



US responds to increase in Zika cases

Health officials pursue Zika research and prepare to combat a formidable foe—the mosquito—despite uncertain funding. Susan Jaffe, *The Lancet's* Washington correspondent, reports.

As the number of confirmed cases of people who have contracted the Zika virus increases across the globe, the knowledge growing about this once rare infection is not reassuring. “The more we learn, the more we get concerned”, said Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases (NIAID), at the US National Institutes of Health (NIH).

The evidence is “now unequivocal that the direct cause of the microcephaly and other congenital abnormalities in the fetuses of [Zika]-infected mothers is clearly the virus itself”, said Fauci. The recent case of a pregnant woman in Washington, DC, who was infected in South America has revealed “the extraordinary and rather virulent neurotropism of the virus”, he said. “This woman had documented viraemia for 10 weeks, which is most extraordinary for a number of reasons [and] it puts the fetus at risk for a very prolonged period of time.” Most infections are spread by mosquitoes although the virus can also be transmitted sexually and through the blood.

As of April 20, 2016, 44 countries have reported cases of Zika virus, including 388 cases in all but seven states of continental USA, according to the US Centers for Disease Control and Prevention (CDC). Although most US infections were acquired while travelling in other countries, eight people were infected in the USA by their sexual partners. Nearly all 503 people with Zika in Puerto Rico and the US territories contracted the disease locally, with only three travel-related cases.

Many people who get the virus may not develop symptoms, said Jesse Goodman, a professor of medicine at Georgetown University

Medical Center in Washington, DC, and former chief scientist at the US Food and Drug Administration. Those with symptoms—which can include a low-grade fever, skin rash, and joint pain—recover after a few days. In rare cases, some may develop Guillain-Barré syndrome,

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which can cause temporary paralysis but can also be fatal among a small proportion of patients. And not all pregnant women who contract Zika will have babies with microcephaly, although the virus and its effects are far from understood, he said. “While everyone is hopeful in the US that we may not have widespread disease here, there is still a risk and the consequences of that are devastating”, said Goodman.

In early February, President Barack Obama requested more than US\$1.8 billion in emergency funding to enable the NIH, CDC, and other agencies to respond to the virus. Since that request, Zika cases in the USA and its territories have risen nearly 15-fold in about 10 weeks. As *The Lancet* went to press, the funding request—recently bumped up to \$1.9 billion—was the subject of intense negotiations between Democrats and Republicans in Congress and between Congress and the White House. Senate Republicans have hinted they might support about half that amount but there’s no guarantee their counterparts in the House of Representatives will agree. In the meantime, NIH has

moved money from Ebola and other programmes targeting diseases such as malaria and tuberculosis, so that it can begin developing diagnostic tools and a vaccine, said Fauci. “When we do get the money we’ve asked for, and we don’t know exactly how much of it we will get at this point, hopefully we will be able to pay back the money we mortgaged out of those other areas because we don’t want them to suffer”, he said.

The fight for funding

“We just had our 91st case diagnosed”, said Representative Debbie Wasserman Schultz, a Democrat from Florida. Her state has recorded more Zika cases than any other state, with most in the southern counties she represents. She is also a member of the House Committee of Appropriations where her Republican colleagues want more information about how the Obama administration will spend the Zika money before approving it. “I think they’re making excuses”, she said. “We have now been through two debates in two different full appropriations committee [meetings] where the Republicans are continuing to rob

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Anthony Fauci testifies about the Zika virus at a Senate committee hearing

Peter to pay Paul.” Republican leaders have the information they need and have been briefed by White House officials, she said. “The Zika virus is an emergency and given how rapidly Zika is advancing and the fact that we don’t know where it’s going to go next, it’s certainly scarier than we originally thought”, she said.

Florida state officials have declared a public health emergency in at least 15 counties with Zika cases and Florida’s Senator Marco Rubio, the former Republican presidential hopeful, supports President Obama’s \$1.9 billion emergency request.

Representative Tom Cole, the Oklahoma Republican who is chairman of the House appropriations health subcommittee, said its questions about the request are not unreasonable and the federal government has sufficient funding for Zika while the committee deliberates. “I think there is a tendency to either politicise this or think Congress will reflexively do anything the administration asks and that’s just not the case, we never do”, said Cole, who visited Zika hotspots in Brazil in March, met with CDC officials there, and has discussed the US response with the Secretary of Health and Human Services Sylvia Matthews Burwell.

“Let us do our job to make sure we do this as prudently as possible and we will get there”, he said. “Nobody thinks this is not a serious challenge”, said Cole. He also points out that the Republican-led Congress doubled the president’s funding request for the NIH last year; “we will probably go above what he asked for this year”.

“Not waiting”

Although the NIAID has no designated Zika funds, Fauci said his agency is working to develop a vaccine to prevent or treat the virus. “We are not waiting”, he said.

One of the most promising candidates is now in predevelopment, and doses are in production in

preparation for a phase 1 clinical trial expected to start this September. If the drug proves to be safe and effective, it will move into a phase 2 trial early next year. “It would have to take place where there is a lot of infection and we are currently negotiating with people in a variety of those regions including Brazil, Puerto Rico, and other South American countries”, said Fauci.

How long it will take before an effective vaccine is available is difficult to predict. “If the infections stay at a high rate, it takes less time to prove or disprove efficacy”, he said. “If the infection rate goes way down, it might take longer.”

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Fauci said his agency is already negotiating with several pharmaceutical companies to market the drug, but this effort also faces challenges. Companies are reluctant to invest in products that may not be widely used, and so the government offers to share the financial risk, said Fauci. But if, as in the case with Zika, sustained government funding over a sufficient time period is uncertain, that’s a problem. “If there isn’t a guarantee that there will be money there, often there is a reluctance on the part of some pharmaceutical companies to get involved if they think that the federal government is not a reliable partner”, he said.

While clinical research and the funding debate continues, protection from the Zika virus will depend largely on avoiding the mosquitoes that carry it.

The mosquito wars

“In Florida, we deal with mosquitoes all year round”, said Wasserman Schultz. Her congressional district runs from the Atlantic coastline to

the Everglades, the largest subtropical wetlands in the USA, home to the Everglades National Park, a protected wildlife refuge and a seemingly infinite mosquito population.

The *Aedes aegypti* mosquito, which commonly carries the Zika virus, “is incredibly hard to get”, Robert Eadie, head of the health department in Florida’s Monroe County, which includes Key West, part of the Florida Keys at the southern tip of the state. He spoke at the CDC’s Zika Action Plan Summit for local officials held earlier this month. This mosquito “is the one that lives in your house and it has resisted efforts by man to control it for years and years and years”.

Despite Monroe County’s \$10 million mosquito control programme, when Key West was hit with an outbreak of dengue fever—another virus carried by *A aegypti*—in 2009, it took 14 months and the assistance of the CDC to defeat it, he recalled.

The CDC is battling *A aegypti* and Zika on several fronts, said Lyle Petersen, director of CDC’s division of vector-borne infectious diseases: using larvicides in its many breeding grounds and attacking adult mosquitoes in Puerto Rico with outdoor insecticide spraying near the homes of pregnant women. A “big cornerstone of the response” in continental USA, will be quickly finding locally acquired Zika cases when they occur, and then targeting mosquito control in those areas.

After years of cuts in federal and local funding for mosquito control, Zika is “a pretty major wake up call to rebuild those capacities”, said Petersen. The virus is the latest “major pathogen that has come into the Americas” in recent years—after chikungunya, dengue fever, and West Nile virus—“and it won’t be the last”.

“We’re living in an interconnected world where these pathogens can travel all over the planet, and they are only an airplane flight away.”

Susan Jaffe