A "mild" illness takes off

In early February 2015, doctors in the impoverished northeastern part of Brazil noticed a surge in the number of people complaining about a mild illness, with and without fever, characterized by rash, fatigue, joint pains, and red eyes. The illness was brief and recovery was spontaneous. A mild form of dengue, a mosquito-borne disease hyperendemic throughout the country, was initially suspected, but tests were negative in the vast majority of samples. Chikungunya, another mosquito-borne disease first detected in Africa in 1952, had hopped to Brazil in September 2014 and was likewise suspected. Again, tests results were negative.

At the end of March, Brazil informed WHO that nearly 7,000 cases of an illness characterized by skin rash had been reported in six northeastern states. Laboratories had performed a battery of tests on more than 400 blood samples. 13% of the samples were positive for dengue, but negative for several other viruses known to cause skin rash. The causative agent remained elusive.

The first promising clue came in late April from a laboratory in Bahia State where researchers began to suspect that the disease might be spread by the area's ubiquitous and dense mosquito population. On a long shot, they tested for Zika, an exotic and poorly understood virus, carried by mosquitoes, that had never been seen in the Americas. Though the results were positive, doubts remained. Testing for Zika is technically challenging as the virus cross-reacts immunologically with dengue and chikungunya viruses, both present in Brazil at that time.

A week later, on 7 May, tests conducted at Brazil's national reference laboratory conclusively identified Zika in several samples. A new mosquito-borne disease had indeed arrived in the Americas, though no one knew what that might mean.

Mixed reviews

The finding was startling, yet difficult to interpret. The appearance of a virus in a new geographical area is always cause for concern, as the population will have no pre-existing immunity to slow the virus down. Spread can be explosive, quickly flooding health services with the sick and the worried well. As another concern, viruses in the same flavivirus family as Zika are known to undergo small genetic changes as they sweep through a vulnerable population that help them acquire epidemic potential. Though the changes are small and their significance is poorly understood, epidemic strains can deliver surprises as an outbreak evolves, sometimes behaving in previously unexpected ways.

On balance, though, the long history of Zika virus disease was reassuring. The virus was first detected in 1947 in a sentinel monkey, identified as Rhesus 776, in Uganda's Zika forest as part of a research project on jungle yellow fever. Over the next six decades, only 14 naturally occurring human cases were identified, by virus isolation, worldwide, all in a narrow equatorial band stretching across Africa and Asia [table 1]. Two additional cases were reported: one in a European volunteer who was experimentally infected in Nigeria and a second in a laboratory worker in Portugal. All illnesses were mild and brief, followed by full and uneventful recovery.

- Table 1: Zika virus infections in humans 1954–2007, confirmed by virus isolation pdf, 84kb

A small group of dedicated scientists continued to conduct Zika experiments aimed at assessing the potential risk to the African people and, possibly, to the world at large. As far back as 1952, they speculated that Zika and other newly discovered African viruses might have effects on the central nervous system or produce congenital changes in the foetus if pregnant women were infected. But that was pure speculation. For all practical purposes, Zika looked like a medical curiosity that posed little, if any, threat to public health.

In Africa, researchers believed that transmission was largely confined to jungles and forests where canopy-dwelling mosquitoes preferred to draw their blood meals from monkeys. Human infections were incidental to this dominant transmission pattern. If the virus had any epidemic potential whatsoever, no one noticed.

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