

## Cuba Confronts Zika: All Hands on Deck

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The world sat rapt as President Barack Obama touched down in Havana in March 2016, the first US President to visit Cuba in 88 years. Across the island, Cubans anticipated Obama's arrival with hope-tinged disbelief; it was hard to fathom that rapprochement had come this far after decades of estrangement and hostility. The capital's streets were abuzz, with Cubans throwing themselves into urban beautification efforts to receive the US First Family in style. Yet, Havana also buzzed with something else, a threat that transcends politics, national borders and differences of opinion: the mosquitoes that transmit Zika, dengue and chikungunya. These arboviral infections are spread by two *Aedes* mosquitoes (*aegypti* and *albopictus*)—highly adaptable creatures that bite during the day and thrive in hot urban climates.

Although Zika had been detected in humans in Uganda and Tanzania as far back as 1952, outbreaks of the nonfatal virus were not confirmed in the Americas until 2014. But in Brazil, where the latest outbreak began spreading swiftly, some 1.5 million suspected Zika cases were reported by February, 2016,[1] with growing concern that the virus could be sexually transmitted. Just a month prior to President Obama's visit, WHO declared Zika a global public health emergency.[2] This was only the fourth such declaration by WHO, the others for epidemics of polio, H1N1 influenza and Ebola. The WHO warning included a possible link between Zika and autoimmune and neurological complications, such as fetal microcephaly and Guillain-Barré syndrome (GBS). The global alarm reflected data from Brazil indicating a dramatic increase in microcephaly incidence from 5.7 per 100,000 live births in 2010 to 99.7 per 100,000 between November 2015 and January 2016.[3]

On April 13, researchers from the US Centers for Disease Control and Prevention (CDC) indeed confirmed evidence of a causal relationship between Zika infection in pregnant women and fetal microcephaly.[4] Scientists investigating the link had already warned: "If Zika virus infection is confirmed to cause congenital microcephaly, this could lead to a large international burden of infant neurological morbidity." [5]

### Detect, Prevent, Respond

Known for its population health approach emphasizing community participation and intersectoral strategies,[6] Cuban health authorities issued a national epidemiological alert as early as December, 2015, establishing protocols designed to get ahead of the curve on Zika transmission and impede proliferation of the *Aedes* mosquito. The country, which has a universal health system guaranteeing free, accessible care to over 11 million people, didn't have to re-invent the wheel: Since the 1970s, Cuba has had a national dengue diagnostic and surveillance network supported by provincial Hygiene, Epidemiology and Microbiology Centers, and 30 WHO-compliant diagnostic labs across the country for confirming cases of the four strains of dengue (DEN 1,2,3 and 4) circulating on the island. These labs report directly to the national reference center lab at the Pedro Kourí Tropical Medicine Institute (IPK) in Havana—a WHO/PAHO Collaborating Center for dengue and related arbovirus research—which has a dengue vaccine in development.

### Zika Timeline in the Americas

#### 2014

**February:** First confirmed case of Zika in the Americas (Easter Island, Chile)

#### 2015

**May:** First autochthonous case confirmed in Brazil

**October:** Brazilian health authorities note an "unusual increase" in microcephaly in Pernambuco State

**December 23:** Cuba issues epidemiological alert detailing surveillance, prevention and control measures

#### 2016

**February 1:** WHO declares spread of Zika and possible relation to microcephaly and other neurological conditions in Brazil a global public health emergency

**February 22:** Cuba adopts 11-step National Zika Action Plan, mobilizes 9000 armed forces reserves and active members for fumigation

**February 26:** Nationwide meetings held in Cuban communities about Zika prevention, containment and treatment

**March 2:** In Cuba, PAHO Director Carissa F. Etienne meets with regional health, government and civil defense authorities

**March 16:** first autochthonous case diagnosed in Cuba

**March 22:** 35 countries in the hemisphere reporting Zika

**March 24:** Cuba confirms six Zika cases, all but one imported; one person infected is a pregnant Cuban woman returning from international posting in Venezuela

**April 8:** Cuba confirms eighth imported Zika case

**April 12:** USA confirms Zika in 30 states (700 people infected, 69 pregnant women and 7 sexually transmitted)

**April 13:** CDC announces evidence establishing causal link between Zika and microcephaly and other serious brain anomalies

**April 14:** Cuba confirms it has diagnosed 10 cases of Zika: 9 imported and 1 autochthonous (of the 10, 2 are pregnant women)

**April 20:** CDC reports imported cases in 41 states and Washington DC, plus autochthonous cases in Puerto Rico, American Samoa and US Virgin Islands

By the time Cubans were toasting the New Year, four strains of dengue and chikungunya were present in the country, but no cases of Zika. Yet, with over 18,000 Cuban doctors working in Brazil and the island's soaring popularity as a tourist destination, Cuban health officials were concerned it was only a matter of time before imported cases of Zika started appearing. The prospect was especially alarming to epidemiologists, since Zika symptoms are usually so mild that most infected people go undiagnosed, so much so that three out of four carriers are asymptomatic, making control even more difficult.

As the Americas outbreak spread, the data suggesting a causal relationship between Zika and neurological and autoimmune

problems in newborns put Cuban health authorities on high alert. Any factor endangering children has always been a priority for the health system and the national Maternal-Child Program. In this case, Zika also threatened the birth rate itself in this country where low fertility (children per woman) and crude reproductive rates (daughters born per woman) are coupled with a rapidly aging population.[7]

In February, Cuba issued a national 11-point Zika Action Plan, based on PAHO guidelines for controlling the disease: detect, prevent and respond. The plan prioritizes 46 municipalities categorized as high risk[8] and underscores the need for strict epidemiological surveillance. Aggressive vector-control measures were implemented, including participation by 9000 active and reserve soldiers in fumigation of homes, offices, schools and other facilities; reduction of environmental risk factors through more systematic garbage pickup; repairs of public infrastructure (closing open sewers and water leaks); and methodical weeding of overgrown areas. In addition, participation by local health authorities and communities was strengthened, counting on them to identify vector-control problems and suggest solutions.

This ‘all hands on deck’ strategy kicked off with a media campaign to inform the public of the dangers and the measures being taken. Above all, it aimed at enlisting their help: neighborhood meetings led by local family doctors and community polyclinic specialists outlined how Zika is transmitted, described the symptoms and warning signs, announced an active screening initiative (including door-to-door visits by medical students to screen for unexplained fevers), detailed steps for ensuring homes were free of potential vector-breeding sites, and posted fumigation schedules for each health catchment area.

Daily health ministry meetings collect data related to these measures—essential for capturing an epidemiological snapshot of arboviruses in the country—and yield information shared with the public via comprehensive media updates. Data analyzed in these meetings include how many people (Cubans and international visitors) have presented at health facilities with unexplained fever and how many have been hospitalized, the number of patients with laboratory-confirmed arbovirus diseases, the international epidemiological picture for Zika, and homes and institutions flagged for noncompliance with weekly fumigation schedules.

The Action Plan’s strategy and progress are also dissected in weekly meetings attended by all authorities involved in the national detection, prevention, control and treatment programs, such as the Ministries of Health, Tourism, Industry, and Economy and Planning, as well as Civil Defense, the armed forces, IPK and others.

### Initial Results

After the Plan had been in place for one month, officials announced encouraging but mixed results. Some 82% of government workplaces had complied with environmental cleanup measures, while 92% of the highest-risk neighborhoods in the country had been fumigated externally (i.e. on the street using fumigation trucks). Meanwhile, although compliance indices for weekly in-home fumigation were increasing—from week 2 through week 3 of the first fumigation cycle, homes not fumigated fell from 7.4% to 0.5%—this was deemed insufficient.

“Since we launched the Zika Action Plan, we’ve seen a progressive decline in incidence of fever, dengue infection and mosquito infestation,” says Dr Francisco Durán, the Ministry of Public Health’s Director of Epidemiology. “But we also identified problems, including lax environmental cleanup and noncompliance with fumigation by some of the population in homes and workplaces.”[9] Absentee home owners were among the worst offenders and encouraged to leave keys with trusted neighbors so their houses could be sprayed. Failure to fumigate would result in fines under Article 18 of Law 272, Attorney General Darío Delgado warned in the national press.[10] “Fumigating every week isn’t pleasant,” says Havana resident Maria González, “I take my grandson to the park for the 45 minutes the house has to remain closed afterwards and it still smells awful when we get home, but it’s for everybody’s health.”



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*Dr Francisco Durán, Cuba’s National Director of Epidemiology*

Another factor identified during the first month-long fumigation cycle was misinformation circulating about what chemicals were being sprayed, coupled with questions about their efficacy. In response, an explanation of the chemicals used in residential fumigation was disseminated by Cuban media—a mixture of gasoline and cypermethrin at 25% dilution. For families with house-bound members, or people with asthma or other respiratory problems, an alternative mixture (cypermethrin and water) was made available and does not require vacating the home.

The ‘tourism tsumani’ under way in Cuba is also a consideration. “The owners of the house I rent in Havana have it fumigated,” said US anthropologist Molly Mandell, who is pursuing research in Cuba, “but not the bedrooms.” Dr Durán acknowledges that the emerging private sector has presented a challenge: “Some small business owners resist fumigating, so we consider this a high-risk sector. But the education and media campaigns have helped, as have fixed fumigation schedules allowing for better planning.” Meetings were held across the country with homeowners who

rent to travelers to underscore the importance of vector control and fumigation and to be attentive to foreign visitors who develop fever, to get them medical attention so they can be diagnosed and treated. “It’s still not perfect, but compliance rates have improved as a result,” says Dr Durán. To date, Cuba has registered 10 cases of Zika infection, all but one imported, and two of those infected are pregnant women.[9]

### Learning from the Ebola Experience

Any outbreak of infectious disease in developing countries, like the Ebola epidemic in Africa, can adversely affect tourism and fragile economies, serving as cautionary tales. WHO/PAHO highlight two specific lessons learned from Ebola that should be applied to Zika and similar outbreaks: 1) accurate, up-to-date and easily understandable information must be furnished to health care providers and the public to ensure proper diagnosis and treatment, and 2) standard protocols must be enacted to effectively detect, control and contain the disease. Crucial to avoid panic is a consistent, easy-to-understand communications strategy—the absence of which contributed to an uneven, sometimes chaotic, response to Ebola. During that outbreak, “34 countries enacted trade and travel restrictions against WHO guidelines and in violation of Article 43 of International Health Regulations.”[11]

Diseases respect no borders, a fact of contemporary life thrown into stark relief by the Ebola experience. Arboviruses transmitted by mosquitoes are particularly worrisome, given the combination of climate change and international travel that promotes propagation of *Aedes* mosquitoes and transmission of the diseases they carry. For health care providers, the challenge becomes more complex still since Zika symptoms can look very similar to dengue and chikungunya, plus there is no treatment. Diagnostic testing, meanwhile, is limited to costly molecular polymerase chain reaction (PCR) analyses that must be performed between day one and day five of infection, while the virus is still in the bloodstream. Although Zika antibodies can be detected after this window, they are so similar to dengue and yellow fever, there is risk of misdiagnosis. The epidemiology of Zika, coupled with the link to fetal microcephaly, especially in contexts with weak public health systems, constitutes an international health tinderbox.

Instead of reacting by closing its borders and shutting down its international cooperation programs, Cuba announced it would not curtail travel or cease commercial relations with countries experiencing Zika outbreaks. Moreover, the country updated its own international health regulations (put into effect on March 1)[12] to identify travelers with fever at all points of entry. Thermal imaging scanners measuring travelers’ body temperature were installed at all airports, ports and marinas; anyone presenting in Cuba with fever is monitored, diagnosed and treated, and their status reported to the Ministry of Public Health’s National Epidemiology Division and the Ministry’s Central Health Management Division. Arriving international students must present a Certificate of Health issued no more than three months before travel.

Additionally, all professionals returning from overseas collaboration are under medical observation for ten days prior to their return to Cuba; if fever is detected, they cannot travel until its cause is diagnosed and treated. Upon arrival in Cuba, they are taken directly from the airport to specialized health centers where they

are observed for at least five hours, their temperature taken at arrival and departure, a clinical exam performed, and blood tests analyzed for malaria at on-site labs; each person must be deemed healthy before they can return to their homes, where followup is provided by their local family doctor.

Cubans returning from or traveling to Angola—where hundreds of deaths have been attributed to a yellow fever outbreak in 16 of the country’s 18 municipalities, a situation the WHO has said “constitutes a potential threat to the entire world”[13]—receive vaccinations against that re-emerging disease, also carried by the same vector as Zika.

### Zika-Related Disorders

Cuba took steps to orient health professionals regarding specialized consultations for pregnant women even before scientific evidence linked Zika to fetal microcephaly. “Among dengue, chikungunya and Zika, dengue causes the highest morbidity; it’s also the most lethal,” says Dr Durán. “However, the mounting evidence suggesting causality between Zika and microcephaly, GBS and other neurological disorders in fetuses is extraordinarily serious.”[9] In February, an in-depth training seminar at IPK (Cuba’s reference center for tropical diseases), attended by specialists countrywide established diagnostic and treatment algorithms and set national protocols, including those for surveillance and treatment of pregnant women. These protocols were circulated to family doctors and OB-GYNs with specific instructions for monitoring women during pregnancy. In the presence of Zika, the 13 standard antenatal checkups provided every Cuban mother-to-be, are complemented by the following:

- From earliest stages of pregnancy, discuss personal Zika protection measures to be taken with each pregnant woman;
- Look for warning signs during every consultation (mild fever; nonpurulent conjunctivitis; red, itchy rash; and joint pain);
- Measure uterine height and amniotic fluid volume at 20 weeks of gestation;
- Perform ultrasounds in the first, second, and third trimester, with the last conducted at 28 weeks;
- Undertake targeted genetic testing and virologic studies on pregnant women fitting certain criteria; and
- Administer ultrasounds every 15 days when fetuses show head circumferences two deviations below the standard mean in any stage of gestation

These measures bolster surveillance already in place for fetal microcephaly—a congenital malformation that occurs in some 20 cases a year in Cuba.[9] Additionally, cranial circumference measurements are taken of every newborn during the first 24 hours of life and data collected on cases of congenital infection due to Zika. All results are reported to the National Registry of Congenital Malformations.

As of this writing, two expectant Cuban mothers have been confirmed with Zika and are being monitored closely. While pregnant women were not eligible for international cooperation posts (requiring a minimum two-year commitment) even before Zika, any Cuban woman becoming pregnant during an international posting is treated as if she were in Cuba; once she is certified as healthy, she travels back to Cuba for further monitoring and followup. As evidence regarding the possible link between Zika



and congenital malformations and other neurological disorders emerges, health officials continue to adapt and update protocols for this vulnerable population.

### Sustainable Surveillance & Control

The need to eradicate *Aedes* breeding sites is taking on added urgency as Cuba enters the May–October rainy season, marked by increased rainfall and warmer temperatures—perfect conditions for mosquito proliferation. Indeed, since the first epidemiological advisory was issued in December 2015, the country's health authorities have emphasized that stamping out mosquito breeding sites is the only way to prevent arthropod-borne viruses. Fumigation, applying mosquito repellent and wearing protective clothing (other measures featured in the national plan) only protect against adult mosquitoes, whereas eliminating breeding sites and larvae is a much more effective strategy. This message is hammered home at every opportunity and by the highest levels of health authorities and government. “We cannot let down our guard, nor back away from our fight against eradicating this vector, especially now that we’re heading into the rainy season,” said Health Minister Roberto Morales in a recent intersectoral videoconference.[14]

In order to maintain effective surveillance and control over time as lower risk perception and fumigation fatigue set in, two new plans are being set in motion: the Phase II Plan and the Sustainability Plan. The first is designed to kill larvae before they hatch by treating standing water and spraying interior walls, exterior areas and water tanks with larvicide. Cuban industrial and biotechnology sectors have joined the fight as well: locally-produced repellent and biolarvicide drops for treating standing and stored water are now sold in stores and pharmacies, and in-home foggers will be available for purchase soon.



*Fumigating at-risk neighborhoods in Havana*

The Sustainability Plan is a series of actions to help people incorporate mosquito surveillance and control into their home and work routines. Every 24 days, 100% of homes, offices and public spaces in the highest-risk areas will be inspected for breeding sites and fumigated inside and out in a 100-meter ring—the radius of the average adult mosquito. This is complemented by a ‘fever blockade,’ led by community polyclinics. Any patient presenting with fever of unknown cause will be hospitalized and tested for arthropod-borne viruses. While awaiting test results, the patient’s home will be inspected and fumigated, as will the 100-meter radius around their property. “It’s impossible to completely eliminate mosquitoes, no matter how vigilant we are,” says Dr Durán. “But we have to try and get the infestation index below 0.05.” [Eds—vectors found in less than 0.05% of premises inspected][9]

### Snapshot: Arboviruses in Cuba

**1909:** Yellow fever eradicated

**1981:** First dengue epidemic (serotype 2); 344,203 cases, with 158 fatalities. Subsequent outbreaks in 1997, 2001–2002 and 2006

**2012:** Clinical trials for dengue vaccine commence on monkeys at Pedro Kourí Tropical Medicine Institute

**December 2015:** 28 cases of chikungunya diagnosed in Cuba (all in 2015; no more cases to date)

**January 1–April 14, 2016:** 1208 cases of dengue diagnosed (serotypes 2 & 3)

**January 1–April 14, 2016:** 10 cases of Zika diagnosed

### Global Cooperation, Global Disease Control

The spread of Zika throughout the Americas, Asia, and parts of Africa, and now with imported cases appearing in Europe, underscores the importance of international cooperation in the control, diagnosis and treatment of arthropod-borne viruses. To this end, PAHO established a regional platform supported by 22 reference laboratories across the Americas to diagnosis dengue and other arboviruses, share epidemiological findings and develop research. In February, the Arbovirus Diagnostic Laboratories Network (RELDNA) appointed Cuban specialist Dr María Guadalupe Guzmán as President and issued new guidelines to improve confirmation of suspected Zika cases. The backbone of the guidelines is a new algorithm for detecting Zika and other mosquito-borne viruses. “This algorithm...will contribute to more accurate diagnosis and more efficient surveillance,”[15] says Dr Guzmán, head of the Department of Virology and the IPK’s deputy director for research.


Forging cooperation and marshaling funds to fight Zika is necessary, but not easy. In March, Google donated US\$1 million

to UNICEF to map outbreaks and disease burden, analyze data and support development of vaccines and diagnostic tests,[16] while President Obama re-directed \$510 million earmarked for Ebola to the fight against Zika. Nevertheless, as of this writing, Congress has yet to authorize the \$1.8 billion in emergency Zika funding requested by the President,[17] even as the outbreak approaches epidemic proportions in Puerto Rico, with imported cases in 41 states and Washington DC.[18] Meanwhile, the White House has indicated that Cuba and the United States are “committed to deepen scientific and health cooperation, focusing on communicable diseases including arboviruses such as Zika, dengue and chikungunya...[this] policy change has increased the ability for American and Cuban experts to collaborate on important science and technology issues of mutual interest.”[19] As past experience shows, regional cooperation in public health is critical for more efficient application of standard protocols, more accurate epidemiological surveillance and control, and to stimulate joint research in areas affecting population health.

### Final Considerations

Over a century ago, Cuban scientist Dr Carlos Finlay made a breakthrough with his hypothesis that yellow fever was carried by the *Aedes*

*aegypti* mosquito. In an early example of regional collaboration in communicable disease research, he shared his findings with Major Walter Reed of the US Yellow Fever Commission, who confirmed them and announced to the American Public Health Association in 1900 that the vector for yellow fever had been isolated.[20] Flash forward to 2016: Zika has been detected in all countries in the hemisphere save Canada, while imported cases have been diagnosed across the USA and several European countries.

Successfully preventing, controlling, diagnosing and treating emerging and re-emerging diseases like Zika and yellow fever demand global and local community cooperation, robust funding and implementation of standard protocols. In his conversation with Cuban entrepreneurs during his visit to the island, President Obama said: “...Zika and dengue are spreading so fast across the Americas. This is a natural place where the US and Cuba should be working together...mosquitoes don’t care about borders...and the women who are fearful because it may affect their pregnancy, they’re not concerned with ideology, they’re interested in making sure that their children are protected.”[21] From the time of Finlay and Reed to today, protecting and improving people’s health requires political will and global cooperation. No one can escape the significance of this conclusion in the face of Zika. 

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