

American Society of Tropical Medicine and Hygiene

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As One Type of Malaria Declines, New Map Reveals another Strain – Impervious to Interventions – Holding Steady in Parts of Asia and Latin America

New data on prevalence of "the last parasite left standing" unveiled in first-of-its kind map by malaria experts at ASTMH meeting, along with new data on deadliness, lack of treatment

(Philadelphia, Pa., USA – December 5, 2011) With signs of declining malaria deaths in Africa raising hopes of eradicating the disease worldwide, researchers unveiled today at the annual meeting of the American Society of Tropical Medicine and Hygiene (ASTMH) a new malaria map that is the first to identify on a global scale where the long-lasting and potentially deadly form of malaria—a parasite known as *Plasmodium vivax*—has a firm foothold in large swaths of South Asia and parts of Latin America.

"This map helps us understand just how difficult it is going to be to eradicate malaria," said Peter Gething, PhD, who led the University of Oxford's Malaria Atlas Project (MAP) team that produced the study of *vivax* burden. "It shows that in substantial parts of the world, *vivax* malaria is endemic and transmission is significant. Unfortunately, the tools for fighting this type of malaria range from ineffective to non-existent."

Other studies being discussed at ASTMH—the world's largest gathering of public and private sector malaria scientists, clinicians and program professionals—and published in the December issue of the *American Journal of Tropical Medicine and Hygiene*, add to mounting evidence that *vivax* malaria may be killing people far more often than previously thought; confirm that existing treatments are inadequate and potentially toxic to millions; and shed light on the level of precaution that travelers should take when visiting these regions (see *Backgrounder* for further information).

While not as deadly as the *Plasmodium falciparum* malaria parasite that is predominant in Africa, *vivax* is more common throughout the world, with an estimated 2.85 billion people at risk of infection. And with its unique ability to relapse by hiding in the liver for months or even years, *vivax* is harder to detect and cure.

The MAP team produced an analysis last year depicting only where *vivax* is known to exist. Malaria experts immediately called for a map pinpointing where the disease is most prevalent, noting that such

a tool is essential to mounting an effective fight against this form of malaria.

Hotspots for *vivax* malaria highlighted by MAP include substantial parts of India. Rates are high even in urban areas like Mumbai, where malaria—once thought of largely as a disease of rural areas—was previously uncommon. Papua New Guinea also has a high rate of infections and transmission, as do significant parts of Indonesia and Myanmar (including Yangon). In the Americas, the area of greatest concern is a large but sparsely populated portion of the Northern Amazon, most of which is in Brazil. But the hotspot also includes parts of Peru, Colombia and Venezuela. In Central America, almost all of Nicaragua is a hotspot for *vivax* malaria, as are parts of Honduras and Guatemala.

In Africa, Gething said that while *vivax* is known to exist, infection rates appear to be "very, very low" for most of the continent, though the map indicates a moderate but stable level of *vivax* transmission in parts of the Horn of Africa and throughout Madagascar.

Stealth Disease Burden: "Large Reservoir" of Vivax Infections Hiding in the Liver

Researchers considered an area to be a *vivax* malaria hot spot if the data analysis yielded infection rates that exceeded 7 percent. Gething noted that this threshold might be considered relatively low for *falciparum* infections. But he said it's high for *vivax* in part because the figure accounts only for parasites that are detectable in the blood, and also because *vivax* disease rates have proven hard to reduce.

He noted that in areas where *vivax* is endemic, at any given time, there are many people carrying *vivax* parasites only in their liver, from which they periodically emerge to cause new infections in the blood stream. But, he said, this "large reservoir" of *vivax* is difficult to quantify with existing surveillance tools, chiefly because there is currently no simple test for detecting the liver parasites.

"One person with *vivax* actually can represent multiple malaria infections over many years in a single community and each time the parasite moves from the liver to the blood, it contributes anew to disease burden and transmission," Gething said.

The disease burden caused by *vivax* relapse, he said, is exacerbated by a lack of treatment options. Medicines such as the artemisinin combination therapies (ACTs) that are used to cure *falciparum* infections can help treat acute bloodstream *vivax* infections. But only one drug—primaquine—can clear *vivax* parasites from the liver and thus provide a long-term cure to this type of malaria.

However, in a cruel twist of evolution, a hereditary condition that may have evolved in response to malaria exposures can make the drug toxic, sometimes fatally so, to some people who live in *vivax*-endemic areas. At ASTMH, another team of researchers from the Malaria Atlas Project will present a map depicting the prevalence of the condition, known as G6PD deficiency, within malaria-endemic countries. Preliminary data indicate that this condition is relatively common in *vivax*-endemic Southeast Asia, though the highest rates are found in sub-Saharan Africa. The condition is also observed in the Americas, though at lower rates.

"We hope that by mapping the prevalence of G6PD deficiency we can provide evidence that will help contribute towards determining the risks and benefits of using primaquine, which is an important, yet

potentially dangerous drug," said Rosalind Howes, the lead investigator on the project.

Even when primaquine is not toxic, the fact that it requires a 14-day regimen has made it impractical for areas where people have little or no access to even modest levels of health care—which is the majority of the malaria-endemic regions of the world.

Meanwhile, bednets and indoor spraying, which, coupled with ACTs, have helped reduce malaria deaths in Africa, appear to have had little impact on *vivax*. One reason is that the mosquitoes that transmit *vivax* typically bite outdoors, rather than indoors in the home. And RTS,S, the malaria vaccine candidate in Phase 3 trials that may soon be commercially available, does not target *vivax*.

This persistence of the *vivax* parasite in the face of a massive global campaign to eliminate malaria has prompted some malaria fighters to dub it "the last parasite standing."

Malaria experts say even though *vivax* still appears to be less deadly than *falciparum*, growing evidence of its link to fatalities warrant giving it a higher profile in the global malaria eradication campaign.

"It's time to step-up the fight against *vivax* malaria and stop looking at this form of the disease as relatively mild and tolerable," said Peter J. Hotez, MD, PhD, noted infectious disease expert and president of ASTMH. "We expect to emerge from this year's conference with a far better view of the state of *vivax* infections around the world and with new knowledge on treatment challenges that can guide a global strategy focused on eradicating all forms of malaria."

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About ASTMH

<u>American Society of Tropical Medicine and Hygiene</u>, founded in 1903, is a worldwide organization of scientists, clinicians and program professionals whose mission is to promote global health through the prevention and control of infectious and other diseases that disproportionately afflict the global poor.