EMBARGOED UNTIL 3:00 PM EST (20:00 GMT) ON MONDAY, NOVEMBER 6, 2017

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At ASTMH Annual Meeting, Researchers Report Breakthrough in Malaria Breathprinting That Could Pave Way to Electronic Nose to 'Smell' Disease

Analysis of breath samples accurately diagnosed malaria in African children; study also finds infected patients exhale odor that attracts mosquitoes

BALTIMORE (6 November 2017)—Scientists have discovered that people with malaria exhale a distinctive "breathprint," insights they have used to develop a new breath test which was highly successful in diagnosing malaria in a group of African children, according to a new study presented today at the American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting.

It is the first study to identify a specific set of compounds in human breath that can serve as evidence or diagnostic markers for malaria. The analysis also is the first to find that people with malaria exhale a compound identical to a plant-produced vapor that is known to attract mosquitoes, which could be accelerating the spread of disease.

"We were able to determine whether the children were infected or not based on the composition of six different compounds that were detectable in a sample of their breath," said Chad Schaber, who presented the results of the study, produced by a team of biologists and bioengineers from Washington University in St. Louis. "We took breath samples from 35 children and we correctly determined the malaria status—whether they had malaria or not—for 29 of them, which is an 83 percent success rate."

The researchers say that simple tools like breath-testing for diagnosing malaria are urgently needed—both to direct life-saving treatment to infected individuals and to conduct surveillance as part of a new global push to eliminate and eradicate the disease. While there are now relatively simple rapid diagnostic tests, or RDTs, for malaria that require only a finger-prick of blood, they have limits, such as producing positive results after an infection has subsided. More troubling are the growing number of reports of *Plasmodium falciparum* malaria parasites (the

world's most deadly form of the disease) that don't produce the protein most of the tests rely upon to detect disease.

Schaber and his colleagues report that the 83 percent accuracy rate of their breath test was lower than the 90 percent or better accuracy of other tests: RDTs or the more labor and technology-intensive method of examining blood samples with a microscope. These blood sample tests are considered the gold standard for malaria diagnosis yet challenging to implement in rural, resource-strapped areas. But the researchers hope to improve the success rate of their breath tests with further refinements to the technology. For example, they are working with engineers who have developed compact electronic noses, or eNoses, devices the size of a credit card or smaller that can be designed to detect a specific set of odors.

An eNose is under development for other purposes, including one attached to locusts to help detect bombs and aid in search and rescue missions. Schaber said the same technology potentially could be used to develop a portable malaria breathalyzer and breath tests for other diseases as well. There is already a prototype eNose under development for diagnosing tuberculosis with a breath sample.

Discovering Malaria's Unique Breathprint

The researchers said they saw malaria as a prime candidate for breath-based diagnosis based on past research indicating that, as the malaria parasite invades the human body, it may alter compounds humans naturally exhale. But that research involved a small trial in which a group of adult volunteers had been deliberately infected with a relatively low level of disease. A similar study had not been done in an area where malaria naturally occurs, they said, where infections are far more intense, or with children, who are more vulnerable to the disease than adults.

To develop a breath test, the researchers recruited 35 children ages 3 to 15 who had arrived at a pediatric care center in Lilongwe, Malawi, suffering from fever and other symptoms that can indicate malaria. The children already had been tested for malaria—17 had tested positive and 18 tested negative. The goal of the study was to determine whether a breath test could be developed that also could distinguish the infected from the uninfected.

The children provided a breath sample by blowing into a simple balloon-like bag. The breath sample was then pumped into a tube packed with an absorbent material, sealed and sent to a lab at Washington University in St. Louis. Researchers also obtained the original blood samples taken from the children at the clinic to further validate the malaria diagnosis by examining them under a microscope.

Back at their lab, the researchers determined that malaria infections appeared to alter the concentrations of six different compounds known to naturally occur in human breath. They used this measure to classify the breath samples as either infected or not infected with malaria. They then compared the breath diagnosis with the microscopic analysis of blood samples and found the breath test correctly determined malaria status—infected or not— for 83 percent of the children studied.

Malaria Breath and a Potential Role in Spreading Disease

Meanwhile, Schaber and his colleagues also report another curious finding: when they analyzed the breath of children with malaria, they discovered it also contained two types of compounds

known as terpenes. Terpenes are typically linked to strong odors exuded by plants, such as pine trees and other conifers. One of the terpenes identified in the malaria breath samples is the same one produced by certain plants that attract mosquitoes that feed on their nectar.

Schaber and his colleagues observed that the parasite appears to be “hijacking” the mosquitoes’ pre-existing attraction to the odor to encourage them to bite infected humans, thus extracting parasites in the bargain and facilitating the spread of disease. Malaria spreads through a complex cycle in which mosquitos transmit parasites to humans and then humans transmit them back to mosquitos.

“The terpene is probably a survival mechanism for the parasite, but this compound also might be useful in boosting the effectiveness of mosquito traps used in malaria control efforts,” said Audrey Odom John, principal author of the study and associate professor of Pediatrics and of Molecular Microbiology at Washington University School of Medicine.

“The malaria parasite has been outwitting human interventions for thousands of years, which is why we need these innovative collaborations between biologists and engineers to develop new tools that can give us the upper hand,” said Patricia F. Walker, MD, DTM&H, FASTMH, and President of the American Society of Tropical Medicine and Hygiene. “It sounds almost like something from science-fiction, but the ability to detect disease with a breath test may be closer than we ever could have imagined or hoped for.”

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