PHOTO: AP PHOTO/FELIPE DANA

INFECTIOUS DISEASE

Mosquito hunters search for Zika vectors

Yellow fever mosquito is confirmed, but others may contribute

By **Gretchen Vogel**

Zika virus, the once obscure pathogen now widely feared for causing birth defects and other problems, has spread very far very quickly since an outbreak was first noticed in northeast Brazil in early 2015. It has reached more than 40 countries across the Americas, even making it to the Cape Verde islands, off the western coast of Africa. More than a million people have become infected.

As public health officials try to contain the epidemic, researchers are racing to answer a key question with important implications for which areas are at risk, and what methods might work to slow its spread: Which mosquitoes are transmitting the virus? Answering the question is no small challenge. Scientists need evidence from both lab-raised and wild-caught mosquitoes to make the case that a given species is guilty.

Just last week, a team in Rio de Janeiro announced that it had nabbed several *Aedes aegypti* infected with Zika—the first infected mosquitoes found in Brazil. The species, the yellow fever mosquito, has long been the prime suspect, but some scientists believe the Zika virus must have other carriers to have spread so quickly—and they have field and lab studies underway to resolve the issue. Until that evidence is in, "we shouldn't jump to conclusions," says Duane Gubler, a virologist at Duke-NUS Medical School in Singapore.

A. aegypti has earned suspicion because it spreads dengue and chikungunya as well as yellow fever and is common in urban areas of Brazil where major outbreaks have occurred and throughout Latin America. But evidence of wild mosquitoes infected with Zika has been lacking. It is harder than one might expect to find them. In dengue outbreaks, says Sander Koenraadt, an entomologist at Wageningen University in the Netherlands, researchers typically find that fewer than 1% of sampled mosquitoes are infected with the dengue virus, even where people are falling sick. "You have to look at a lot of mosquitoes to find [infected ones]," Gubler says. The mosquitoes "infect people and die before anyone shows up at the hospital" with disease symptoms, says Oliver Brady, an entomologist at the University of Oxford in the United Kingdom.

> ***"You have to look at a lot of mosquitoes to find [infected ones]."***
> **Duane Gubler**, Duke-NUS Medical School

For the insects to transmit a virus, they must take up infected blood from a human or animal and become infected themselves. The virus then has to travel from their gut to their saliva. Only some species are susceptible to particular viruses.

To test whether a given species is able to transmit a virus, researchers feed insects on infected blood in the lab and a week or so later collect saliva from them. If the saliva contains infective virus, the species is considered a "competent" vector. Not all lab-competent vectors spread disease, however. That depends on several factors, such as how often the species bites, whether it feeds primarily on humans or other animals, and how long it lives. To confirm that a species is transmitting disease, researchers also need to find virus-infected mosquitoes in the wild.

The team that reported the first Zika-infected mosquitoes in Brazil, led by Ricardo Lourenço-de-Oliveira, an entomologist at the Oswaldo Cruz Foundation (Fiocruz) in Rio de Janeiro, vacuumed up mosquitoes from homes and streets in Rio de Janeiro neighborhoods that were home to people complaining of Zika symptoms. Over 10 months they collected more than 1500 mosquitoes, identified them, and tested pooled samples of the same sex and species for the presence of Zika and other viruses. Nearly half were *A. aegypti*, and most of the rest were *Culex*

Researchers in Brazil have captured thousands of mosquitoes to test them for Zika and other viruses.

quinquefasciatus, another common mosquito in urban Brazil. Roughly 5% were other species. A species called *A. albopictus*, widely known as the Asian tiger mosquito, which can also transmit Zika in the lab and has been found infected with the virus in Mexico and Gabon, made up only about 2% of the catch, Lourenço-de-Oliveira says. They found Zika virus in three sets of female *A. aegypti* mosquitoes, but none of the other species.

The lack of virus in *C. quinquefasciatus* is somewhat reassuring, Lourenço-de-Oliveira says, but the case is not closed. Constância Ayres, an entomologist at Fiocruz in Recife, Brazil, says that her lab has evidence that the species is a possible vector; they have found Zika virus in the saliva of *C. quinquefasciatus* that had fed on infected blood. (Her team has submitted its work for publication.)

Lab tests can be misleading, however. "There is a classic discordance between what you see in the lab and what happens in the wild," Brady says. "*Albopictus* and *aegypti* are both highly competent in the lab" as vectors for dengue. "But in Europe, where we have widespread *albopictus* and almost no *aegypti*, you don't have huge dengue outbreaks."

Ayres and others are still searching for Zika in the wild. She and her colleagues have collected and identified more than 5000 mosquitoes in the Recife area since March, from homes where confirmed Zika patients lived and from urgent care centers. She is waiting for promised grant money before she can run the polymerase chain reaction tests to find which viruses the mosquitoes are carrying, she says.

Culex mosquitoes transmit several viruses related to Zika, and it would not be particularly surprising if both *Culex* and *Aedes* species could spread Zika, Ayres says. Gubler agrees that *Culex* is a plausible carrier. He notes that several Zika relatives spread by *Culex* mosquitoes, including the West Nile virus, target the nervous system, which Zika also seems to do.

If *Culex* mosquitoes can transmit Zika virus, that will make slowing its spread even more difficult. *C. quinquefasciatus* is found as far north as Iowa and Indiana in the United States, although people there are protected by window screens and other factors. In Latin America, most vector control methods are targeted at *A. aegypti*. Those efforts have made barely a dent in curtailing spread of the Zika virus so far, notes Paul Reiter, an entomologist at the Pasteur Institute in Paris. Targeting multiple vectors at once will only make the job harder. "If [*C.*] *quinquefaciatis* is a vector," he says, "we can forget anything about mosquito control." ■

PHOTO: DARKO VRCAN/ALAMY STOCK PHOTO

EVOLUTION

Dogs may have been domesticated more than once

But all living dogs have Asian roots

By **David Grimm**

For years, scientists have debated where dogs came from. Did wolves first forge their special relationship with humans in Europe, or in Asia? The answer, according to a new study, is yes. On p. 1228, researchers report that genetic analysis of hundreds of canines reveals that dogs may have been domesticated twice, once in Asia and once in Europe or the Near East, although European ancestry has mostly vanished from today's dogs. The findings could resolve a rift that has roiled the canine origins community—but the case isn't closed yet.

"These are fantastic data that are going to be extremely valuable for the field," says Peter Savolainen, a geneticist at the Royal Institute of Technology in Stockholm and the leading proponent of Asian dog origins. But Robert Wayne, an evolutionary biologist at the University of California, Los Angeles, whose work has shown that dogs arose in Europe, says the results—although plausible—are too preliminary to settle the question. "The story is still a bit of a muddle."

The study includes a unique specimen: the inner ear bone of a nearly 5000-year-old dog unearthed from Newgrange, a football field–sized mound of dirt and stone on the east coast of Ireland, built around the time of Stonehenge. Researchers led by Laurent Frantz, an evolutionary geneticist at the University of Oxford in the United Kingdom, sequenced this specimen's entire nuclear genome—the first complete genome from an ancient dog to be published—and compared it to the nuclear DNA of 605 modern dogs from around the world. The team then created a family tree for the animals, which revealed a deep divide between European dogs (like the Newgrange canine and the golden retriever) and Asian dogs (like the shar pei and free-ranging village dogs from Tibet and Vietnam). "I was like, 'Holy shit!'" says project leader Greger Larson, an evolutionary biologist at Oxford. "We never saw this split before because we didn't have enough samples."

To figure out when this divide occurred, the Newgrange specimen was critical. Researchers used it, in conjunction with the complete genomes of several modern dogs and wolves, to calculate a genetic mutation rate for canines. This rate suggests that the East-West split happened sometime between 6400 and 14,000 years ago. The analysis also revealed a "genetic bottleneck" in Western dogs—a reduction in genetic diversity typically tied to a sharp decline in a population's numbers, as can occur when a small band of individuals splits off from the main group. (A

Asian dogs like this Tibetan mastiff have been separated from European breeds such as Labradors for more than 6000 years.

Mosquito hunters search for Zika vectors
Gretchen Vogel (June 2, 2016)
Science **352** (6290), 1152-1153. [doi: 10.1126/science.352.6290.1152]

Editor's Summary

Science (print ISSN 0036-8075; online ISSN 1095-9203) is published weekly, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005.