Without known vertebrate host**
 - Aedes flavivirus
 - Barkedji virus
 - Calbertado virus
 - Cell fusing agent virus
 - Chaoyang virus
 - Culex flavivirus

- *Culex theileri flavivirus*
- *Donggang virus*
- *Hanko virus*
- *Ilomantsi virus*
- *Kamiti River virus*
- *Lammi virus*
- *Marisma mosquito virus*
- *Nakiwogo virus*
- *Nhumirim virus*
- *Nienokoue virus*
- *Palm Creek virus (PCV)*
- *Spanish Culex flavivirus*
- *Spanish Ochlerotatus flavivirus*
- *Quang Binh virus*
- **Aroa virus group**
 - *Aroa virus (AROAV)*
 - *Bussuquara virus (BSQV)*
 - *Iguape virus (IGUV)*
- **Dengue virus group**
 - **Dengue virus (DENV)**
 - **Kedougou virus (KEDV)**
- **Zika Virus Group**
- **Virus Group IV (ZIKV) ((+)ssRNA)**
- **Japanese encephalitis virus group**
 - *Bussuquara virus*
 - *Cacipacore virus (CPCV)*
 - *Koutango virus (KOUV)*
 - *Ilheus virus (ILHV)*
 - *Japanese encephalitis virus (JEV)*
 - *Murray Valley encephalitis virus (MVEV)*
 - *Alfuy virus*
 - *Rocio virus (ROCV)*
 - *St. Louis encephalitis virus (SLEV)*
 - *Usutu virus (USUV)*
 - *West Nile virus (WNV)*
 - *Yaounde virus (YAOV)*
- **Kokobera virus group**
 - *Kokobera virus (KOKV)*

- *New Mapoon virus (NMV)*
- *Stratford virus (STRV)*
- ***Ntaya virus group***
 - *Bagaza virus (BAGV)*
 - *Baiyangdian virus (BYDV)*
 - *Duck egg drop syndrome virus (BYDV)*
 - *Ilheus virus (ILHV)*
 - *Jiangsu virus (JSV)*
 - *Israel turkey meningoencephalomyelitis virus (ITV)*
 - *Ntaya virus (NTAV)*
 - *Tembusu virus (TMUV)*
- ***Spondweni virus group***
 - *Zika virus (ZIKV)*
- ***Yellow fever virus group***
 - *Banzi virus (BANV)*
 - *Bouboui virus (BOUV)*
 - *Edge Hill virus (EHV)*
 - *Jugra virus (JUGV)*
 - *Saboya virus (SABV)*
 - *Sepik virus (SEPV)*
 - *Uganda S virus (UGSV)*
 - *Wesselsbron virus (WESSV)*
 - *Yellow fever virus (YFV)*

Viruses with no known arthropod vector

- ***Tamana bat virus (TABV)***
- ***Entebbe virus group***
 - *Entebbe bat virus (ENTV)*
 - *Sokoluk virus*
 - *Yokose virus (YOKV)*
- ***Modoc virus group***
 - *Apoi virus (APOIV)*
 - *Cowbone Ridge virus (CRV)*
 - *Jutiapa virus (JUTV)*
 - *Modoc virus (MODV)*
 - *Sal Vieja virus (SVV)*
 - *San Perlita virus (SPV)*
- ***Rio Bravo virus group***

- *Bukalasa bat virus (BBV)*
- *Carey Island virus (CIV)*
- *Dakar bat virus (DBV)*
- *Montana myotis leukoencephalitis virus (MMLV)*
- *Phnom Penh bat virus (PPBV)*
- *Rio Bravo virus (RBV)*

Non vertebrate viruses

- *Soybean cyst nematode virus 5*

Viruses known only from sequencing

- *Aedes flavivirus*
- *Aedes cinereus flavivirus*
- *Aedes vexans flavivirus*
- *Culex theileri flavivirus*

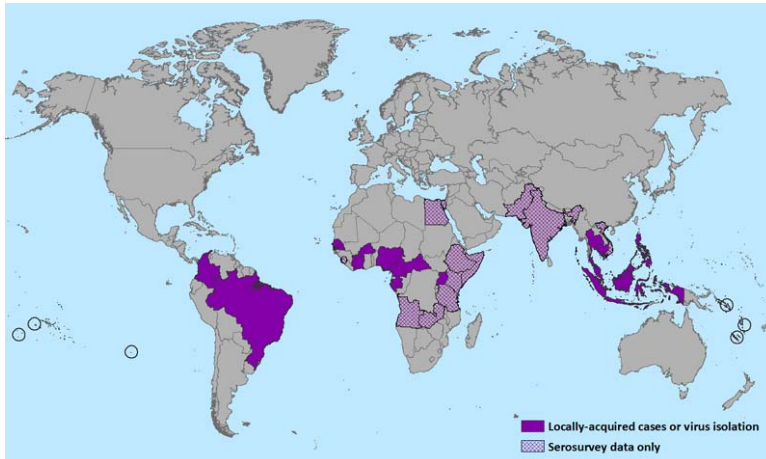
ZIKA (ZIKV) Transmissions, considered an emerging pathogen

Zika virus is spread to people through mosquito bites. The most common symptoms of Zika virus disease (Zika) are fever, rash, joint pain, and red eye. The illness is usually mild with symptoms lasting from several days to a week. Severe disease requiring hospitalization is uncommon.

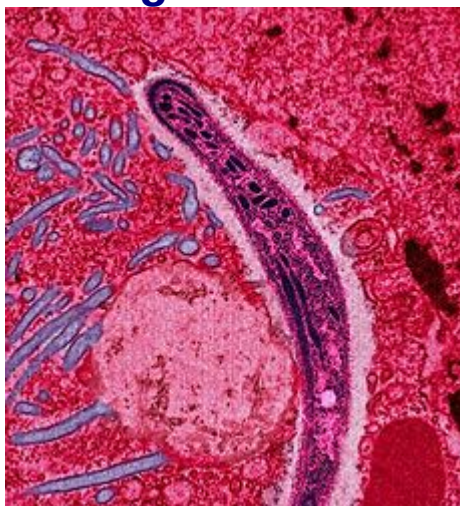
Outbreaks of Zika have occurred in Africa, Southeast Asia, and the Pacific Islands.

Because the *Aedes* species mosquitoes that spread Zika virus are found throughout the world, it is likely that outbreaks will spread to new countries. Zika virus is not currently found in the United States. However, cases of Zika have been reported in returning travelers.

There is no vaccine to prevent or medicine to treat Zika. Travelers can protect themselves from this disease by taking steps to prevent mosquito bites. When traveling to countries where Zika virus (see below) or other viruses spread by mosquitoes have been reported, use insect repellent, wear long sleeves and pants, and stay in places with air conditioning or that use window and door screens. Zika Virus has attacked Colombia and Brasil heavily:

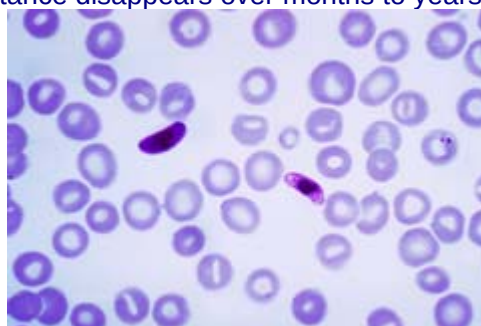


Malaria in Widening Area Resists Drug, Lancet



Study Finds

Malaria is a mosquito-borne infectious disease of humans and other animals caused by parasitic **protozoans** (a group of single-celled microorganism) belonging to the genus *Plasmodium*. Malaria causes symptoms that typically include fever, **fatigue**, vomiting, and **headaches**. In severe cases it can cause **yellow skin**, **seizures**, coma or **death**. The disease is transmitted by the biting of mosquitos, and the symptoms usually begin ten to fifteen days after being bitten. If not appropriately treated, people may have recurrences of the disease months later. In those who have recently survived an infection, re-infection typically causes milder symptoms. This partial resistance disappears over months to years



if the person has no continuing exposure to malaria

The disease is transmitted most commonly by an infected female **Anopheles** mosquito. The mosquito bite introduces the parasites from the mosquito's saliva into a person's **blood**. The parasites travel to the liver where they mature and reproduce. Five species of *Plasmodium* can infect and be spread by humans Most deaths are caused by *P. falciparum* because *P. vivax*, *P. ovale*, and *P. malariae* generally cause a milder form of malaria The species *P. knowlesi* rarely causes disease in humans. Malaria is typically diagnosed by the microscopic examination of blood using blood films, or with **antigen**-based rapid diagnostic tests Methods that use the **polymerase chain reaction** to detect the parasite's **DNA** have been developed, but are not widely used in areas where malaria is common due to their cost and complexity.

BANGKOK — The world's best drug for treating malaria, a medicine that is the key to saving millions of lives in Africa and beyond, is losing its efficacy in a

much larger swath of territory than was previously known, according to research that was released Friday.

The study, in *The Lancet Infectious Diseases*, a medical journal, raises the troubling prospect that resistance to the drug, artemisinin, might one day severely hamper treatment of a disease that kills hundreds of thousands of people every year.

"This should focus minds," said Charles Woodrow, one of the authors of the study. "We have to eliminate these very resistant parasites. The fear is that if we don't, we would reverse all the gains that have been made."

For several decades, artemisinin has been considered an anti-malaria wonder drug, rapidly ridding the body of the parasite that is introduced into the body by a mosquito and infects the blood.

Early signs of trouble with the drug were cited a decade ago by scientists working in western Cambodia. Falciparum malaria, the deadliest form of the disease, was increasingly resistant to treatment with artemisinin, which is derived from a plant used in traditional Chinese medicine and is often used in conjunction with other drugs. The new study in *The Lancet* shows that resistance to the drug extends more than 1,500 miles away from Cambodia, along the border between Myanmar and India.

It was not known whether resistance had spread overland or whether new diagnostic tools were revealing a situation that had previously gone undetected.

The *Lancet* article concluded that resistance to artemisinin treatment "extends across much of Myanmar."

One of the sites where resistance was prevalent was 15 miles from the border with India.

"The pace at which the geographical extent of artemisinin resistance is spreading is faster than the rate at which control and elimination measures are being developed and instituted, or new drugs being introduced," the authors of *The Lancet* article wrote. "A vigorous international effort to contain this enormous threat is needed."

There is no immediate replacement for artemisinin, which has helped contribute to steep declines in mortality rates from the disease.

Scientists say any possible substitute is years if not decades away.

Scientists are particularly concerned about the declining efficacy of artemisinin because it appears to follow a pattern seen in previously used malaria drugs, like chloroquine. Such drugs were, in their time, mainstays of malaria treatment but are no longer considered useful because the parasite became resistant.

The *Lancet* study found that nearly 40 percent of the samples it gathered from patients across Myanmar showed resistance to artemisinin.

“It’s probably not a matter of if but a matter of when the rest of the world will be seeing this problem,” said Voravit Suwanvanichkij, a medical doctor who works with charities that offer health care to people along the Thai-Myanmar border.

Dr. Voravit said Myanmar’s decrepit health care system and the lack of government control in many parts of the country had abetted the development of drug resistance.

“In a place like Burma, where you have a health system that is so inadequate, you have the perfect setup for something like this,” Dr. Voravit said, referring to the country by its alternate name. “There are a lot of fake and adulterated drugs on the market.”

Scientists say counterfeit drugs and patients who do not finish their course of medication encourage drug resistance by giving the parasite greater opportunity to mutate.

Drug resistance appears to be most acute in western Cambodia, where a standard three-day course of drugs is no longer effective for many patients, scientists say. Additional doses are needed to mop up the malarial parasites.

Researchers’ great fear is that resistance to artemisinin will spread to Africa. Ninety percent of the estimated 584,000 annual deaths from malaria occur in Africa, according to the World Health Organization. Emergence of artemisinin resistance in southeast Asia poses a serious threat to the global control of *Plasmodium falciparum* malaria. Discovery of the K13 marker has transformed approaches to the monitoring of artemisinin resistance, allowing introduction of molecular surveillance in remote areas through analysis of DNA. We aimed to assess the spread of artemisinin-resistant *P falciparum* in Myanmar by determining the relative prevalence of *P falciparum* parasites carrying K13-propeller mutations.

AFRICAN DENGUE

Up to 33% of the population is exposed to Dengue by the age of 19:
KENYA IMMUNE TEST – DENV 2

Table 1: Prevalence of anti-DENV-2 serocomplex antibodies (IgM, IgG and IgA) based on indirect ELISA tests by health facilities, Western Kenya, 2010 (n=422)

Health Facility, n (%)	Positive, n (%)	Negative, n (%)	P-value
Alupe Sub-district Hospital 124 (100)	15 (12.1)	109 (87.9)	0.236 ^a
KEMRI/CIPDCR Alupe Clinic 176 (100)	12 (6.8)	164 (93.2)	
Anderson Medical Centre 122 (100)	9 (7.4)	113 (92.6)	
Total sample size 422 (100)	36 (8.5)*	386 (91.5)	

Data are presented as n (%). ^a= χ^2 test. *8.5% prevalence by indirect ELISA test

MALARIA

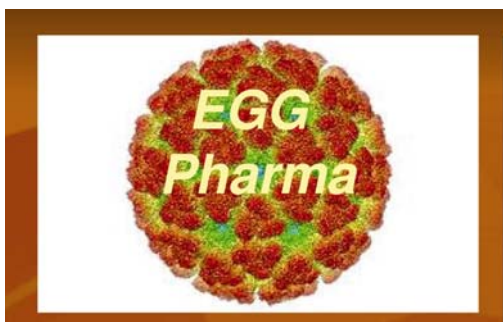
Malaria has remained a major public health problem in Nigeria. It accounts for over 60% outpatient visits and 30% hospital admissions in Nigeria. The disease has impacted negatively on the economy with about 132 Billion Naira (·\$802 million) lost to the disease as cost of treatment and loss in man-hours.

Malaria is an infectious disease caused by the parasite of genus Plasmodium. The four identified species of this parasite causing human malaria are Plasmodium falciparum, P. vivax, P. ovale and P. malariae. In Nigeria 98% of all cases of Malaria is due to Plasmodium falciparum. This is the species that is responsible for the severe form of the disease that leads to death. It is transmitted from bites of an infected female anopheles mosquitoes to man.

Malaria is highly endemic in Nigeria. It poses a major challenge to the country as it impedes human development. It is both a cause and consequence of underdevelopment and remains one of the leading causes of morbidity and mortality in the country (2). Malaria accounts for about 63% (1) of all visits to public health facilities (Out-patient –attendances). Thirty percent of hospital admissions are also due to malaria. It is responsible for 29% of childhood death, 25% of infant mortality and 11% of maternal mortality (3, 10).

The economic loss to Nigeria due to malaria is estimated at \$802 million USD annually due to loss of man hours resulting from sickness absence and cost of treatment. It is a major cause of absenteeism from work and school. It contributes to poverty and results in poor pregnancy outcome.

In Lagos State, malaria is responsible for 70% of outpatient attendance at the secondary healthcare facilities and over 80% of all tracer diseases reported by primary healthcare facilities (HMIS). The most vulnerable groups are under fives, pregnant women, visitors from non-endemic areas, those with sickle cell anaemia, HIV/AIDS.



EGG SUMMARY CONCLUSIONS

After 75 years of single-action malarial drugs, the malaria virus has become resistant to all known medicines, including the Cortem Cloro-artemethinin drugs of Novartis, and are mainly ineffective to date. Currently the CDC and WHO have been holding out for a Vaccine, which has not arrived, and the latest vaccine from Sanofi for Dengue was only 31% effective after a series of shots over 2 years, which clearly shows the diversity and sophistication of these Malaria and Dengue viruses, as well as their speed of adaptation.

ACT Rx however, uses three separate Ayurvedic cures to combine into one therapy, which makes it impossible for the mosquito and viruses to adapt, and thus can cure 100% of the time without creating resistance. Moreover; the tri-act therapy uses Berberine to flush the plasmids out of the liver so that they can be cleared by the actions of the other two Artemethinin, and Artemether.

EGG's patented tri-act system uses no needles, so it can safely be deployed by non-professionals and nurse practitioners, and parents of afflicted children. This is necessary in Asia and Americas, where the epidemic of Dengue, Chikungunya and Malaria has totally overwhelmed the medical community, and there are no spare treatment facilities even in Brasil (see page 3) and India, so that patients are seen in make-shift tents!

The speed of the growth of Dengue and Chikungunya, and to some degree malaria, is due to the fact that asymptomatic patients are able to pass on the virus without showing symptoms, or even, the infected persons knowing of their infection. Once infected, they can carry the virus and infect other mosquitoes if bitten, for years, and even decades. It is known that malaria patients can, in fact, have episodes of relapse of malaria symptoms over 30 years from the time of original infection.

Thus, the need for Act Rx Tri-act Therapy for all is needed to end this epidemic. Indeed, 75% of the population of Latin and Asian cities means that the mosquitos have a nearly 100% success rate spreading the disease. Thus, EGG will help the governments by lowering the cost of a 2 day cure of Dengue or Chikungunya, or 5 day cure for Malaria by lowering the cost to \$35 (and %70 for malaria), thereby allowing the whole community to be cleared of the virus completely, and stop the acceleration of the epidemic, which has increased by 8 times in Brasil, and 2x's in Colombia over last year!