PNAS OPINION

Urban malaria may be spreading via the wind—here's why that's important

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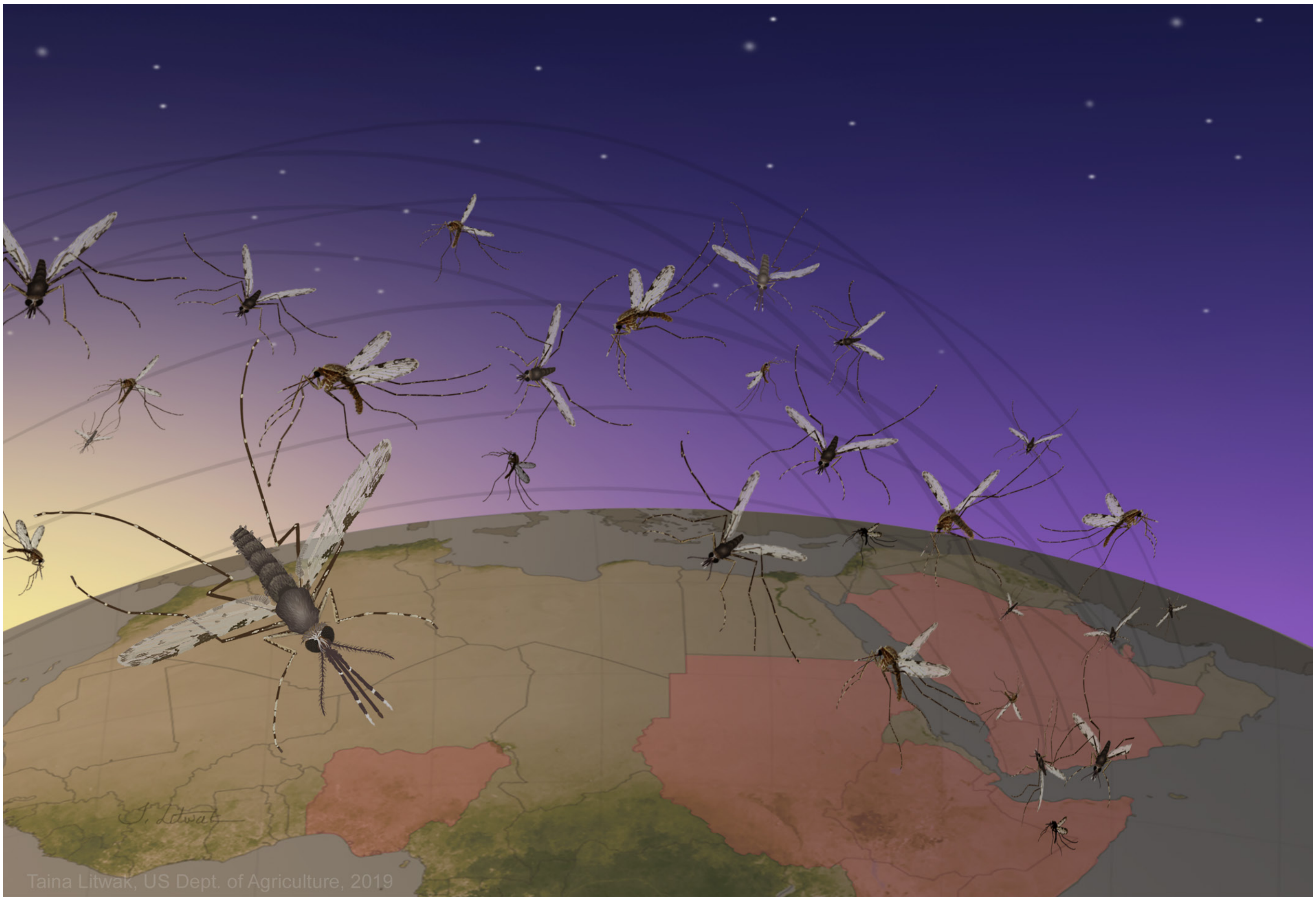

Until now, malaria in Africa has been primarily a rural problem. But the recent establishment and expansion of the invasive urban Asian vector *Anopheles stephensi* will likely drastically change Africa's risk landscape. Image credit: Taina Litwak (Scientific Illustrator, United States Department of Agriculture).

Malaria remains the most important vector-borne disease in Africa, with over 590,000 deaths annually (1). Although until now, malaria in Africa has been primarily a rural problem, the recent establishment and expansion of the invasive urban Asian vector *Anopheles stephensi* will likely drastically change Africa's disease risk landscape. Urban malaria will become a bigger threat (2–6). Unlike all other African malaria vectors, *An. stephensi* larvae thrive in container habitats (e.g., abandoned tires or cisterns) near human dwellings, similar to the urban yellow fever mosquito, *Aedes aegypti*. Thus, human populations in the continent's rapidly expanding megacities, such as Kinshasa and Lagos, and metropolises, such as Khartoum and Abidjan, are now more vulnerable to malaria (2, 3, 5, 6).

It is hard to overstate the public health importance of this paradigm shift (4–6). Existing surveillance and vector-control strategies are ill-equipped to rapidly pivot to tackle urban, container-breeding *Anopheles,* and this seemingly minor change in vector ecology may ultimately derail transcontinental malaria elimination progress, which has achieved dramatic reductions in malaria's burden over the past three decades (6).

Currently, there's a widely accepted hypothesis that people unwittingly imported *An. stephensi* into the Horn of Africa via human-mediated transport, on ships or possibly airplanes (2, 3, 7, 8). This supposition most likely stems from the first discovery of *An. stephensi* in Africa being about 20 kilometers from the port of Djibouti, and influenced by the established mode of spread of common invasives

Author contributions: T.L., R.B., J.W.C., D.R.R., and Y.-M.L. developed the concept; T.L., R.B., J.W.C., D.R.R., T.R.B., and Y.-M.L. led the data collection and analysis; and T.L. wrote the paper with contributions from all authors.

The authors declare no competing interest.

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Published April 27, 2023.

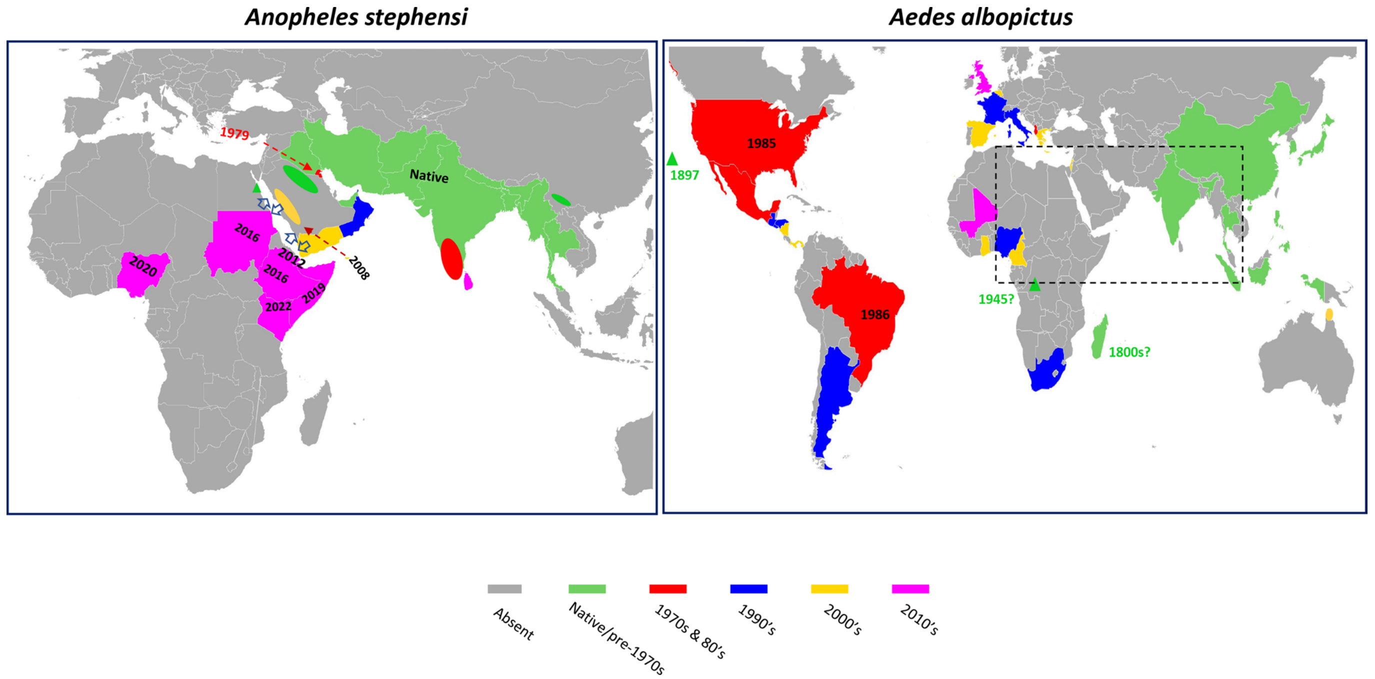

Fig. 1. **Range expansion by decade (color) of *An. stephensi* compared with *Ae. albopictus*. Regions within (select) countries are distinguished where the species have been reported from especially restricted areas. Key dates are listed ("?" indicates uncertainty about arrival date). Schematic wind directions seasonally prevailing around Bab el Mandeb and the Tokar Gap, Sudan, from the northeast from November to April, and from the southwest from May to October, are shown (blue arrows). Image credit: Based on data from refs. 2, 15, 16, 18, and 19.**

such as *Ae. aegypti* and *Ae. albopictus* (9, 10). While invasive *Aedes* typically disperse through inadvertent carriage of desiccation-tolerant eggs (9, 10) and *An. stephensi* shares the same man-made containers as larval sites (11), *Anopheles* eggs are highly sensitive to desiccation. They lose viability within 48 hours and seldom survive over a week without moisture (12), thus limiting opportunistic and mass carriage of eggs typically needed for successful establishment (referred to as "propagule pressure") (9, 13). Nonetheless, immature *An. stephensi* could potentially develop in stagnant freshwater sources on board ships and, together with adults, survive the journey into new ports by maritime transportation (8, 9, 13). Herein, we examine the available data and propose an alternative, though not mutually exclusive, hypothesis: *An. stephensi* range expansion is mediated through long-distance, windborne migration (14), which better accounts for its pattern of new population establishment through Asia and Africa.

Speedy Spread

Examining the global establishment pattern of *Ae. albopictus*, which has been facilitated by shipments of cargo and especially used tires, offers clues as to the dispersal strategy of *An. stephensi*. Both species expanded their native range from Asia during approximately the same time period (15, 16). Within its first decade of major range expansion, in the 1980s, *Ae. albopictus* leapt to Europe (Albania), as well as North and South America. By the second decade, it had reached mainland Africa and other distant regions of Europe and the Americas. By the third, it had invaded Australia (Torres Strait islands; Fig. 1). By comparison, *An. stephensi* slowly spread across Asia for over three decades: reaching Goa in the 1970s, to the southernmost tip of India in the 1980s, to Lakshadweep Islands in 2001, and to Sri Lanka in 2017. In its fourth decade of range expansion, *An. stephensi* crossed the Red Sea into the Horn of Africa, at least 4 years after reaching the southern and western coasts of Arabia (Fig. 1). In Africa, it was first detected in Djibouti (2012), in Ethiopia and Sudan (2016), and Nigeria (2020; Fig. 1). Its rapid penetration into central Africa from the coast also contrasts with *Ae. albopictus*, which took three decades to reach inland Africa.

Thus, in four decades, *An. stephensi* expanded to only one, adjoining continent. *Aedes albopictus*, in contrast, leapt to five continents (arriving at very distant ports and on multiple islands), traveling thousands of miles between its origin and destinations (Fig. 1). The spatio-temporal pattern of range expansion of *An. stephensi* across Asia, Arabia, and into and across Africa presents a compelling signature of a diffusion process that sharply contrasts with the huge leaps of *Ae. albopictus* establishment via ship-mediated transport.

Genetic Clues

So far, the distribution of *An. stephensi* around African ports is only documented from Djibouti (3), suggesting that it's probably a rare event. Accordingly, low genetic diversity in African populations would be expected, reflecting a series of bottlenecks due to the transport of small numbers of *An. stephensi* larvae and/or adults on a ship and their subsequent establishment and spread overland by cars across hundreds of kilometers. Sequence analysis of Ethiopian *An. stephensi* populations using the mitochondrial COI and CytB genes revealed considerable diversity in Ethiopia (17). This suggests an exceptionally large colonizing event or multiple invasions into Africa over a relatively short period of time.

Indeed, the establishment of *An. stephensi* populations at the southern and western regions of the Arabian Peninsula by 2008, 30 to 250 km away from the African coast, could have produced multiple invasions (Fig. 1). Carter et al. (17) suggested that the source of the African invasion is most likely to be from southern Asia, with notably low haplotype similarity between Ethiopian and close-by Arabian samples. However, the low sample size of mosquitoes ($n = 8$) that were available from a single location on the eastern Arabian Peninsula precluded a conclusive inference about the source populations. In fact, subsequent studies revealed high genetic similarity between populations from Yemen and those from Djibouti, Sudan, and Ethiopia (18, 19). A report of new invasive populations in northern Kenya (20) also revealed that the Kenyan population was most related to mosquitoes from Yemen, Nigeria, and India, which supports gradual windborne migration from western/southern Arabia. Notably, if the sources of the multiple invasions were directly from SE Asia by human-assisted maritime or air transport, it would be difficult to explain why the invasion was only in the Horn of Africa, and not across the continent and beyond.

Busy Highways

Researchers have routinely recorded the desert locust (*Schistocerca gregaria*), a serious pest that threatens food security (21), crossing the Red Sea aided by winds from the Arabian Peninsula to Northeast Africa. Moreover, a third to a half of all the mosquito fauna of Mali, including *Anopheles* malaria vectors, regularly engage in high-altitude windborne migration as gravid females (14), extending other reports, including from SE Asia. Once established along the southern and western regions of the Arabian Peninsula at or shortly after 2008 (Fig. 1), mosquitoes, aided by favorable high-altitude winds, might cross the Red Sea (approximately 30 to 250 km in a direct crossing, depending on departure location) in 1 to 7 hours, assuming typical windspeeds of 10 meters per second. Such flight durations are common for many insects, including *An. stephensi* based on flight mill studies (22). By contrast, no evidence known to us demonstrates *An. stephensi* dispersal by human vehicles.

Crucially, understanding *An. stephensi*'s mode of spread will help in better assessing risk in different regions.

The new distribution records of *An. stephensi* reflect localities where entomological surveillance has been ongoing, near cities and main roads (6). Yet, despite this sampling bias, the species appears to be spreading inland [rather than along coasts with major ports (8)], where it is present in small, relatively remote rural communities, many of which have only begun to be surveyed (23, 24). Notably, the isolated record of *An. stephensi* from Nigeria in 2020 is over 100 kilometers from the nearest port and major airport and is not on a main road (24). This lends further support for long-range windborne migration on the prevailing easterly winds—especially during September to November, when easterlies blow from the southern region of the Arabian Peninsula and northern East Africa (21).

The proximate cause for the timing of the invasion into Africa is therefore the gradual expansion and establishment of populations in southern and western Arabia (Fig. 1). The ultimate cause is more speculative. Although we cannot rule out the effects of climate change or a novel adaptation in *An. stephensi*, we suspect that the key factor was the shift from a nomadic to a settled lifestyle across Arabia following the discovery of oil in 1938, coupled with the sharp increase in human density and urbanization across the Peninsula (population density grew more than 10-fold from 1940 to 2010, compared with 2.9-fold worldwide) (25). Presumably, an increase in the density of human settlements, accompanied by proliferation of larval and resting sites, as well as suitable hosts, facilitated the survival and establishment of windborne mosquitoes that otherwise would perish, forming new bases from which range expansion could further proceed. This anthropogenic process may play a role in the range expansion of other windborne human-commensal mosquitoes, among other pests.

Seeking Data

Testing the hypothesis that *An. stephensi* engages in high-altitude windborne migration and comparing the expected pattern of spread with transport by vehicles is especially important during the early stages of its expansion, when large portions of the habitable continent are still free of this invasive species (Fig. 1). A combination of approaches could be used to prove or disprove the hypothesis of windborne spread. Wind-trajectory analyses can identify putative source populations of recently established populations (backward wind-trajectory analysis) and also identify putative newly invaded sites from established populations (forward wind-trajectory analysis). Subsequent on-the-ground surveillance data could ascertain whether select locations assessed as high (or low) probability for natural windborne transport, and low likelihood for human-aided transport, confirm these predictions. Population genetics analysis of *An. stephensi* populations will also be key, to help discriminate between source populations that are connected by prevailing winds, rather than via human transport. In tandem, aerial sampling at 100 to 350 meters above ground (14) situated ~5 to 20 kilometers downwind from localities with high densities of *An. stephensi* will determine whether this species—particularly gravid females harboring more than 100 eggs each—undertake high-altitude flights (14). These activities can be integrated with urgently needed updated vector surveillance and control operations (1, 4, 6).

Crucially, understanding *An. stephensi*'s mode of spread will help in better assessing risk in different regions. The risk of invasion into other continents (e.g., South America) is negligible via windborne dispersal, but remains high if ships and airplanes are involved. Conversely, typical ground barrier methods, such as port interception or limited-barrier insecticide spraying, are ineffective for containment of aerial invasives. If ship-borne transport (or airplane transport) is the primary means of long-range spread and colonization, new vector populations would concentrate near busy international ports before subsequently dispersing along major transportation routes. By contrast, wind-borne migrants will radiate from high-density source populations mostly along the direction of prevailing winds, which may change seasonally. Mitigation strategies for *An. stephensi* in Africa may benefit from approaches used against agricultural migrants (e.g., planthoppers, moths, locusts) that employ wind-trajectory analyses to better identify the main source populations and predict those regions for intensive control operations. Moreover, elimination of *An. stephensi* from Africa depends on understanding the processes of its spread to prevent re-introductions.

Finally, efforts to understand how this invasive mosquito spreads—and to integrate that knowledge into the campaigns to combat it—may help prepare us for the next mosquito invasion. And there are important implications here beyond *An. stephensi*. These insights could inform efforts to combat numerous invasive species, whether they pose a threat to human health, to animal and plant health, or impact food security or ecosystem stability.

ACKNOWLEDGMENTS. We thank Drs. Martin Donnelly (London School of Hygiene and Tropical Medicine) for initial discussion; Kristin Sloyer (University of Florida) and Carole Long and Alvaro Molina-Cruz (National Institute Health - NIH) for reading earlier versions of this manuscript and for helpful discussions; and Thomas Wellems, Carolina Barillas-Murry, Ms. Wendy Hamm, Fatoumata Bathily, and Mr. Sam Moretz for the support of our program at NIH and the International Center for Excellence in Research in Mali. This study was supported by the Division of Intramural Research, National Institute of Allergy and Infectious Diseases (NIAID), NIH, Bethesda, MD. Y.-M.L. is supported by the Armed Forces Health Surveillance Division–Global Emerging Infections Surveillance (P0050_23_WR). D.D.R. is supported by a Rothamsted Research grant from the United Kingdom Biotechnology and Biological Sciences Research Council. P.A.A. is supported by NIAID Grant R01AI132409 and the Davis Family Endowment. The opinions or assertions contained herein are the private views of the authors, and are not to be construed as official, or as reflecting true views of the U.S. Department of the Army, Navy, or the Department of Defense.

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